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Angiogenesis as a Target in Cancer Prevention/Treatment by Phytochemicals

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Angiogenesis is the growth of new vascular capillary channels from pre-existing vessels, and is of fundamental importance in expansion of primary tumors and their metastasis to distant organs. We have investigated the effect of green tea, Brahma rasayana (BR) and curcumin on angiogenesis and in cancers of the prostate gland or breast. Much of the biological effects of green tea appear to be mediated by its major polyphenolic constitutent, epigallocatechin gallate (EGCG). BR is a popular rasayana which contains several plant extracts and has been shown to have maximum immunomodulatory activity against tumor cells. Curcumin is the major active component of turmeric and has been shown to have anti-cancer activity in several animal tumor systems including colon, duodenal, stomach, prostate and breast carcinogenesis.

We have investigated the effects of these agents on angiogenesis in an *in-vitro* model using human umbilical vein endothelial cells on matrigel and mouse subcutaneous matrigel plug model. Data show that these agents inhibit the tube formation on matrigel and reduce cell migration in matrigel plug model as well as resulted in decreased gelatinolytic activity. BR treatment also reduces tumor incidence, tumor growth and metastatic spread caused by MAT-LyLu cells in Copenhagen rats. Angiogenic factors such as Factor VIII, VEGF, MMP-9 and MMP-2 expression was significantly lower in tissues from BR treated animals. Methanolic extract of BR was also found to inhibit the proliferation, reduce cell migration, attachment and tube formation on matrigel. These results suggest that these phytochemicals may inhibit tumor promotion and progression by inhibiting angiogenesis. The importance of angiogenesis in tumor growth is widely recognized and will provide new approaches to target, cure or prevent tumor angiogenesis by treatment with safe and cost effective novel phytochemicals.

We have also evaluated the anti-proliferative activity of EGCG using both *in vitro* with MDA-MB- 231 breast carcinoma cell line and *in vivo* with nude mice xenograft model. EGCG decreased the proliferation of the tumor cell line by arresting the progression of the cell through G1 phase of the cell cycle. Furthermore, EGCG were capable of delaying the tumor incidence as well as reducing the tumor burden in athymic nude mice. Data showed that EGCG induced apoptosis and suppressed invasiveness of MDA-MB-231 cells in a dose dependent manner. A fragmented DNA ladder was detected by electrophoresis in cells treated with ECGC indicating apoptosis. These studies have clinical significance since the ability of polyphenol to activate the apoptotic program and decrease the invasiveness of tumor cells might determine the success of chemotherapy.

Predicting and Controlling Selective Alkylation of DNA

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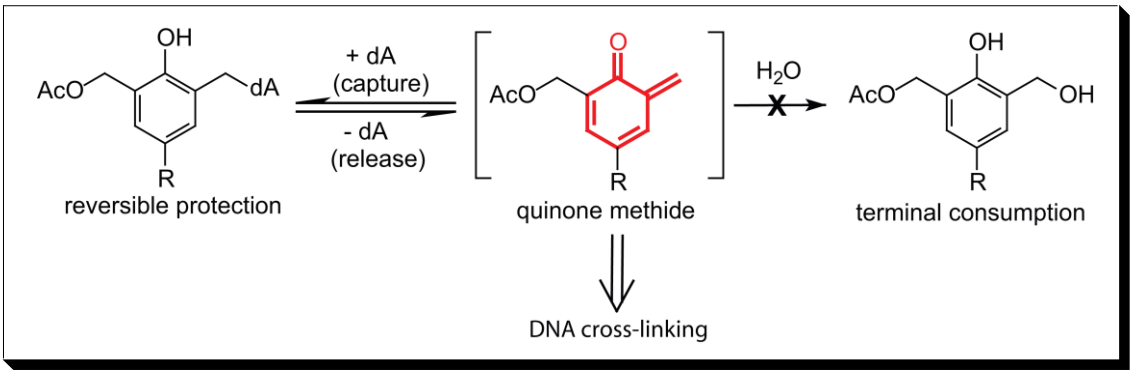
Highly electrophilic quinone methides are generated during metabolism of numerous compounds ranging from food preservatives to anti-cancer drugs. These species readily alkylate strong and weak nucleophiles of DNA, and the stability of the resulting adducts can be predicted from the nature of the participating nucleophile and the electronics of the transient electrophile [1]. The most nucleophilic nitrogens within the nucleobases form the predominant adducts, but these adducts also form reversibly. The consequence of this reversibility is evident by the surprising persistence of quinone methide reaction and by the time-dependent evolution of products that originate from simple quinone methides and their bioconjugates [2]. The major adducts essentially act as a reservoir for continually regenerating quinone methides over extended periods. As an example, the presence of dA increases the half-life for quinone methide reactivity by 100-fold under aqueous conditions by generating the dA N1 adduct reversibly and suppressing irreversible formation of the water adduct [3]. Single-stranded DNA also has the capacity to trap and transfer a quinone methide cross-linking agent to its complementary strand of DNA. Intra- and interstrand reaction remains reversible and yet is only weakly susceptible to quenching by external agents such as non-complementary DNA, thiols or water. Selective delivery of a quinone methide to a chosen sequence of DNA has similarly been demonstrated using an oligodeoxynucleotide-quinone methide conjugate. This bioconjugate efficiency forms internal self-adducts reversibly. Continual recapture of the reactive quinone methide intermediate acts as a safety catch to protect this bioconjugate from non-specific targets. Only when the self-adduct associates with a complementary sequence does the quinone methide transfer to the chosen strand and establish a cross-link. This overall process represents a new approach for directing a highly reactive intermediate to a precise target and may ultimately provide a general approach to gene specific reactions in vivo.



Scheme 1. dA suppresses quinone methide quenching and facilitates its cross-linking of DNA.

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Multifunctional Agents for Tumor Imaging and Phototherapy

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Optical imaging has attracted a great attention for studying molecular recognitions because; minute fluorescent tracers can be detected in homogeneous and heterogeneous media with existing laboratory instruments. In our preliminary study, a clinically relevant photosensitizer (HPPH, a chlorophyll-a analog) was linked with a cyanine dye (with required photophysical characteristics, but limited tumor selectivity) and the resulting conjugate was found to be an efficient tumor imaging (fluorescence imaging) and photosensitizing agent (PDT). Compared to HPPH, the presence of the cyanine dye moiety in the conjugate produced a significantly higher uptake in tumor than skin. At a therapeutic/imaging dose, the conjugate did not show any significant skin phototoxicity, a major drawback associated with most of the porphyrin-based photosensitizers. These results suggest that tumor-avid porphyrin-based compounds can be used as "vehicles" to deliver the desired fluorescent agent(s) to tumor. The development of tumor imaging or improved photodynamic therapy agent(s) by itself represents an important step, but a dual function agent (fluorescence imaging and PDT) provides the potential for tumor detection and targeted photodynamic therapy, combining two modalities into a single cost-effective "see and treat" approach. The synthesis, photophysical characteristics and in vitro/in vivo biological significance of a series of photosensitizer-cyanine dye conjugates will be discussed.

Chemical Genetic Approaches for Dissecting Signaling Cascades

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Our laboratory focuses on the development of chemically based tools to decipher signal transduction pathways on a genome-wide scale. Using chemistry and genetics in one regime, our laboratory is interested in developing and utilizing novel chemical genetic approaches to dissect signaling cascades. Recently, we have applied a chemical genetic approach to identify novel targets of Cdk5 kinase in Alzheimer Disease (AD). This study revealed more than 30 novel substrates of Cdk5 kinase in mouse brains. Using novel chemical tools developed in our laboratory, Cdk5's fatal role in AD will be presented.

Second part of the presentation deals with engineering unnatural nucleotide specificity in G proteins. G proteins are a large family of proteins comprising approximately 0.5% of mammalian genomes. To date, their functional study has been hampered by an absolute dearth of inhibitors due to technical challenges. In this study, we used H-Ras, the prototypical small G protein, to develop a system answering this need. Convergent engineering of the nucleotide and of its binding pocket resulted in the production of two complementary small molecule/mutant protein pairs that allow an absolutely specific "on" and "off" control over the activity of engineered G protein. Importantly, the highly conserved nature of the guanine nucleotide binding pocket augurs well for the possible translation of this system to other G proteins.

Recent Trends and Discoveries at the Interface of Chemistry and Biology - Case of Natural Product Science

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The field of phytopharmaceutical research and development is now witnessing a major transformation both in terms of concept and in practices. With the advent of super-advanced hyphenated techniques, such as LC-NMR, LC-MS/MS, LC-MS/NMR, GC-MS, development of new spectroscopic methods and high-throughput bioassay techniques, the research in plant-based drug discovery has immensely progressed in recent years. The emerging new field of metabolimics and associated technological advancements also holds great promises for the future of this exciting discipline.

Biodiversity is an outward manifestation of chemical diversity. Plants contain a fascinating array of natural products. Since last three decades, we have been focusing our efforts to harness the chemical diversity present in the floral diversity. In the process, we have employed state-of-the-art technologies, including modern chromatographic techniques, sophisticated and sensitive spectroscopic techniques and a range of biological screening methods. As a result, we have identified various new classes of potential pharmacophores against various diseases.Different clinically important enzymes were targeted such as β-glucosidase, thymidine phoshphorylase, acetylcholinesterase, butyrylcholinesterase, β-glucuronidase, phosphodiesterase, tyrosinase and urease, which led to the discovery of potent and novel pharmacophores. Along with this, a battery of *in-vitro* and in vivo bioassays were employed to identify new antibacterial, antifungal, antiparasitic, antioxidant, antiangiogenic and antiglycation agents.During this presentation, recent trends and future prospects of technological developments in phytopharmaceutical research will be discussed and examples of their utility will be demonstrated by taking the examples of our own research work.

Highlight in Synthesis and Isolation of Bioactive Molecules

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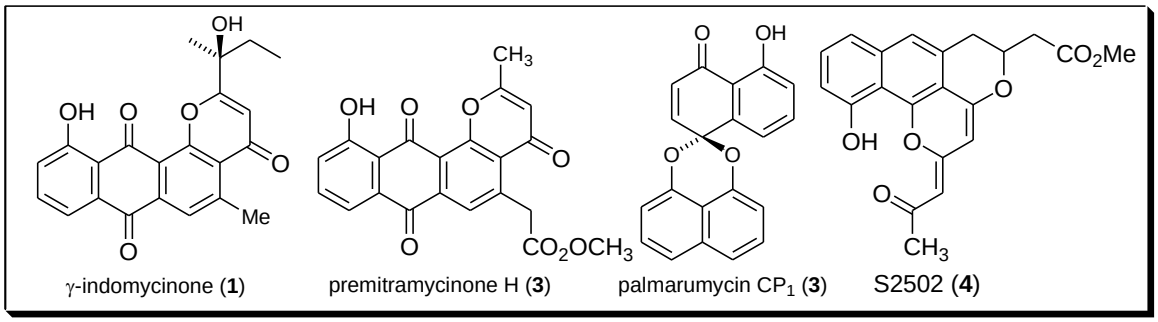
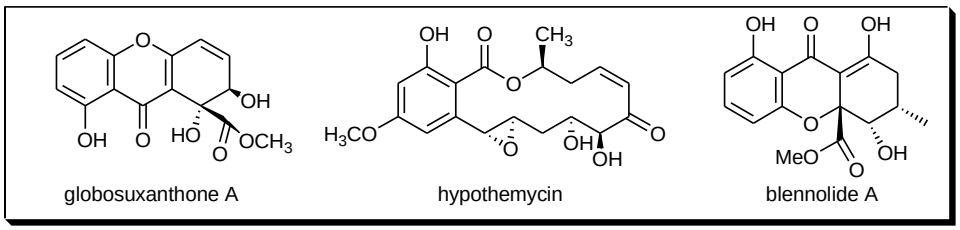
The lecture has two parts. In the first part, a number of polyketide-derived naturally occurring antibiotics of the anthrapyrane-type are presented. These include γ-indomycinone (1) and premitraymcinone H (2). [1] Further targets are the palmarumycines (3), a group of bioactive spiro-bis-naphthalenes, and S 2502, a new antiviral agent, produced by genetic engineering using genes of Streptomyces nogalater producing originally nogalamycin expressed in Streptomyces lividans. S2502 and S2507 exerted outstanding activities against herpes simplex, influenza B, adeno, and cytomegalo viruses. [2]



In the second part, recent results in the isolation of bioactive metabolites from endophytic fungi are presented. A few examples of increasing diversity of the products by dimerization or by production of open chain or cyclic products are shown. A new method for elucidation of the absolute configuration by combination of solid stated CD measurement and TDDFT calculations is outlined. Some results include globosuxanthone A [3], hypothemycin, [4] and blennolide A, the first monomer to be isolated from the dimeric secalonic acid type mycotoxins.



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Recent Advances in Drug Development Design, Synthesis and Biological Evaluation of Substituted 2-alkylthio-1,5-diaryl-imidazoles as selective COX-2 Inhibitors

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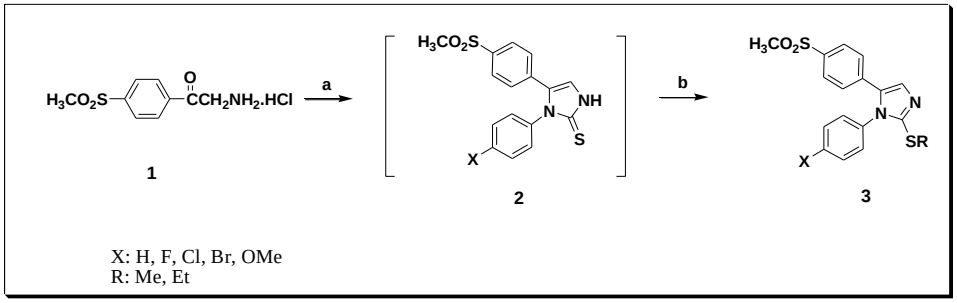
Before the 20th century, medicines consisted mainly of herbs. In the mid-nineteenth century efforts were made to isolate the active compound from of medicinal herbs. Chemists made literally thousands of analogues of the active compound to improve what nature had provided. The mechanism by which a drug worked at the molecular level was rarely understood and drug research very much focused on what is known as the lead compound, so that, the active principle isolated from the plant. In recent years, medicinal chemistry has undergone a revolutionary change. Rapid advances in the biological sciences have resulted a much better understanding of how the body functions at the cellular and molecular levels. Therefore, most researches begin by identifying a suitable target in the body and designing a drug to interact with the target. Advances in molecular genetics and mapping the DNA of humans and microorganisms resulted to increasing the number of new receptors and enzymes which are potential for drug targets. The more selective a drug is for its target, the less chance that it will interact with different targets and the less chance that it will have side-effect. For example in the field of antimicrobial agents, the best targets to choose are those which are unique to the microbe and which are not present in man.

In the present study design, synthesis and biological evaluation of substituted 2-alkylthio-1,5-diarylimidazoles as selective COX-2 inhibitors are described and the title compounds were prepared according to the following Scheme.



Scheme 1

New Techniques in Combinatorial Chemistry - Synthesis of Biologically Active Compounds on Solid Supports

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The design and creation of small molecules displaying specific and strong interactions with biological systems is a pivotal area in organic syntheses. The fact that many biologically active molecules such as drugs and pesticides contain this motif shows how particular suitable heterocycles are for this purpose and that novel strategies are needed for their selective, straightforward and modular creation. In the first part of the lecture, we build a bridge between our concepts of multifunctional linkers for solid-phase chemistry leading to diverse heterocycle libraries and the synthesis of natural products incorporating the heterocycle motif. In particular, the synthesis of benzoannelated nitrogen heterocycles such as indoles, benzotriazoles, and benzotriazinones will be discussed on selected examples. Key features are the introduction of diversity by various metal-mediated and -catalyzed processes like Heck reactions, Hartwig-Buchwald amination reactions, or Bartoli indole syntheses.

In the second part, combinatorial approaches towards drug delivery of small molecular probes will be presented.

Asymmetric Desymmetrization: Conceptual Creation to Synthetic Explorations

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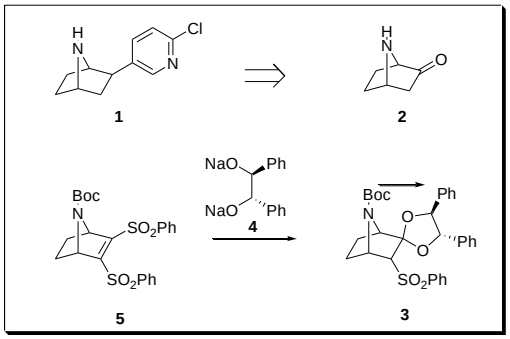
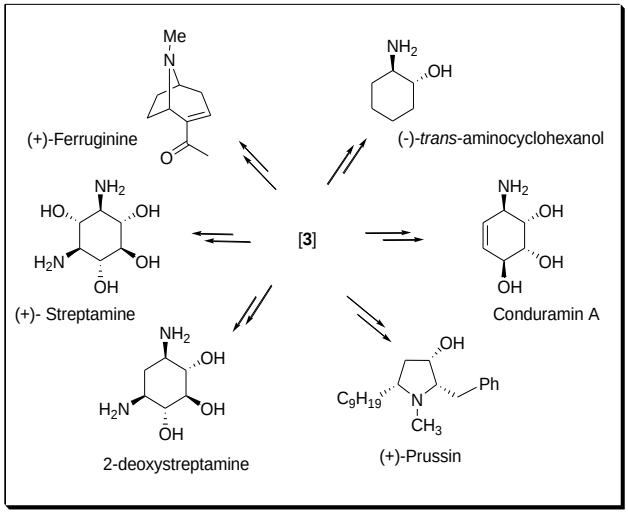
Asymmetric synthesis via enantiotopic differentiation of meso compound employing chiral reagents / catalysts is an attractive strategy for the synthesis of enantiomerically pure compounds. In the context of our earlier interest in the synthesis of epibatidine (1); a powerful analgesic (non-opioid, 200-500 times more potent than morphine), we developed a strategy to obtain optically pure 7-azabicyclo[2.2.1]heptan-2-one skeleton (2) via asymmetric desymmetrization of meso-5 using chiral alkoxide (4) as enantiotopic differentiating reagent. However, further development of 1 veined due to the detection of pronounced toxicity.



Scheme 1

Nevertheless, having developed a conceptually new and short strategy for the synthesis of **3,** also endowed with attractive structural framework, we explored its synthetic potential for the synthesis of several important natural products and other useful compounds as shown in Scheme 2



Scheme 2

Concept and details of the synthetic endeavors will be presented.

The Nature of Protein Folding Reactions

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The nature of the barriers that slow down protein folding reactions from their diffusion limited rates is poorly understood. A fundamental question is whether an enthalpy-entropy mismatch occurs at one point along the reaction coordinate, leading to a single dominant free energy barrier.In this case, the folding reaction is expected to be two-state or all-or-none. Alternatively, there might be small distributed free energy barriers which are easily crossed by diffusive motion of the polypeptide chain during folding.

The Passerini and the Ugi reaction, Recent Development

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The Passerini reaction (P-3CR) [1] produces an α-acyloxy carboxamide in one-pot from an aldehyde, a carboxylic acid and an isonitrile (Scheme 1, Eq. 1), while the Ugi four-components reaction (U-4CR) [2] involves an additional component: an amine leading to an α-acylamino amide. They have been the subjects of intensive researches for the past decades for generating the molecular complexity and diversity. [3] In this talk, we will briefly present the development of (a) oxidative P-3CR; [4] and oxidative Ugi type reaction; [5] (b) enantioselective Passerini reaction [6].

References:

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Quinolines and Isoquinolinones as Inhibitors of poly(ADP-ribose)polymerases (PARPs)

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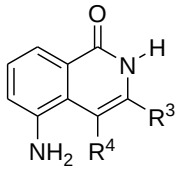
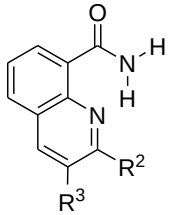
The poly(ADP-ribose)polymerases (PARPs) catalyse the transfer of ADP-ribose units from the substrate NAD^+ to acceptor proteins, biosynthesising polyanionic poly(ADP-ribose) polymers[1]. The major isoform, PARP-1, senses sites of damage in DNA through its Zn-fingers and binding to these damaged sites activates the enzymatic activity. Inhibitors of PARP-1 may have applications in the treatment of many disease states, including cancer, haemorrhagic shock, cardiac infarct, stroke, diabetes and inflammation. Recent clinical trials of inhibitors of PARP-1 have shown that PARP-1 inhibitors potentiate the anticancer activity of DNA-damaging drugs, such as temozolomide, and can be used as a monotherapy to treat tumours which are already DNA-repair deficient.

The consensus pharmacophore for inhibition of PARP-1 is a benzamide with N—H constrained *anti* to the carbonyl—arene bond. Most current inhibitors are benzamides or fused benzamides. We have designed 3-substituted and 4-substituted derivatives of our lead agent 5-aminoisoquinolin-1-one (5-AIQ) as inhibitors of PARP-1, aiming to increase potency while retaining the great water-solubility of 5-AIQ. The 3-substituted 5-AIQs were synthesised *via* the corresponding 3-substituted 5-nitroisocoumarins by several routes: cyclisation of 2-alkynyl-3-nitrobenzoates with electrophiles (Hg^{2+}, ICl, PhSeCl) [2]; tandem Hurtley coupling / cyclisation of β-diketone enolates with 2-bromo-3-nitrobenzoic acid; tandem Friedel-Crafts acylation / rearrangement / decarboxylation of 5-nitroisocoumarin with aroyl chlorides [3]. Examples of 4-substituted 5-AIQ derivatives were prepared by a novel double-bond migration / intramolecular Heck reaction of N-(3-(substituted)allyl)-2-iodo-3-nitrobenzamides. A new class of PARP-1 inhibitor, the quinoline-8-carboxamides (Q8Cs), uses intramolecular hydrogen bonding to constrain the benzamide pharmacophore in the correct conformation. 2-Substituted Q8Cs were synthesised by quench of 8-lithio-2-R-quinolines with trimethylsilylisocyanate. An efficient route to 3-substituted Q8Cs was developed in which diversity was introduced in the last step: palladium-catalysed Stille, Sonogashira and Suzuki couplings of 3-iodo-Q8C. The substituted 5-AIQs and substituted Q8Cs showed inhibition of PARP-1 activity, ranging from 10× more potent to >25× less potent than 5-AIQ.



General structure of 3- and 4-substituted 5-AIQs



General structure of 2- and 3-substituted Q8Cs

Acknowledgements

We are grateful to the Association for International Cancer Research, KuDOS Pharmaceuticals Ltd., UK Government ORS Scheme and the University of Bath for financial support.

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Synthesis and Evaluation of Drug-Dextran Conjugates for Selective Liver-Targeted Drug Delivery

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Liver-specific targeting is critical for a number of liver-associated diseases, such as viral hepatitis and hepatic cancer. Furthermore, preferential delivery of immunosuppressive agents to the transplanted liver is expected to both reduce systemic toxicities of these drugs and improve graft (liver) survival. Available conventional therapies are nonspecific and cause severe side effects. The treatment can be compromised due to dose-limiting toxicity in other tissues. Therefore, alternative strategies are required for the preferential delivery of drugs to the liver to both reduce the systemic toxicities of these drugs and improve their therapeutic effects. Dextran (~20 kDa) has a preferential uptake by the liver compared to other tissues and accumulates in the liver. Dextran functions as a polymer carrier because it is water-soluble, biodegradable, and non-antigenic natural polysaccharide. The dextran prodrugs of lamivudine (3TC) and methylprednisolone (MP) were synthesized and characterized. 3TC and MP are used as the antiviral drug against hepatitis B virus and immunosuppressive agent, respectively. The prodrugs preferentially accumulated in the liver, where they gradually regenerated the active drugs. 3TC was coupled to dextran (~25 kDa) using a succinate linker, and the in vitro and in vivo behavior of the conjugate was studied using size-exclusion and reversed-phase analytical methods. In vitro, the conjugate slowly released 3TC in the presence of rat liver lysosomes, whereas it was stable in the corresponding buffer. In vivo in rats, the accumulation of the conjugated 3TC in the liver was 50-fold higher than that of the parent drug. The high accumulation of the conjugate in the liver was associated with a gradual and sustained release of 3TC in the liver. Methylprednisolone succinate (MPS) was attached to dextran 25 kDa using linkers with 1–5 Gly residues. The release characteristics of the conjugates in pH 4.0 and 7.4 buffers, blood, liver lysosomes, and various lysosomal proteinases were determined using a size-exclusion and/or a reversed-phase HPLC method capable of simultaneous quantitation of MP, MPS, and all five possible MPS-peptidyl intermediates. Rat lysosomal fractions degraded the conjugates to MP and all the possible intermediates at a rate directly proportional to the length of the peptide. These newly developed dextran conjugates of MP show promise for controlled delivery of MP in lysosomes. These studies indicate the feasibility of the synthesis of drug–dextran conjugates and their potential use for the selective delivery of drugs to the liver.

Design and Synthesis of New Pyrrolobenzodiazepine Anticancer Agents

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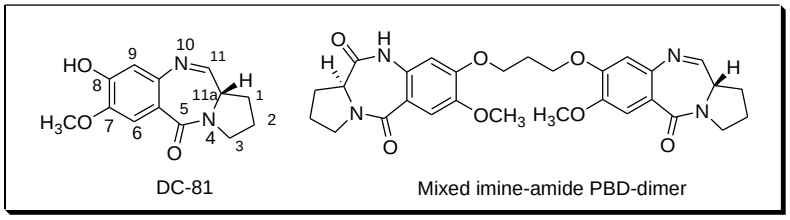
During the last few years major advances in molecular and cellular biology have led to breakthroughs in the field of cancer research. The most important is the identification of genes that are intimately involved in cancer initiation, progression, invasion and angeogenesis, particularly those genes that cause cancer and those that promote or inhibit programmed cell death. It is evident that DNA is an important cellular target for many anticancer agents. Pyrrolo[2,1-*c*][1,4]benzodiazepines (PBDs) are naturally occurring compounds isolated from various *Streptomyces* species. The PBDs exert their biological activity through covalent binding with in the minor groove of DNA [1,2]. Most of the methods reported in literature are based on the solution phase synthesis of the tricyclic PBD compounds.

In recent years there has been a growing interest in the design and synthesis of PBD linked hybrids and in this connection a large number of C-8 linked hybrids have been synthesized and explored their potential as anticancer agents [3]. Over the past few years we have been pursuing the structure-activity relationship (SAR) investigation in the area of chemotherapy. On the basis of SAR studies, a number of novel PBDs have been synthesized in an attempt to increase their potency against tumour cells and DNA sequence selectivity. Furthermore, we have also been interested in the selective delivery of this class of compounds at the tumour site using ADEPT, GDEPT and PMT strategies.



Scheme 1

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Design and Development of Phototriggers for Biomolecular Caging

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Biomolecular caging is a technique in which a bioactive molecule is rendered inactive by covalently linking it to a photolabile group, and when required the biomolecule can be released in its active form in site-, time- and concentration-controlled fashion by photoirradiation.[1]. It presents a novel strategy for investigating wide range of cellular activities and also gives rise to many practical applications of chemical, biochemical, catalytic, medical and physiological significance. For instance, while biomolecular arrays based on photocleavable cages are of central importance in the field of nanotechnology, pro-drug activation *via* photolysis is important in the field of medicine and health care. Several types of photolabile groups including phenacyl–, *o*–hydroxycinnamoyl–, *o*–nitrobenzyl– esters and amides have been considered for caging applications. However, the success of this strategy, particularly in biological systems, is largely dependent on the photocleavability of the cage under physiological conditions. Recently we have examined the efficacy of nitronaphthyl, phenacyl and anthryl related chromophores and found that some of these chromophores are useful for biomolecular caging under physiological conditions [2]. The cages can be easily prepared and the release of bioactive component from the cage can be triggered in aqueous media employing biologically benign photons of different wavelengths. Synthesis, photochemistry and applications of these chromophores in biomolecular caging, particularly with respect to controlled drug delivery will be presented. Further, future prospects of developing orthogonally photocleavable chromophores, IR-active chromophores, two-photon excitable chromophores and other advances made in the area will be discussed.

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1,2-Dialkynylimidazoles as Anticancer Aza-enediynes

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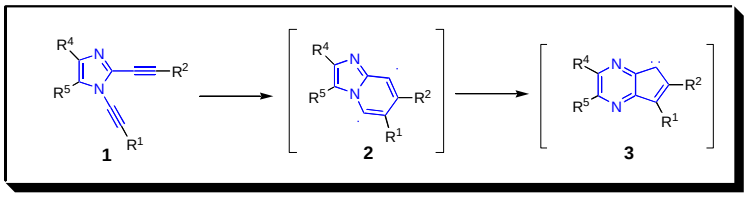
In an approach to selective anticancer compounds inspired by the fascinating chemistry of the enediynes, we have explored alternative diradical-generating cyclizations that may be more readily applied to targeting specific proteins for covalent inactivation [1-3]. These efforts have lead to the discovery of a novel thermal cyclization and rearrangement of 1,2-dialkynylimidazoles (**1**) [4]. Under relatively mild conditions, these dialkynylimidazoles afford imidazo[1,2-*a*]pyridine products through the trapping of 5,8-didehydroImPy diradical intermediates (**2**) [5]. If the diradicals **2** are not trapped, they can undergo rearrangement to afford cyclopentapyrazine carbene intermediates (**3**), which participate in H-atom abstraction, C-H bond insertion, and alkene addition reactions (Scheme 1) [6]. Compared to enediynes, the lower energy barriers required for DAIm cyclization and the similarity of the resulting reactive intermediates to known protein-targeting drugs, indicate that the cyclization shown in Scheme 1 may be harnessed to create selective, irreversible inhibitors of a number of therapeutically relevant anticancer targets.



Scheme 1

In this talk, we will present our latest work demonstrating the facility of DAIm cyclization, x-ray crystallographic and DFT studies of these compounds and their thermal cyclizations, and the potent and unique cancer cell cytotoxicity of these compounds.

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Understanding the Organic Chemistry in Aqueous Medium

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Over the past 15 years chemistry has emerged has a distinct discipline of science and is intimately associated with the welfare of the society. However, this long history of development of chemistry has appeared as both blessings and a curse. Most of the strategies of assembling the target molecules (drugs and pharmaceuticals) employ reactions that are old and use chemicals that are detrimental to environment. The common approach adopted in the practice of medicinal chemistry research is somehow to make the designed molecule. However, in addition to the principle objective to produce compounds that lead to API, it is necessary to develop a robust process with high purity and yield. Also is equally (even more) important is to develop an eco-friendly procedure. While the scale of the reactions in the early stage of the programme is usually small, the cumulative footprint generated by numerous laboratories across the globe is significant. The delay to reengineer the discovery route for scale up has impact on the timeline and cost. Thus, the influence of green chemistry on medicinal chemistry research can not be overlooked. Solvents define a major part of the environmental performance of a process and also has impact on the cost, safety and health issues. The annual use of solvents by the chemical industries in Europe alone was almost 4 X 10^6 tons in 2004. Organic solvents account for 85% of the mass utilisation of pharmaceutical manufacturing process with an usage of £4 billion per annum. With a typical recovery efficiency of 50-80%, organic solvent use is the major contributor to the burden of environment pollution. The potential of water as a organic reaction medium has been recognized as significant advancement of sustainable development it is the cheapest, most abundant, non-inflammable, non-toxic solvent and provides ease of product isolation [1]. Water is the most preferred solvent according to Pfizer solvent selection guide. Although the beneficial effect of water in influencing reaction rate and selectivity indicate that water is not merely an environmentally friendly alternative reaction medium its exact role in accelerating organic reactions remains unclear. The present deliberation will highlight an understanding of the molecular basis of catalysis by water by "electrophile-nucleophile dual activation" [2] through "cooperative hydrogen bond network" [3] its projected generalization [4] and implication in underpinning certain enzymatic selectivities for the synthesis of natural toxins [5].

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Natural Product Synthesis: Does It Satisfy Only the Scientific Curiosity or Some Thing More

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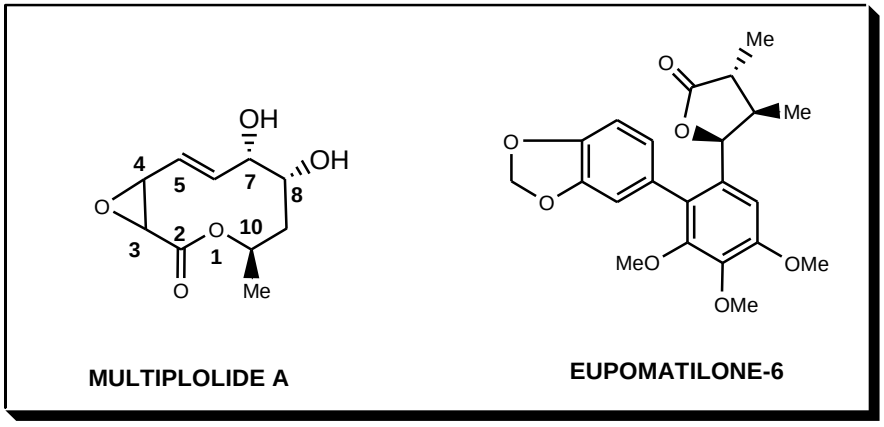
More than 50% of drug molecules are directly or indirectly related to natural products skeletons. In spite of this proven data, the importance of classical natural product chemistry as it relates to isolation, structural elucidation and screening is diminishing. The new role of natural product chemistry is focused on bioactivity driven natural product isolation. The fermentation of micro organisms, bioassay of various fractions and subsequent isolation of natural products have given new impetus to this area and some brilliant, complex and structurally intriguing natural products were reported. There are inherent issues in determining the correct chemical structures coupled with stereo chemical assignments. The scarcity of the natural product from natural resources frequently debars from conducting the complete biological screening and its chemical modification for structure activity relationship.

In this regard the total synthesis of natural product comes to our rescue, first to provide absolute stereo chemical structure, enough quantity for complete biological testing and derive new structurally modified natural products.

Our group is engaged in this activity for long period of time. The following natural product synthesis shall be discussed.



MULTIPLOLIDE A **EUPOMATILONE-6**

The total synthesis of eupmatilone-6 revealed that a wrong structure was assigned to this natural product. We carried out the synthesis of many stereo isomers of eupomatilone-6 and first provided proof for the relative stereo chemistry. Later we synthesized the single enantiomerically pure eupomatilone-6 and concluded the absolute stereo chemical assignment.

In case of multiplolide A, the stereo chemical assignment of the oxirane ring was never established. Therefore both the distereomers of multiplolide A were synthesized and absolute stereo chemistry of multiplolide A was established.

Tuning of Selectivities in the Metalation of Benzoic Acids. Application to the Synthesis of Analogs of Gossypol Antagonists of Bcl-2 Family Proteins

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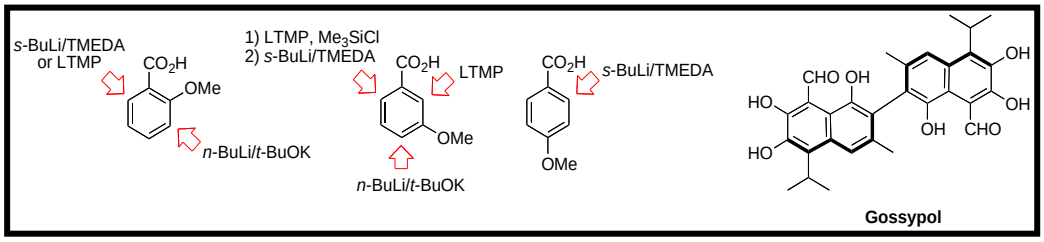
There are a number of carboxylic acid derivatives such as secondary and tertiary amides, esters, *a*-amino alkoxides, oxazolines, acetals, imidazolidines, imidazoles and cyclohexylimines which are widely used for directed ortho-metalation (DoM). The advantages of the tertiary amide directing metalation group (DMG) include ease of preparation, priority over directors during the metalation step, utility in polysubstituted aromatic systems, and resistance to nucleophilic attack. The resistance to nucleophilic attack can be a problem if one wishes to convert the tertiary amide group into another functionality. In fact, the main disadvantages of *N*,*N*-dialkylamides as DMGs are their resistance to hydrolysis and the paucity of methods for their transformation to other useful functionalities. Comins and Brown [i] and Reitz and Massey [ii] have tried to address the hydrolysis problem by developing *tert*-amide DMGs which are readily converted into secondary amides, the cleavage of which, via the *N*-nitrosoamide, has long been known. Snieckus has shown [iii] that *N*-Methyl-*N*-[bis(trimethylsilyl)methyl]-benzamides and their monotrimethylsilyl analogues are ortho-lithiated and that the derived ortho-substituted products can be transformed, in two steps, into the corresponding benzyl alcohols or benzaldehydes. Secondary benzamides, although useful in directed metalation syntheses usually suffer from problems which arise from the lack of solubility of the dianion generated.

When the carboxylic acid substituent is employed as a DMG, substantial selectivity toward metalation can be obtained.[iv] The CO_2Li DMG is of modest strength when compared to some of the strong ortho-directors, but it permits a remarkable degree of control of the regioselectivity of metalation between nonequivalent ortho centers. Regioselective routes to very simple substituted benzoic acids with a variety of functionalities that are not easily accessible by other means have been developed. The mechanism of the ortho-metalation is discussed. As an application of the previous results, the total synthesis of analogs of Gossypol is described.



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Design and Synthesis of Novel M1 Receptor Agonist and AChE Inhibitors for the Treatment of Alzheimer's Disease

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Etiopathology of Alzheimer's disease (AD) is associated with beta amyloid formation, mainly in response to hypocholinergic function, which leads to impairment in memory and cognitive abilities. It is quite evident from many research studies that the most striking therapeutic strategy emerging from hypocholinergic concept of AD is the upregulation of cholinergic function obtained by acetyl cholinesterase (AChE) inhibition and or by activation of muscarinic acetylcholine receptor 1 (M1 receptor). In this regard, we have synthesized both M1 receptor agonist and AchE inhibitors for the possible treatment of AD. In one of the clinical studies, arecoline, an alkaloid from areca nut, showed a significant improvement in memory and cognition in dementia patients, but was later found to be carcinogenic and tends to be hydrolyzed due to the presence of ester functional group of arecoline in stomach (pH<7). This led to emergence of many structurally modified arecoline derivatives as M1 receptor's agonist in AD research. In our laboratory, we have synthesized and characterized several alkyl/aryl derivatives of arecoline thiazolidinones, arecoline emides and arecoline morpholines as M1 receptor agonist and screened by several in vitro and in vivo pharmacological studies. Piperazine derivatives are known to inhibit AchE in worms. In this connection, piperazine derivatives were synthesized with condensing various pharmacologically active alkyl and alkyl halides group as AchE inhibitors. Some derivatives of arecolines showed potent M1 receptor agonist activity and some piperazine derivatives as potent AChE inhibitor.

Exploring Structural Diversity in Nucleoside Drug design

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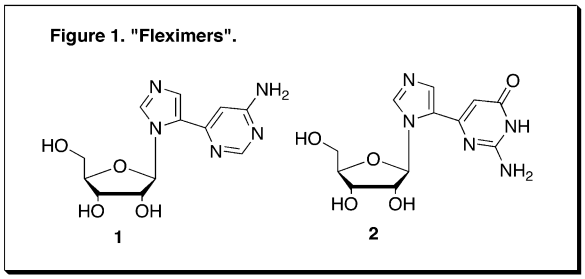
One focus for the ongoing research in the Seley-Radtke laboratories has involved the design and synthesis of structurally unique nucleosides to explore fundamental aspects of nucleic acid structure, function, and stability, as well as to investigate enzyme binding site parameters. With the increasing number of crystal structures for biologically relevant enzyme-substrate/inhibitor complexes, it has become apparent that many binding sites are more flexible than previously thought and can therefore adjust to fit a wide range of substrates. Significant to this observation, it has also been shown that flexible inhibitors such as tenofovir and etravirine are able to evade drug resistance mutations in viral HIV due to their inherent flexibility [1].

As a possible means to explore this phenomenon in the enzyme systems of interest in our research, we have strategically designed a series of structurally innovative nucleosides that possess a heteroaromatic purine ring split into its two components (i.e. an imidazole and pyrimidine ring), thereby conferring additional degrees of conformational freedom and torsional flexibility to the ligand [2-4]. As a result, these molecular "chameleons" can adapt to the environment of a binding site in order to maximize and complement structural interactions, without losing the integrity of the crucial contacts involved in the enzyme's mechanism of action. Simply stated, the flexibility of the putative drug complements structural changes in the drug target, and the result could be a more potent inhibitor, with broad implications for overcoming viral mutations.

As expected, the increase in rotational degrees of freedom allowed the fleximer base to sample alternative binding modalities [5] and to interact with secondary amino acid residues not previously involved in the mechanism of action [6]. Notably, the fleximer nucleotide was able to retain biological activity despite mutations to active site residues critical to catalysis [6], and also exhibited a catalytic efficiency more than twice that for GTP, the natural substrate [7]. These findings are significant, and as such, indicate that flexible nucleoside analogues should find use in drug design by revealing alternative binding modes that can help guide inhibitor design.



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Eradication of M.TB Infection in Two Months with LL-3858 (Sudoterb) A Preclinical Study

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Tuberculosis is a chronic respiratory disease, caused by Mycobacterium tuberculosis, continues to present as a major global health problem with approximately 8 million new cases and close to 3 million deaths each year. The combination drugs together are effective in treatment against sensitive *M. tuberculosis* infection in 4 – 6 months time, but is not effective against MDR strains. In past 30 years very little efforts have been made to develop new drug to treat tuberculosis caused by MDR strains and latent tuberculosis. Thus, there is an urgent need to develop new drug against tuberculosis that is safe, effective and reduces the total treatment time when given alone or in combination. LL3858, was found to be the most active (MIC_{50} 0.12 and MIC_{90} 0.25µg/ml) against sensitive and resistant strains. LL3858 is mycobactericidal and has synergy with Rifampicin. Mono therapy of *M. tuberculosis* infected mice with LL3858 (12.5 mg /kg) demonstrated a complete absence of growth in organs of 33% of animals after 3 months. Combination of LL3858 with first line anti TB drugs i.e. isoniazid Rifampicin, and Pyrazinamide i.e. LL4858 (LIRZ) induced complete eradication of mycobacterial load from the target organs of animals infected with sensitive or resistant strains of *M. tuberculosis* after 2 months treatment with once daily dose. Furthermore, LL4858 also prevented relapse in mice upto two months post treatment, indicating that the present combination LL4858 is superior then the existing combinations of anti TB drugs. Further, the combination is bioavailable non-genotoxic and has an LD_{50} 2500mg/kg in mice. The combination also did not show any adverse effect on the nervous, cardiovascular, respiratory and autonomic systems in rodent and non rodents.

The results of our study suggest that **LL4858** is a novel combination consisting of a novel antimycobacterial compound (LL3858) that is safe, nontoxic and provides effective cure against tuberculosis in 2 months in our Preclinical studies.Phase II EBA study inplanned.

Designer Molecules Containing Heteroaromatic Amino Acids

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A common approach to restrict the conformational degrees of freedom in small peptides involves designing structurally rigid non-peptide scaffolds which, when inserted in the appropriate sites in peptides, produce the specific secondary structures required for binding to their receptors leading to the development of potent agonists/antagonists. The number of reports on the development of constrained non-peptide scaffolds used in peptidomimetic studies is increasing rapidly. Newer concepts are emerging where the fundamental building blocks used by nature, like amino acids, sugars and nucleosides, are amalgamated to produce nature-like, and yet unnatural, de novo structural entities with multifunctional groups anchored on a single ensemble. Furan amino acids (Faa) and pyrrole amino acids (Paa) belong to a new class of heteroaromatic amino acid building blocks that have been developed by us recently and used extensively in peptidomimetic studies.

It is now well known that the secondary structural motifs so common in proteins are not restricted to the α-peptide backbone alone, but can be seen in many designer oligomers. Among the most studied families of non-natural oligomers that show interesting secondary structures are the β-, γ- and δ-peptides, which bear particular significance because of their similarity to α-peptides. The conformationally constrained scaffolds of furan and pyrrole amino acids, which belong to the family of γ- and δ-amino acids, have emerged as important synthetic monomers leading to many *de novo* structural entities that have displayed interesting secondary structures and also useful properties like binding with DNA and G-quadruplex. The presentation will give a brief overview of some of our latest results in these areas of research.

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Metallo-Nucleosides: Synthesis and Biological Evaluation of Hexacarbonyl Dicobalt 5-Alkynyl-2'-Deoxyuridines

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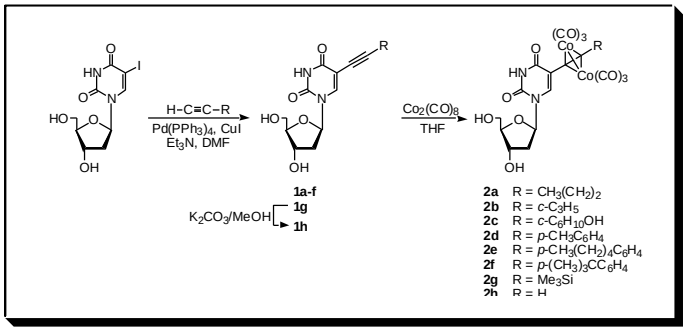
Reactions of 5-alkynyl-2'-deoxyuridines (**1**) with dicobalt octacarbonyl $Co_2(CO)_8$ in THF at room temperature gave hexacarbonyl dicobalt nucleoside complexes (**2**, 77-93%). The metallo-nucleosides were characterized including an X-ray structure of a 1-cyclohexanol derivative. In crystalline form the Co-Co bond is perpendicular to the plane of uracil base, which is found in the *anti* position. The level of growth inhibition of MCF-7 and MDA-MB-231 human breast cancer cell lines was examined and compared to results obtained with the alkynyl nucleoside precursors. The cobalt compounds displayed good antiproliferative activities with IC_{50} values in the range of 5-50 μM. Interestingly, the coordination of the dicobalt carbonyl moiety to 5-alkynyl-2'-deoxyuridines led to a significant increase in the cytotoxic potency for alkyl/aryl substituents at the non-nucleoside side of the alkyne but in case of hydrogen (terminal alkyne) or a silyl group a decrease of the cytotoxic effect was observed. As demonstrated using examples for an active and a low active target compound the cytotoxicity was significantly influenced by the uptake into the tumor cells and the biodistribution into the nuclei [1, 2]



Other synthetic transformations of 5-alkynyl-2'-deoxyuridines, to modified furanopyrimidines, will be discussed as well.

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Recent Advances in Carbon-Carbon and Carbon-Heteroatom Bond-Forming Reactions Mediated by NHCs and Other Nucleophiles

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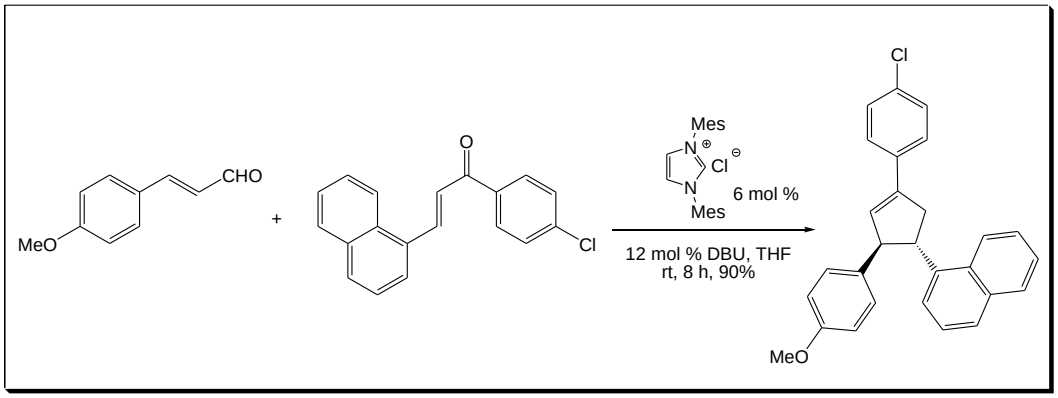
In recent years we have uncovered a number of carbon-carbon and carbon-heteroatom bond forming reactions involving zwitterionic species generated by the addition of isocyanides, N-heterocycles, nucleophilic carbenes such as dimethoxycarbene and *N*-heterocyclic carbenes (NHCs) to activated alkynes. NHCs are known to react with a variety of electrophiles in a reversible or irreversible manner. Organocatalysis falls in the first category and Multicomponent reactions (MCRs) in the second. Very recently we have utilized NHC catalyzed homoenolate annulation in the stereoselective construction of γ- and δ-lactones and cyclopentenes. The lecture will focus on these and related reactions.



Scheme 1

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New Insights of Asymmetric Supramolecular Chemistry in the Synthesis of Biologically Active Compounds: Fishing Intermediates of Catalyzed Reactions by ESI-MS

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Enantioselective total synthesis of Quinolactacin B, PDE5 inhibitor, and asymmetric b-carboline moieties were achieved in few steps and higher yields. The syntheses features the use of ruthenium catalytic asymmetric hydrogen reaction to introduce the chirality in dihydro-b-carboline, and a new supramolecular approach based on cyclodextrin host-hest complexes were also studied. Based on the Noyori's work, the hydrogenation using both (S,S)- or (R,R)-TsDPEN-Ru complex produce dihydro-b-carbolines possessing the desired absolute configuration, the corrected asymmetric center of the natural products. Mechanistic approach of the supramolecular induction was rationalized based on electrospray ionization mass spectrometry studies through on-line reaction monitoring.

Synthesis of Proline Derivatives by Asymmetric 1,3-dipolar Cycloaddition Reactions of Azomethine Ylides and Alkenes

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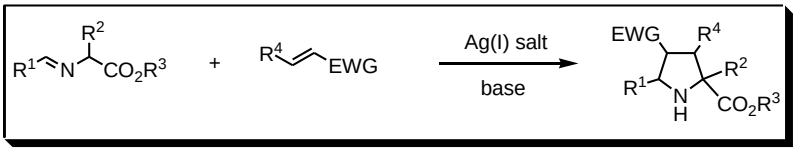
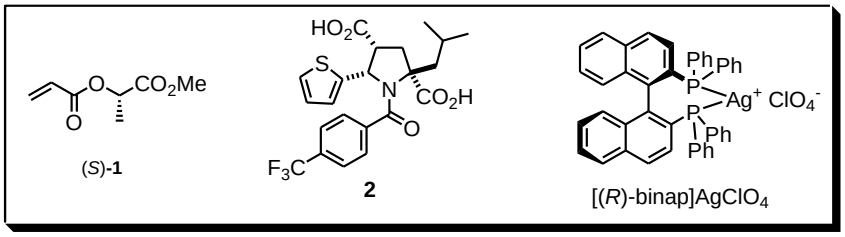
The asymmetric 1,3-dipolar cycloaddition of azomethine ylides and alkenes provides a direct access to the synthesis of enantioenriched highly substituted pyrrolidine or proline derivatives in a high diastero- and enantioselective form [1]. The most direct way for the preparation of the corresponding dipoles is to generate in situ a metallo-azomethine ylide from α-imino esters derived from amino acids (Scheme 1). There are three main strategies for the asymmetric 1,3-dipolar cycloaddition of azomethine ylides: a) by attaching a chiral auxiliary to the imino group or to the ester in the dipole, b) by attaching the chiral auxiliary group to the dipolarophile, and c) by using a chiral catalyst. We will present our work in this field using the last two strategies.



We have found that the use of chiral acrylates **1** derived from methyl (*R*)- and (*S*)-lactate as dipolarophiles with imino esters in the presence of AgOAc as catalyst and KOH as base at room temperature afforded the corresponding cycloadducts with high regio-, diastereo- and enantioselectivity [2]. This methodology has been applied to the synthesis of substituted prolines, which are hepatitis C virus RNA polymerase inhibitors **2** [3]. For the enantioselective version Ag(I) complexes with phosphorus ligand such as phosphines and phosphoramidites have been used as chiral catalysts. The employment of binap-$AgClO_4$ complex has allowed to recover, just by simple filtration, and to reuse this catalyst during 5 runs [4]. Different phosphoramidites derived from binol have also been used as the first monodentate chiral ligands in this type of enantioselective 1,3-dipolar cycloaddition of azomethine ylides and alkenes.



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Thiazolidinones, Pyrazolo-1,3-oxazin-2-ones and Thiazolyl-N-substituted Amides as Anti-inflammatory Agents. Dual Acting Agents for the Treatment of Various Disorders with Mild Anti-inflammatory Action as a Beneficial Additional Property

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Inflammation is a multifactorial process. It is the organism response to various stimuli and is related to a number of disorders which require prolonged or repeated treatment. Cyclooxygenase (COX) and lipoxygenase (LOX) produce two groups of arachidonic acid metabolites, that play a key role in inflammation. Non-steroidal anti-inflammatory drugs (NSAIDs) mainly act via the inhibition of the COX-1 and COX-2 isoenzymes. As COX-1 selective inhibitors were blamed for inducing GI tract irritation and mild bleeding diathesis and COX-2 selective inhibitors were associated with increased risk of myocardial infraction and cardiovascular thrombotic events, investigators turned to dual acting agents that combine COX and LOX inhibiotory activity.

Inflammation or high tendency to inflammatory response escorts many diseases from microbial infection to Alzheimer's disease. Thus, mild anti-inflammatory activity might be a beneficial, additional property to many agents designed for the treatment of other disorders.

Our team works in the investigation of new anti-inflammatory agents for years. We have synthesised a number of new series of thiazolidinones, thiazolyl-N-substituted amides and N-substituted pyrazolo-1,3-oxazin-2-ones and evaluated their anti-inflammatory activity. Anti-inflammatory activity was estimated in vivo using the carragenan induced paw oedema model and in vitro by the inhibition of soybean lipogygenase, ovine cycloxygenase-1 and human cycloxygonase-2. Some of thiazolidinone derivatives were revealed to be of the most potent anti-inflammatory agents combining COX and LOX inhibitory activity. Dual acting molecules appropriate for use as anti-microbial agents or as potent drugs for the treatment of Noonan Syndrome were found among these compounds.

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The Representation of Chemical Structures for Drug Design

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Chemists have developed a variety of models for representing the structure of molecules: from the constitution through the 3D structure to molecular surfaces: [1]We have developed various methods for calculating chemical descriptors for the constitution, for the 3D structure, [2] or for molecular surfaces. [3]The relationships between the structure of a molecule and its reactivity or its biological activity are too complex to be cast into explicit mathematical equations. In such situations, the modeling of the relationships between structure and properties by inductive learning methods such as statistical analyses, pattern recognition methods, or neural networks [4] offers the only amenable solution. Application of these methods to the separation of molecules with different biological activity, to finding new lead structures, to the definition of the diversity of a library, to the analysis of high-throughput screening data, and the prediction of ADME properties will be given.

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Advances in QSAR Studies on Calcium Channel Blockers

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Calcium channel blockers (CCBs) have got potential therapeutic uses against several cardiovascular and non-cardiovascular diseases. The three principal structural classes have been found to act as potent calcium channel blockers and they are phenylalkylamines, 1,4-dihydropyridines (DHPs), and benzothiazepines. Recently, a few more classes of CCBs have been studied. All these classes of CCBs have been found to be the most effective drugs against vasospastic angina. These drugs selectively inhibit Ca^{2+} influx into heart muscles by blocking slow inward channels for Ca^{2+} or inhibit Ca^{2+} influx into vascular smooth muscles. The result is negative inotropism of smooth muscle relaxation, which is translated into hypotension.We intend to present a comprehensive review, including the most recent studies, on quantitative structure-activity relationship (QSAR) and molecular modeling studies on all kinds of CCBs. These studies lead to highlight the essential structural features and physicochemical properties that the compounds should possess to act as potential CCBs. These studies also describe vividly the mechanism of interaction of CCBs with the calcium channel.

Design and Synthesis of Lipid Vesicles for Gene Delivery: From Structure to Function

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Recent advances in genomics and molecular biology reveal that almost all diseases have a genetic component. In some cases, such as cystic fibrosis or hemophilia, mutations in a single gene result in disease. Even viral or bacterial infections have a genetic component - the genes of the invading pathogen.

Gene delivery is the process by which DNA sequences encoding specific genes are delivered to cells. As the genetic and molecular basis for a number of diseases is elucidated, the promise of gene therapy continues to grow. Although initial efforts in gene therapy focused on delivering a normal copy of a missing or defective gene, current programs are applying gene delivery technology across a wide spectrum of disease conditions.

Several laboratories the world over are involved in the development of non-viral DNA delivery vehicles. Lipid molecules when endowed with suitable charge characteristics, they complex with other macromolecules such as double-helical DNA or proteins. These complexes have nanometric dimensions and such nanoparticles contain condensed DNA in the form of nanoparticles with radii of 20-100 nm. They often have the ability to induce gene transfer across eukaryotic cells. We have prepared a number of lipid systems which induce gene transfer effectively. Based on their molecular structure it is possible to make a correlation of their function.

In this presentation, I would like to describe our efforts to this direction.

Gene to Drug *in silico:* A Molecular Bioinformatics Endeavor

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The world wide genome sequencing efforts and the concurrent developments in scientific software implementations on massively parallel computer architectures grant us the opportunity to dream that drug design could be undertaken against suitable biomolecular targets to develop individualized medicine almost in an automated way. Currently however, without the help of any database, an inspection of a DNA sequence does not tell us whether it is likely to be a gene and if it is a gene for messenger RNA, what the likely three dimensional structure of its protein product is. Also drug design softwares fall short of expectations even if the structures of drug targets are known.Addressing the above issues from a physico-chemical perspective, we have developed a novel semi-empirical model for whole genome analysis (*ChemGenome*) based on DNA energetics, an all atom energy based computational protocol for narrowing down the search space for locating tertiary structures of small globular proteins (*Bhageerath*) and a binding free energy based methodology for active site directed lead molecule design (*Sanjeevini*). The *ChemGenome* could distinguish genes from non-genes in 331 bacterial genomes and 20 eukaryotic genomes with > 90% accuracy. The start and stop site prediction accuracies of *Chemgenome* are either at par or exceed the current standards. *Bhageerath* could successfully bracket native-like structures to within 3 to 6 Å in the 10 lowest energy structures for 50 small alpha helical globular proteins. The *Sanjeevini* drug design protocol could sort drugs from non-drugs for a few drug targets helping in addressing both affinity and specificity issues in drug design. Progresses recorded in the areas of genome analysis, protein structure prediction and drug design and the software tools developed and made freely accessible at www.scfbio-iitd.res.in together with challenges and promises there of will be presented.

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A Chiral Dirhodium Tetracarboxylate Complex as NMR Auxiliary for Enantiodifferentiation of a Great Variety of Functional Groups

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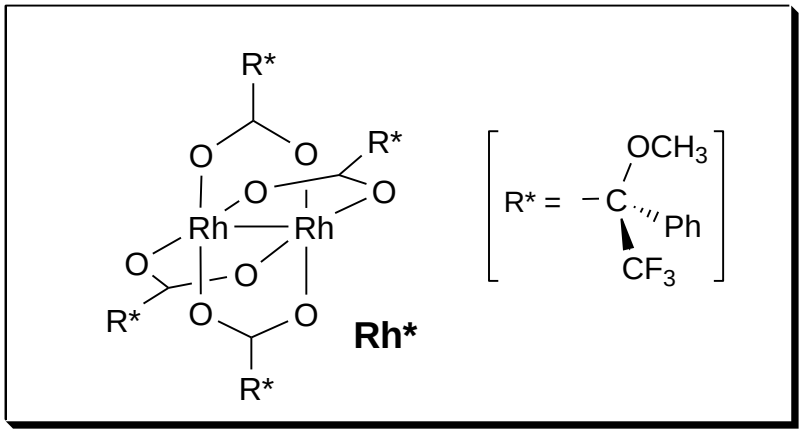
In the dirhodium method[1], *in-situ*-adducts between chiral ligand molecules and the enantiopure dirhodium complex $Rh^{(II)}_2[(R)\text{-}(+)\text{-MTPA}]_4$ (**Rh***, MTPA-H = methoxytrifluoromethylphenylacetic acid ≡ Mosher's acid; see structure above) are generated by dissolving equimolar amounts of both components in $CDCl_3$ und recording the ^1H and ^{13}C NMR spectra of the mixture. Ligand signals are dispersed by chiral discrimination within the diastereomeric adducts so that the enantiomeric ratio of the ligand can be determined easily.

This method is particularly useful for soft Lewis-base ligands where phosphorus, sulfur or selenium are the binding sites; chiral lanthanide shift reagents [2] generally fail with those ligands. Recently, we found that chiral discrimination of hard Lewis-acid bases is easy as well, although the donor property of oxygen is poor and complexation to **Rh*** is weak. This is of particular interest for ether compounds [3] where most other NMR auxiliaries fail, too [4].

The basic features of adduct formation (**Rh*** ← ligand) and various applications for soft and hard Lewis bases ligands will be demonstrated.



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Modulation of Functional Activity of Enzyme by Alterations in Structure and Interactions of Domains by Activating Ions

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Large proteins/enzymes consist of structural domains which have either close interactions or no interactions between them. For several of these enzymes there is a prerequisite of ions for their functional activity as in the absence of these ions no activity is observed. Our studies with several of these enzymes have demonstrated that the ions which act as activators for the functional activity in fact modulate either the cooperativity of the enzyme molecule or the conformation of the substrtae. These results are of significant importance as during in silico mining of lead compounds in drug discovery 3D enzyme structures are used.

Protecting Group Directed Ring-Closing Metathesis (RCM): The First Total Synthesis of Anti-Malarial Nonenolide

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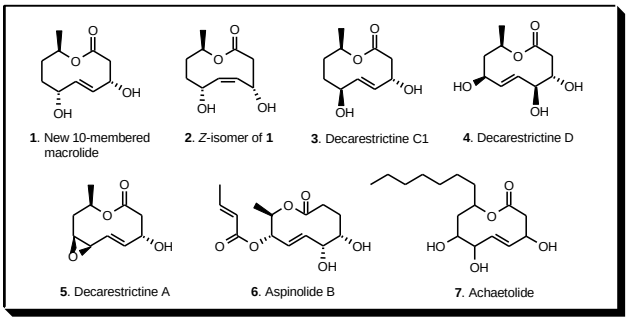
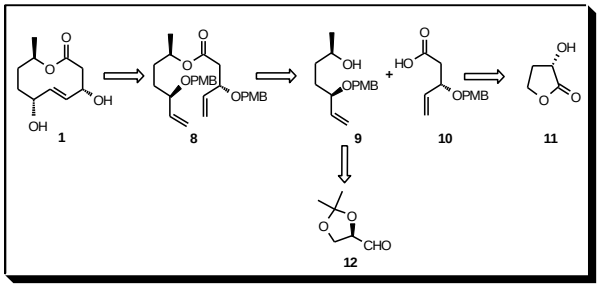
In recent years, secondary metabolites isolated from *Cordeceps militaris* have received attention due to their unique structures and specific biological activities. Cordycepins (3'-deoxyadenosine), with antifungal, antivirus, and antitumor activities, is one of selected secondary metabolites that have been previously isolated from *Cordyceps militaris*. Compound **1** was recently isolated as a white solid from *Cordyceps militaris BCC 2816*; the structure was elucidated and the stereochemistry confirmed by spectral data and X-ray crystallographic analysis [1].

As part of our ongoing programme on the synthesis of natural lactones with ring-closing metathesis (RCM) as key step, we have devised a stereoselective synthesis of nonenolide **1.** The retrosynthetic analysis is depicted in Scheme 1. The macrolactonization step relies on a RCM on a diolefinic ester. Strategic bond disconnection in ester **8** leads to chiral, nonracemic fragments **9** and **10** that could be derived from (*S*)-α-hydroxy-γ-butyrolactone (**11**) and 1,2-*O*-isopropylidene (D)-glyceraldehyde (**12**), respectively.



Some natural nonenolides with chiral centres on both sides of double bond



Retrosynthetic analysis

Despite its effectiveness in the synthesis of rings of all sizes, two factors still limit the scope of the RCM reaction: (a) control over E/Z stereochemistry of the double bond generated is difficult and not demonstrated: stereochemical control is probably of thermodynamic origin. (b) reports that describe the application of RCM to medium sized, particularly 10-membered rings, are still rare, especially when dense functionality close to the reaction center is involved. A dearth of reports on RCM reactions on substrates wherein chiral centers with protecting groups are present adjacent to both the reacting centers, prompted us to investigate the outcome of such RCM reactions with promise in the synthesis of nonenolides with chiral centers on both sides of the double bond.

Calculations on ruthenium metathesis have been instrumental in delineating a theoretical model that explains, at least qualitatively, the trends in E/Z product distribution.

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Structure Activity Relationship of a Novel Hematoregulatory Peptide

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Hematopoiesis is a lifelong cell renewal process regulated by a family of lineage specific hematopoietic growth factors. Several hematopoietic growth factors such as G-CSF, GM-CSF, and M-CSF have been clinically evaluated for enhancement of host defense in normal and immunocompromised patients and for the treatment of infectious diseases. IN this presentation I will discuss the the structure-activity relationships of low molecular weight hematoregulatory peptides based on a nonapeptide (1, SK&F 107647). Like the macromolecular growth factors, these peptides modulate host defense. A molecular target for this class of compounds has not yet been identified. However, the structure-activity relationships established by this study implicate a very specific molecular recognition event that is pivotal for the biological activities of these peptides.

Serendipitous Discovery of Dual Direct Anticoagulants

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Several anticoagulants including heparin, coumarin, hirudin and argatroban are used in the clinic to treat antithrombotic disorders. Yet, current anticoagulation therapy suffers from numerous limitations and adverse effects. To arrive at better anticoagulants, we began a program few years ago on designing inhibitors of thrombin, a key proteinase of the coagulation cascade. We began by targeting the indirect pathway of thrombin inhibition, which physiologically requires a sulfated polymeric chain of some 16 residues to drive the inhibition process. Following initial studies, we designed sulfated dehydropolymers (DHPs) of 4- hydroxycinnamic acids that exhibited only 10 – 20-fold lower potency than enoxaparin, the clinically used low molecular weight heparin, in ex vivo experiments. Recent work shows that our designed sulfated DHPs prefer to utilize the direct pathway of thrombin inhibition rather than the indirect pathway for which these were designed. Further, the new molecules selectively inhibit thrombin and factor Xa over factor IXa and factor VIIa. Competitive binding studies reveal that the sulfated DHPs bind in or near anion-binding exosite II of thrombin. Mechanistically, these molecules inhibit thrombin through an allosteric disruption of the catalytic apparatus. Overall, sulfated DHPs form a unique class of potent dual direct inhibitors of coagulation because of their novel mechanism of inhibition and their distinct structure, which is unlike any known anticoagulant.

Phytochemicals in Present Scenario

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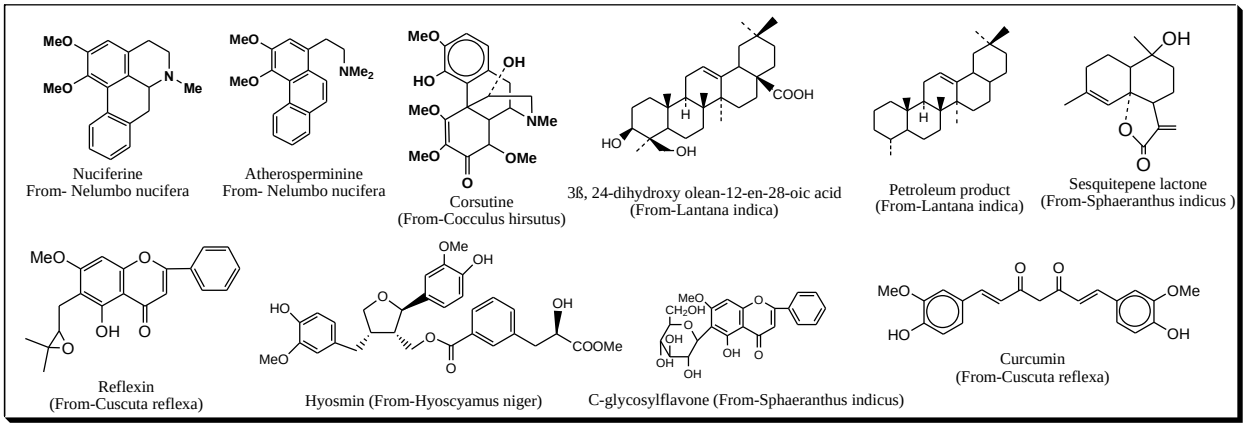
The organic chemistry is nothing but the study of derivatives of small molecule methane which itself is a natural product. Authors focus here in the present context on phytochemicals isolated directly from plants. The use of plants as medicine is as old as human civilization. The earliest record use of medicinal plant for prevention of disease and cure of ailments can be traced in "Rigveda" perhaves the oldest repository human knowledge having been written between 4500 and 1600 BC. India in this regard has unique position in world where a number of traditional systems of medicine e.g. Ayurveda, Yoga &Naturopathy, Unani, Siddha and Homoeopathy are practiced and utilized in the total health care system of the country and all these systems are predominantly dependent upon medicinal plants. The earliest recorded use of a medicinal plant, quite popular a Chinese drug-Ma Huang-a species of ephedra over 5000 years. It may be interesting to note that figures from more than one billion prescriptions dispensed from pharmacies in the United States during 1967 show that about 243 million, or about 23%, of all prescriptions contained one or more products of plant origin. This percentage of plant drugs is probably much the same even today. Some of led compound from plant origin like taxol**,** penicillins, brevetoxin, thromboxane, coniine, thujone, cholesterol, adrenaline, atropine, hordenine, dopamine, hyoscine, cocaine, morphine, reserpine, emetine, papaverine, etc. have surprisingly fascinated the medical world [1]. Following are phytochemicals discovered by author from some important medicinal plants [2-8].



Future prospects

With the increasing loss of much of the world's forests, the potentially remarkable properties of plant constituents not yet discovered and threatened with extinction could be forever lost. If this occurs and reluctancy with phytochemical research prevails, many future drugs and other useful plant products would remain undiscovered and the often surprising chemical structures produced by the genetic diversity of plants might not be envisioned by future chemists. Need of hours is to preserve the plant diversity through bioengineering to monitor higher levels'metabolites to incorporate enough phytochemicals with our food.

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Non-covalent Synthesis with Functional Porphyrins, Calix[4]pyrroles and Related Functional Molecules

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Non-covalent synthesis a powerful method for the construction of various supramolecular structures by simultaneous assembly of preorganized functional molecules. There is continuous interest in designing of preorganized functional molecules and their uses in development of complex structures by non-covalent synthesis [1,2]. Porphyrins, calix[4]pyrroles and related functional molecules are important building blocks due to their easy functionalization at meso and β-pyrrolic positions of the above macrocycles. The non-covalent synthesis is less common than covalent synthesis of complex molecules. One possible way to overcome the limitation inherent in non-covalent synthesis is the use of convent synthesis to develop the functional molecules which may be converted to complex structures by non-covalent synthesis in milder conditions. The design and synthesis of covalent functional porphyrins and related functional molecules have been used for the synthesis of complex structures to mimic the charge separation, electron transfer, signal and energy transfer in biological systems.

Selected functional porphyrins, calix[4]pyrroles and related molecules have been synthesized by modifications of known procedures in milder conditions such as use of ionic liquids and other green synthetic methods. The porphyrins and related molecules have been used to develop complex structures by non-covalent syntheses in non-polar solvents to understand the biological processes and the development of newer materials. The size exclusion chromatography, recent NMR techniques, electron-spray ionization mass spectroscopy and other modern techniques have been used to confirm the complex structures formed by non-covalent synthesis.

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Targeting HIV-1 RNA with Peptide and Non-peptide Conjugates of Polyamide Nucleic Acids

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The two most commonly used anti-HIV-1 drugs target two key enzymes, protease and reverse transcriptase. These drugs have been great success so far in reducing the viral load in AIDS patients. However emergence of resistant strains to these two drugs has made the management of this disease more difficult. Drug resistant strains are usually recognized when the viral load does not fall even after the administration of the combination therapies. Alternative strategies to establish a stable drug line to combat the HIV-1 menace is the thrust of the ongoing antiviral research. The major plunge in this direction has been the accessory and regulatory proteins of HIV-1 as the new antiviral drug targets. However, the biggest drawback with these targets is that they are not sufficiently explored and their role inside the cell and the mode of action in virus production and maturation is not well understood at the molecular level. Another major strategy, extensively worked upon, to inhibit the HIV-1 replication is by targeting regulatory conserved and nonmutable sequences on the viral genome using antisense technology. In the last one decade with the advancement in the field of antisense technology and gene silencing polyamide nucleic acid (PNA) has emerged as a very potential antisense therapeutic molecule to inhibit specific cellular messages. The potential of sequence specific PNAs conjugated with cell penetrating peptides (CPP) or with RNA cleaving neamine moiety of neomycin, has been demonstrated as effective antiviral and virucidal agents. Using this technology we have successfully targeted transactivating response (TAR) element, conserved primer binding site (PBS) and dimerization site (DIS) on the HIV-1 RNA genome to block the viral replication and infection. The anti-HIV-1 PNA-CPP conjugates are not only antiviral but are also strong virucidal agents that has potential for external topical formulations designed to block HIV-1 infection or as a prophylactic agent for inactivation of HIV-1 in the circulating plasma prior to attachment and entry.

Chemoenzymatic Approaches to Studying Carbohydrate-Recognizing Proteins

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The important roles of carbohydrates have been increasingly recognized. Compared to monosaccharides of five- or six- carbons, sialic acids containing a 9-carbon backbone are much more complex. Structural modifications on sialic acid residues further increase the complexity of sialic acid-containing structures. Currently, more than 50 sialic acid structures have been found in nature. These include three basic forms: *N*-acetylneuraminic acid (Neu5Ac), *N*-glycolylneuraminic acid (Neu5Gc), deaminoneuraminc acid (KDN), and their modified forms with substitutions, such as 8-*O*-methylation, 8-*O*-sulfation, 9-*O*-lactylation, 9-*O*-phosphorylation and single or multiple *O*-acetylation at C-4, C-5, C-7, C-8, and/or C-9 positions [1]. Most of these naturally existing modifications are post-glycosylational modifications [2].

Sialic acids have been predominantly found as the terminal carbohydrate units on glycoproteins and glycolipids of vertebrates or as components of capsular polysaccharides and lipooligosaccharides of pathogenic bacteria. As the frontline encountered by other molecules, sialic acids play pivotal roles in many physiologically and pathologically important processes, including cellular recognition and communication, bacterial and viral infection, and tumor metastasis, etc.[1] In order to understand the structure-function relationship of sialic acid modifications, my laboratory has established and developed highly efficient chemoenzymatic methods to obtain structurally defined homogenous sialic acid-containing structures with naturally occurring sialic acid modifications which are difficult to be obtained either by isolation or by chemical synthesis. Their non-natural derivatives can also be obtained similarly [3]. These compounds have been used as invaluable probes for studying the important biological roles of sialosides and sialic acid-recognizing proteins [4].

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Natural and Unnatural Heterocycles from Epoxides and Allylanions

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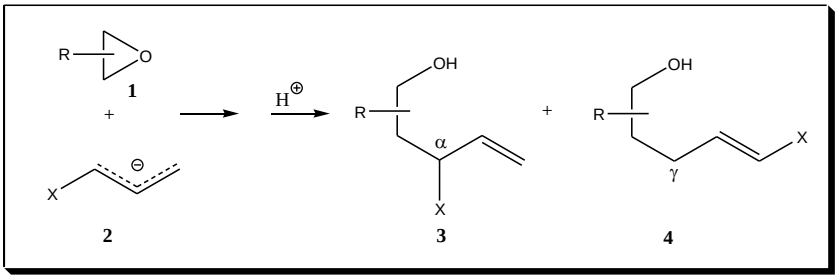
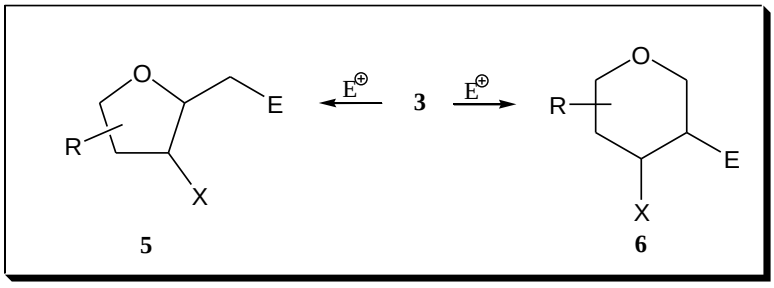
Ring opening of epoxides **1** by nucleophiles is a synthetically very useful reaction. If heterosubstituted allyl anions **2** [X=SiR_3, $P(O)R_2$, SPh] are employed as nucleophiles, regioisomers are possible, but the α/γ ratio can be controlled at least to some extent, e.g. making 4-alkenols **3** the main or exclusive products.

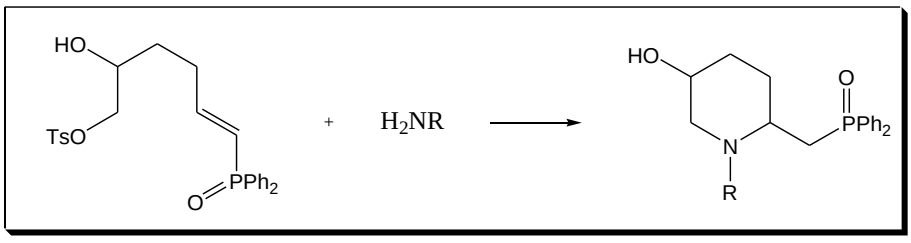


The action of electrophiles on alcohols **3** leads to Markovnikov-controlled formation of functionalised tetrahydrofurans **5**, but the presence of additional substitutents may give rise to pyrans **6**.



The utility of the approach is demonstrated by asymmetric syntheses of the monoterpene artemeseol, of S-(+)-parasorbic acid, of the aminosugar desosamine, and of the antibiotic malyngolide.

Moreover, **3** or **4** can serve as building blocks in pyrrolidine or piperidine synthesis. The ring nitrogen is introduced by use of amino-functionalized epoxides **1** ($R=R^1CHNHPG$) or by Michael-type addition of amines to alkenols **4** [$X=P(O)R_2$], e.g.:



Targets include the antifungal antibiotic (+)-preussin and the piperidine alkaloid pseudoconhydrine.

Recent Trends in Diabetes Therapy: The Mounting Challenges

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Diabetes Mellitus has become one of the leading cause of death in the modern times. The sedentary life style, calorie rich food and lack of means of burning the calorie intake have been responsible for the increasing incidence of this slow killer disease. It is a multifactorial disease, including obesity and cardiovascular diseases and involves a combination of genetic and environmental factors. India has become the diabetes capital of the world with a large number of undiagnosed cases. Although a number of drugs working through different mechanisms have been in use starting from exogenous insulin administration, sulfonylurea ureas, metformin, thiazolidine diones etc…, none of them is alone most effective due to the complexity of the disease involving defects in different targets. A number of drug candidates have failed in advanced clinical stages and many more in the clinical trials. Safety has been an issue and concern in the development of new drugs. Until the clarity on the cause of side effects in human becomes clear, the challenge of drug development continues. Such challenges in the new drug discovery and development will be discussed.

Polymeric Nanoparticles as Novel Non-Viral Gene Carriers

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With the development of genomic and proteomic technologies, the prospect for gene therapy has advanced rapidly. In the last few years, gene therapy has emerged as one of the great scientific challenges in modern medicine. Early clinical trails using viral vectors indicated significant problems primarily as they demonstrated short-lived transgene expression, an inability to persist in host cells and toxicity. These studies highlighted the need to improve vector design if the adverse effects associated with viral vectors are to be avoided. To achieve successful gene therapy, development of proper gene delivery systems could be one of the most challenging tasks. The innumerable reports on the development of new non-viral vectors indicate that gene delivery to cells in a safe and efficient manner remains an intangible end. Several cationic lipids, nanoparticles and dendrimers have been exploited extensively in the production of non-viral vectors. Efficient gene therapy requires vehicles to be engineered that can (i) protect DNA from degradation, (ii) exhibit prolonged circulation times, (iii) efficiently bind to target cells, and (iv) deliver DNA to the nucleus. Although non-viral vectors lead to significant improvements in cellular penetration, protection, and transfection over naked DNA, they have not yet achieved consistent transfection suitable for practical applications. Among all the cationic polymers, branched PEI is the most extensively studied polymer because of its efficient capability to condense DNA and the resulting PEI/DNA complex can act as proton sponge, thus enabling DNA delivery into cytoplasm by rupturing endosomes. Branched PEI contains primary, secondary and tertiary amines in a ratio of 1:2:1 with pK_a values spanning around the physiological pH, providing remarkable buffering capacity. The primary amines are mainly responsible for high degree of DNA binding, but contribute maximum toxicity during transfection, while the secondary and tertiary amino groups provide good buffering capacity to the system. In order to improve its transfection efficiency as well as cell viability, our group has developed a number of transfection reagents based on cationic polymers (PEI and PAA) in the form of nanoparticles as well as nanocomposites. The resulting systems were demonstrated successfully as efficient carriers of nucleic acids (pDNA and siRNA) in a wide range of cell lines even without the addition of lysosomotropic agent. Cell viability was also scored ~90-100%.

Discovering New Asymmetric Catalyses: Chiral Tertiary Alcohols

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Among asymmetric synthesis, the catalytic version of this process has received a great attention in the last few years due to the possibility of preparing chiral molecules from prochiral starting materials by using a chiral catalyst [1]. In general the catalyst belongs to one of the following series: (a) metal-containing catalyst, (b) organocatalyst, and (a) biocatalyst (enzymes or microorganisms). Considering the first group, usually the active species consists in a metal component and a chiral ligand, which gives the anisotropic information necessary in order to get the corresponding induction. Concerning different methodologies involving carbon-carbon bond formation [2], one of the most studied has been the enantioselective addition of an organometallic reagent to a prochiral carbonyl compound [3]. However, this process is especially difficult when ketones are used as the electrophilic component [4], this reaction being of great interest because it could be a way to generate chiral compounds bearing quaternary stereocenters [5]. In this presentation, the last findings in the enantioselective addition of dialkylzinc reagents to proquiral ketones using not only first generation (1), but also second (2) an third generation (3) ligands will be shown (Chart 1) [6]. Especially in the case of the last ligands 3, they are interesting from a practical point of view due the possibility of recovering and reusing them many times.

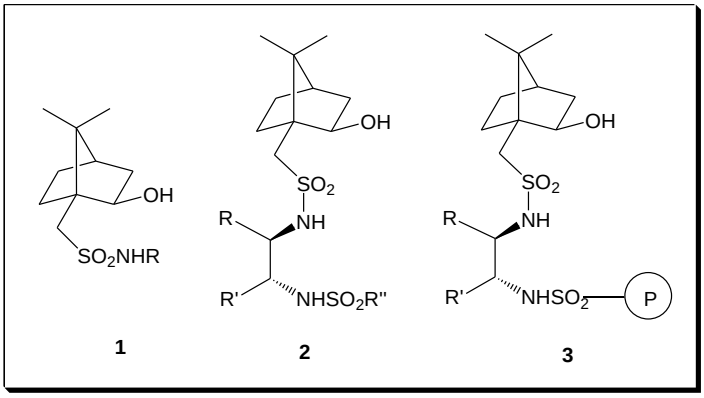

Chart 1

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Interesting Pyrolytic Studies of Some Heterocyclic Compounds

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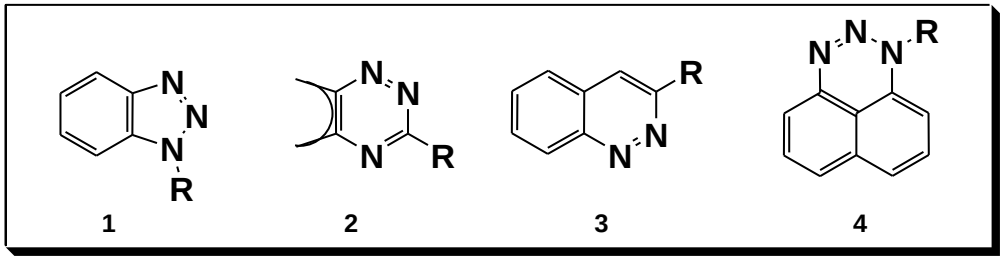
Gas-phase thermolysis using either flash vacuum pyrolysis or static pyrolysis of heterocyclic nitrogen compounds gave direct access to many interesting valuable products which are otherwise difficult to obtain or which needs several synthetic steps.

In this lecture our results on the pyrolytic behavior of benzotriazole 1, 1,2,4-triazine 2, cinnolines 3 and naphthotriazine 4 derivatives will be discussed. Moreover, the mechanism of some of these pyrolytic reactions will be explained.



Scheme 1

Acknowledgement: The support of the University of Kuwait received through research grant no. SC04/05 and the facilities of ANALAB and SAF (grants no. GS01/01, GS01/03, GS03/01) are gratefully acknowledged.

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Design and Development of Drugs to Treat Rare Vancomycin Resistant Microbial Pathogens

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Due to intensive and constant exposure of antibiotics to bacteria, the spread of antibiotic-resistant bacteria occurs much more rapidly in hospitals than in the outside community. An approximate 10% patients requiring long and frequent hospital stay due to surgery or organ replacement or due to opportunistic diseases, are vulnerable to developing resistance even to antibiotic of last resort such as Vancomycin, compared with normal population and lead 1% of this population to death.

Successful introduction of a combination therapy of clavulanate, a β-lactamase inhibitor and amoxicillin antibiotic for the treatment of infections caused by gram-positive cocci prompted us to investigate a new approach involving the shutting off the enzymes which are responsible for resistance and thus reinstating Vancomycin antibiotic sensitivity.

The Vancomycin resistant enterococci (VRE) are characterized by the presence of a zinc binding dipeptidase, namely VanX that removes the cell wall precursor molecule DAla-DAla peptide which is essential for the cell wall synthesis of Vancomycin sensitivite bacteria. Preliminary studies on the synthesis of novel class of VanX inhibitors derived from molecular modeling and enzyme assay suitable for high throughput screening will be presented.

Nitrogen Heterocycles as Important Tools in Drug Research

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Heterocyclic compounds are widely distributed in nature and are essential to life; they play a vital role in the metabolism of all living cells. Since many drugs contain the nitrogen heterocylic component and nitogen heterocycles posses a high order of structural diversity. We have concentrated our effort in synthesis of novel heterocycles by using solid support, solution phase and microwave assisted synthesis. Several synthesized compounds have shown interesting antiparasitic activity.

Solid supported syntheses and solution phase synthesis of novel Heterocycles and their combinatorial chemistry will be discussed.

Greener Alternatives to Expedient Synthesis of Heterocycles and Nanomaterials

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A brief account of reactions involving microwave (MW) exposure of neat reactants or catalyzed by mineral support surfaces, such as alumina, silica, clay, or their 'doped' versions, for the rapid one-pot assembly of heterocyclic compounds [1] from in situ generated reactive intermediates via enamines [2] or using hypervalent iodine reagents [3] will be described that can be adapted for parallel synthesis in multicomponent reactions (Biginelli and Ugi reactions) [4]. The eco-friendly nucleophilic substitution chemistry in water [5] can be manipulated using microwaves to generate cyclic amines via double N-alkylation of primary amines or hydrazines by dihalides or tosylates [6]. Greener protocols for the synthesis of pharmaceutically active heterocycles namely N-aryl azacycloalkanes, isoindoles, and dihydropyrazoles [6], 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, 1,3-dioxanes [7a], pyrazoles, hydrazones [7b] and 3,4-dihydropyrimidin-2(1H)-ones [7c], catalyzed by basic water or polystyrene sulfonic acid (PSSA) in aqueous media or solid supported Nafion®NR50, or (P_4S_{10}/Al_2O_3) under solvent-free conditions will be described.

Aqueous preparation of nanoparticles using vitamins B_1 and B_2 [8a], which can function both as reducing and capping agents and the bulk and shape-controlled synthesis of noble nanostructures via microwave (MW)-assisted spontaneous reduction of noble metal salts using α-D-glucose, sucrose, and maltose [8b] will be presented. A general MW method has been developed that accomplishes the cross-linking reaction of poly (vinyl alcohol) (PVA) with metallic systems such as Pt, Cu, and In; bimetallic systems, namely Pt-In, Ag-Pt, Pt-Fe, Cu-Pd, Pt-Pd and Pd-Fe [9a]; and SWNT, MWNT, and C-60 [9b]. The strategy is extended to the formation of biodegradable carboxymethyl cellulose (CMC) composite films with noble nanometals [10]; such metal decoration and alignment of carbon nanotubes in CMC is possible using MW approach [11] which also enables the shape-controlled bulk synthesis of Ag and Fe nanorods in poly (ethylene glycol) [12]. The application of nano-sized MgO is demonstrated in the green synthesis of 2-amino-2-chromene derivatives in aqueous PEG [13].

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Natural Products as Source of New Chemical Entities: Experience at Nicholas Piramal Research Centre

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Natural products have remained the most consistent and rewarding source of diverse structures exhibiting remarkable biological activities and pharmacological profiles [1,2]. Historically natural products have provided many truly novel, life saving and "first-in-class" drugs for untreatable diseases (e.g. 60% of anti-cancer and 75% of anti-infective drugs are natural products derived). Furthermore, a number of drugs in current use in other therapeutic areas are either derived or inspired by natural products (e.g. opiates and statins). Besides being drugs, many privileged natural products (e.g. cytochalasins, monensin, brefeldin, rapamycin, FK-506, forskolin etc) enabled fundamental advances in cell biology and immunology, and provided inspiration to synthetic organic chemistry. Among the primary sources for the bioactive natural products (medicinal plants, fungi and bacteria), marine biology has provided most remarkable, structurally complex and bioactive substances [3,4]. However much of the marine flora, fauna and associated microbial diversity remain unexplored with great potential for novel drug discovery.

We at Nicholas Piramal Research Centre (NPRC) have integrated the bioactivity-guided isolation of natural products in our drug discovery and medicinal chemistry programs spanning all the therapeutic areas of our interest (cancer, diabetes, inflammation and infection). Our approach, strategy and results in the exciting field of natural products drug discovery will be discussed in this presentation.

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The Advances and development in Nitric Oxide Donors

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The discovery of the physiological and pathophysiological roles of nitric oxide (NO) during the 1980s was one of the most surprising and exciting developments in biological research. NO exhibits a broad range of biological activities. Cellular NO is almost exclusively generated *via* the oxidation of L-arginine, which is catalyzed by nitric oxide synthetases (NOS). Under physiological conditions, NO directly activates soluble guanylate cyclase (sGC) to transform guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP), followed by kinase-mediated signal transduction. The endogenous formation of NO plays a key role in many bioregulatory activities, including smooth muscle relaxation, inhibition of platelet aggregation, neurotransmission, immune stimulation and inflammation. Due to the instability and inconvenience of handling aqueous solutions of authentic NO, there is increasing interest in using compounds capable of generating NO. These compounds are called NO donors, or NO releasing agents. Glyceryl trinitrate (GTN) is one of the most well known NO donors and use of GTN for medicinal purposes dates back more than 150 years.

Apart from organic nitrates, many other chemicals species, with variety of structures can be transformed into NO or can release NO in an *in vitro* or *in vivo* system. In last couple of decades, much attention has been devoted to the development of 'new NO donors' which have offered several advantages over the existing NO donors, such as ability to spontaneously release NO or controlled release or specific tissue targeted release. Recent approach in NO donors drug research is, coupling of NO donor moieties with currently available therapeutic drugs, in order to overcome or reduce the drug toxicity as well as provide additional NO-dependant biological activity. The advances and development in Nitric oxide donors and our work towards development of substituted furoxans and benzofuraoxans as anti-anginal agents will be presented.

Chirality, Asymmetric Induction and Biological Activity of Chiral and Achiral 1, 4-Naphthoquinone Derivatives as Potential Cytotoxic and Antifungal Agents

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The quinone group forms the basis of biological activity of a number of clinical and experimental drugs associated with antitumor and antifungal activity. The clinical significance of this class of compounds has stimulated the synthesis and biological evaluation of new agents retaining the core quinone moiety [1,4]. The diverse biological effects caused by incorporation of hetero atoms in heterocyclic ring retaining the core chromophore shall be discussed in detail.

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Novel Selective Biocatalysis in Nucleoside Chemistry

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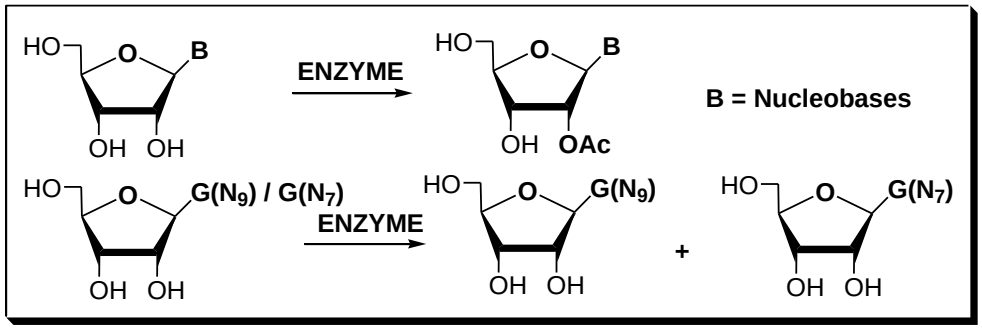
The intrinsic problem in the synthesis of nucleoside derivatives and oligonucleotides involving them is the selective manipulation of different hydroxyl and amino functions present in the compound under mild reaction condition. We have developed an efficient synthesis of different natural and unnatural nucleosides under a research program involving synthesis of modified nucleosides as potential antiviral agents and as oligonucleotide monomers using lipases in one of the crucial steps. Detailed results will be presented in the meeting.



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Perspectives in Organic Sulfur Chemistry: Synthesis of Heterocycles from Ketene Dithioacetals

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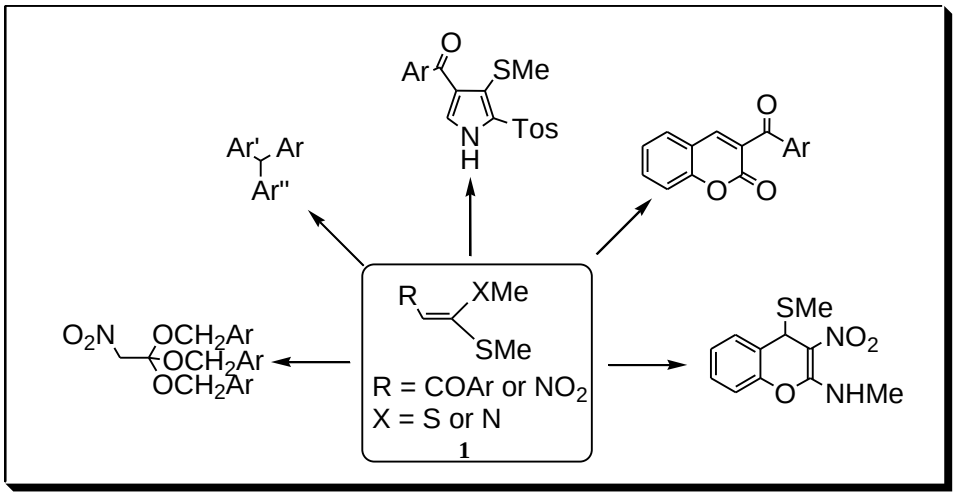
The polarized ketene acetal functional group represented by **1** is well known in synthetic organic sulfur chemistry as a two-carbon push-pull system. While the aroyl or nitro groups in **1** act as powerful electron-withdrawing centers, the two alkylated sulfurs readily donate lone-pair of electrons to make the entire atomic framework highly polarized. Furthermore, the α,β-unsaturated aroyl / nitro groups behave as excellent Michael acceptors; subsequent to the attack of a nucleophile at the β-carbon, one of the alkylsulfanyl group leaves to regenerate the olefinic double bond. Owing to popularity of polarized ketene dithioacetals as a two-carbon synthons, many *S,S*-dialkylated derivatives have been synthesized and have been employed for further cyclization towards the synthesis of heterocyclic derivatives. We have transformed α-oxoketene dithioacetals (OKDTAs) and nitroketene dithioacetals (NKDTAs) into combinatorial libraries of coumarins, chromenes, pyrroles, thiophenes, triarylmethanes, orthoesters etc. by condensing with bifunctional molecules. Details of the studies will be presented in the symposium.



Scheme 1

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Synthesis and Biological Activities of Functionalized 2-(nitroaryl) 5-substituted-1,3,4-thiadiazole Derivatives

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Nitroheterocyclic compounds such as nitroimidazoles, nitrofurans and nitrothiophenes are being extensively used in therapy against amoebic and anaerobic infections. Metronidazole and other nitroheterocyclic drugs such as tinidazole and furazolidone have been used in treatment regimens for *H. pylori* infection with varying degrees of success. Moreover, the antimicrobial property of 1,3,4-thiadiazole derivatives is well documented and their attachment with other heterocycles often ameliorates the bioresponses depending on the type of substitutent and position of attachment. In view of the antimicrobial property of the above pharmacophores, it was envisaged that the combined effect of both nitroaryl and 1,3,4-thiadiazole entities would result in increased antimicrobial activity. Thus we have synthesized and screened a large number of 2-(nitroaryl)-1,3,4-thiadiazoles against clinical isolates of *H. pylori*, which several of them exhibited very potent anti-*H. pylori* activity. Various 5-substituted-2-(nitroaryl)-1,3,4-thiadiazoles prepared in our laboratory also exhibit a wide spectrum of antibacterial activity. Extending the research in this area, we have synthesized the derivatives which contain a quinolone molecule at 5-position of 1,3,4-thiadiazole ring. In continuation of our work on bioactive 2-(nitroaryl)-1,3,4-thiadiazoles, strong antituberculosis effects of 5-substituted-2-(nitroaryl)-1,3,4-thiadiazoles are also reported by us.

Furthermore, in view of antiprotosoal activity of 1,3,4-thiadiazoles, we have designed and synthesized certain 2-(nitroaryl)-1,3,4-thiadiazoles with leishmanicidal activity. Moreover, the potent antitrypanosomal activity of megazole, a nitroimidazolylthiadiazole, switched our search to new, not reported in the literature, 2-(nitroaryl)-5-(substituted piperazinyl)-1,3,4-thiadiazoles; which several of them showed strong trypanosocidal activity with relatively low toxicity.

Anticancer Drug Development, using Multiple Targets Based Strategy, in PI3K/Akt-mTOR-HIF-1 Pathway

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The phosphatidylinositol-3-kinase/Akt (PI3K/Akt) and mTOR signaling pathway –also known as the survival or anti-apoptotic pathway– plays an important role in controlling cell growth, proliferation and survival. Whatever the mechanism, the prevalence of PI3K/Akt-mTOR signaling abnormalities in human cancer cells has suggested the potential use of PI3K/Akt-mTOR and HIF-1 pathway modulators as novel targeted anticancer therapeutic agents. This presentation will detail about our design and synthesis of furoquinoline based novel inhibitors of multiple targets in PI3K/Akt-mTOR-HIF-1 pathway. In particular, one of the compounds in addition to PI3K/Akt-mTOR inhibitory potency, it has shown potent inhibition of hypoxia-induced accumulation of HIF-1α protein in glioblastoma U251-HRE cell line. The inhibitory activities of said compound was confirmed by Western blot analysis using human non-small cell lung carcinoma H-460 cell line (PI3K & mTOR) and U251-HRE cell line (HIF-1α).

Challenges in the Discovery and Development of New Molecules for Pulmonary Delivery

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The origins of inhalation therapy can be traced back to early civilizations. The direct delivery of drugs by inhalation route grew rapidly only in the second half of twentieth century as a result of availability of effective asthma drugs in a convenient, portable delivery systems. Subsequently there was an improvement in the understanding of pulmonary route for systemic delivery of small molecule drugs and biologicals. The large epithelial surface area, high organ vascularisation, the thin nature of the alveolar epithelium and the immense capacity for solute exchange offers an ideal route of delivery of drugs. New delivery systems with efficiency and reproducibility to match the high cost of therapeutic constraints of biologicals are currently in late stage clinical trials. Even small molecules previously administered by other routes are tested via inhalation route. The objectives of pulmonary delivery can be either the administration of the drug for local or for systemic action. Of greater importance is the use of this route for biologicals and small molecules undergoing significant first pass and/or producing undesirable pharmacological effects by conventional routes. Development of a drug to be administered primarily by pulmonary route depends on various factors like, the therapeutic property of the drug, degree of onset and duration of action required, stability of the drug and formulation, suitable delivery system and cost factors. Extensive study of the 'particular' properties that determine efficient drug delivery, use of alternate preparations like liposomes and employing suitable pulmonary delivery systems these problems can be efficiently addressed. The idea of considering a drug molecule developed in the clinical trials using conventional routes for optimized pulmonary delivery is changing to a suitable prior consideration of pulmonary delivery in case of proteins and peptide molecules. The presentation will cover challenges during lead optimization (with respect to physicochemical properties of molecule, ADME, safety and interspecies scaling) and also during early preclinical and clinical development.

Chemistry Methodologies and How Technology can Help Improve Productivity in The 21st Century!"

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R & D Chemistry is a challenging world in which to apply technologies and make structuralchanges. Over the last 20 years there has been significant pressure to increase the rate atwhich new drugs are discovered and developed. Chemists in companies in the USA, Europeand Japan have attacked this problem with a range of different approaches. Some havebeen more successful than others, but all have found both the technologies and structuralissues challenging.A lot has been learnt, and the current methods are significant improvements as a result.However there are still many chemists who have not changed significantly how they work.Many of these approaches taken have not been appropriate for all chemists to apply.A brief history of approaches taken and their strengths and weaknesses are discussed. Then a look is taken at the current technologies and approaches. Finally a look is taken at somekey emerging technologies and how they might affect chemistry into the 21st century including how to integrate Chemistry and Biology somewhat better.

New Synthetic Platforms for Nucleoside Modification: Mechanisms to Structural Diversity

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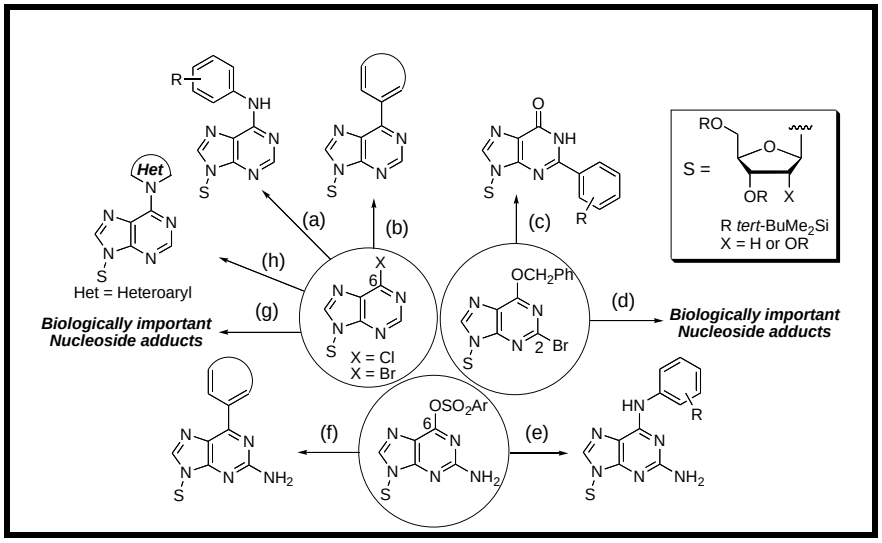
Palladium-catalyzed C-N and C-C bond-forming reactions are state-of-the-art techniques in contemporary organic synthesis [1,2]. We have shown that such reactions can be conducted on the chemically more complex and relatively sensitive nucleoside substrates, leading to new structural paradigms [3,4]. A summary of some of our achievements in this area are displayed in Scheme 1. This talk will focus on selected aspects of palladium-catalyzed reactions of nucleosides as well as our newer developments of reactive nucleoside derivatives for uncatalyzed reactions. Both avenues have provided novel platforms for nucleoside modification as well as the possibility for developing structurally diverse nucleoside analogues.



Scheme 1

References:

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Brugia malayi: Hexokinase Cloning and Characterization

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Understanding the molecular basis of parasitism, particularly linked to human diseases is one of the most important frontiers in biology. It is difficult to analyze the functions of nematode genes with any of the genetic methods used so effectively for many multicellular model organisms and unicellular parasites. Though significant progress has been made in the treatment and control strategies of parasitic infections, these diseases still continue to be a formidable problem due to lack of definite action on parasites. Since the nematodes depend mainly on Glycolysis for their energy metabolism, hexokinase represents an important putative target for antihelmenthic development. The hexokinase of human filarial parasite *Brugia malayi* was cloned and characterized. The parasitic enzyme showed significant difference as compared to host enzyme. These differences can be exploited for designing of specific inhibitors against filarial parasites.

Synthesis of Novel Tetrahydroquinoline and Pyrimidine Heterocycles and Evaluation of their Antifungal Properties

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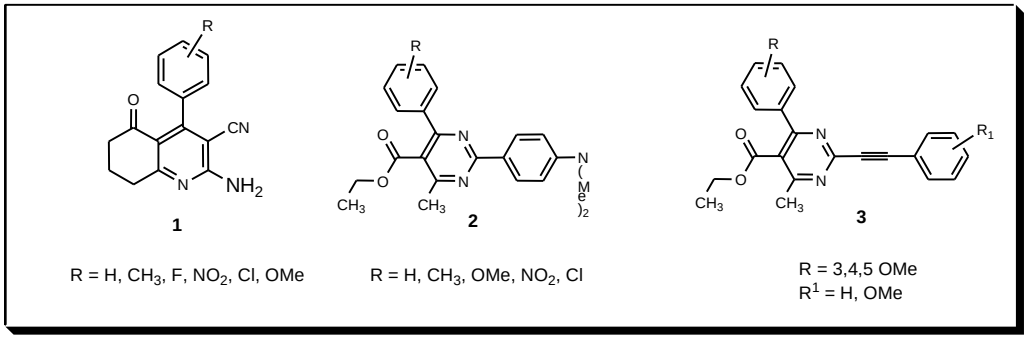
The commercially available antifungal drug Amphotericin-B remains the standard therapy for life-threatening mycoses, however this drug is associated with significant toxicity, including fever, headache, nausea and vomiting, and dose-limiting nephrotoxicity. Also the recent studies have documented resistance of *Candida* species to Fluconazole and other azole and triazole drugs, which have been used widely. A potential approach to overcome this resistance problem is to design new and innovative agents with a completely different mode of action so that no cross-resistance with the present therapeuticals can occur.

Among various nitrogen heterocycles, derivatives of azole such as imidazole and triazole are proved to be clinically potent and useful antifungal agents. However pyrimidine and tetrahydroquinoline derivative have not been extensively exploited as antifungal agents.

In the present work, a series of 2-amino-5-oxo-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile and various analogues **1** have been synthesized in excellent isolated yields starting from various arylidenemalononitrile and 3-amino-2-cyclohexen-1-one in 1-propanol. Likewise tetrasubstituted pyrimidine **2** and **3** were synthesized by sequential functionalization of easily available Biginelli 3,4-Dihydropyrimidine-2(1*H*)-ones via dehydrogenation, chlorination followed by palladium catalyzed C-C coupling Suzuki/Sonogashira reaction. Their antifungal properties have been evaluated and a preliminary QSAR study has been attempted.



Impurities and Process Research

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Ahmedabad – 382 210, India

Formation and control of impurities (Impurity Profiling) is extremely important to establish the quality of Drug Substance and / or Drug Products in pharmaceutical industry. Impurities play a dominant role during drug discovery and development process, analytical method development and validation, polymorphism, chirality determinations, formulation development, stability studies, IPR strategies, marketing competitions and of cource, during ensuring efficacy and safety of Drug Products. Various types of Impurities eg, metallic (heavy and toxic), inorganic, organic, OVI's, polymeric etc and their role in regulatory affairs will be described. The fascinating science involved during impurity formation, their simulation, isolation and characterization, usually not discussed in our academic training, will be highlighted with practical examples.

Design and Development of Novel Inhibitors of Topoisomerase 2

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We are involved in the discovery of non-genotoxic chemotherapeutic agents for cancer intervention targeting certain vital cellular enzymes found abundantly in cancerous cells. To achieve this, we have concentrated our focus on small electrophilic molecules that have the potential to differentially alkylate cellular proteins. Our efforts have been considerably successful in terms of selective in-vitro anticancer potency and reduced murine toxicity. There is evidence that our compounds elicit their anticancer potential by alkylating thiol groups of vital cellular enzymes, thereby incapacitating them. One such sulfhydryl-rich enzyme is human topoisomerase 2 alpha (TOPO-2), a well established target in cancer chemotherapy. TOPO-2 is a nuclear enzyme responsible for the regulation of DNA topology in living cells. It is an important target of many antitumor drugs (e.g. doxorubicin, etoposide, mitoxantrone, m-ASMA). TOPO-2 inhibition can be achieved as a result of protein thiolation. The inhibition or poisoning of the catalytic activity of TOPO-2 has been reported to be due to the binding of the drug with the cystine residues of the enzyme, stabilizing the cleavable complex. This cleavable complex has been shown to be the critical cellular lesion responsible for apoptosis. Selective thiolation can be achieved by certain types of enones which exhibit a preference for electrophilic attack towards thiols, rather than amino or hydroxyl groups, due to the soft acid and soft base character of the enone and the thiol group, respectively. Therefore, it is anticipated that these types of compounds will not exhibit the mutagenic and carcinogenic side effects displayed by most alkylating agents. Although several catalytic inhibitors of TOPO-2 are being clinically used, the compounds being developed by us are structurally divergent from known inhibitors of TOPO-2 and therefore could be of value in treating drug-resistant tumors. Biological activity results obtained on several series of compounds will be presented at the meeting.

Homology Models in Structure Based Drug Design Approaches: Our Experiences in Membrane Proteins

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Membrane proteins form a large number of drug targets and more often than not that the X-ray crystallographic 3-D structures of them are elusive owing to the difficulty of their isolation, purification and crystallization. Therefore, for membrane proteins valuation and validation of homology modeling methods are essential. The current talk addresses the performance of a range of off-the-shelf tools for the protein modeling and their validation. In this lecture I would like to present a critical assessment of the performance of various homology modeling approaches, especially when applied to membrane proteins. Virtual screening approaches have been analyzed and their applicability with a protein target obtained through homology modeling is assessed by taking some examples. Finally, illustrative examples were taken where we employed protein modeling, virtual screening, quantitative structure activity relationships and docking approaches for the lead identification and optimization of selected proteins. The choosen targets are aromatase, p-type ATPases, G-protein coupled receptors and phosphodiesterases.

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Chemical Approaches in Glycobiology

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Polysaccharides constitute one of major classes of bio-macromolecules in living organisms. They are ubiquitous in nature and play crucial roles in a variety of important biological processes, such as embryotic development, signal transduction, mediation of cell-cell interaction and regulation of immune responses [1]. In contrast to the in-depth understanding of the molecular mechanisms of nucleic acid and protein biosynthesis, the pathway for the biosynthesis of polysaccharides, especially complex hetero-polysaccharides, is poorly understood.

A large number of complex hetero-polysaccharides are found on the bacterial cell surface, where they play an essential role in mediating microbe-host interactions, and are important for pathogenicity [2]. A biosynthetic model, termed "wzy-dependent" pathway, has been proposed based on genetic studies. The synthesis begins in the cytoplasmic side of the inner membrane with the addition of N-acetylhexoamine (GlcNAc or GalNAc) to the undecaprenyl phosphate lipid carrier. Additional sugar residues are added to the N-acetylhexoamine in a sequential manner to form a repeating unit by specific glycosyltransferases. The repeating units are then translocated by Wzx flippase to the periplasmic side, where they are linked by Wzy polymerase to generate nascent polysaccharide chain. The Wzz protein is essential for generating a preferred chain length distribution of polysaccharides. So far, this rough biosynthetic picture has never been biochemically characterized in vitro and the underlying molecular mechanism is rather speculative.

In the past several years, my laboratory has established and employed chemical approaches to dissect the molecular details of essential steps in the pathway. We have elucidated repeating unit assembly step by biochemically characterizing each glycosyltransferase and reconstituting the assembly in vitro [3]. The access of a series of repeating unit analogs through chemo-enzymatic synthesis has enabled us to probe the Wzy polymerization activity in a cell free system and start to investigate its detailed mechanism. Furthermore, using a combination of chemical and structural approach, we are beginning to uncover the chain length regulation exerted by Wzz protein [4].

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Design, Synthesis and Evaluation of PPARα/γ Dual Activators

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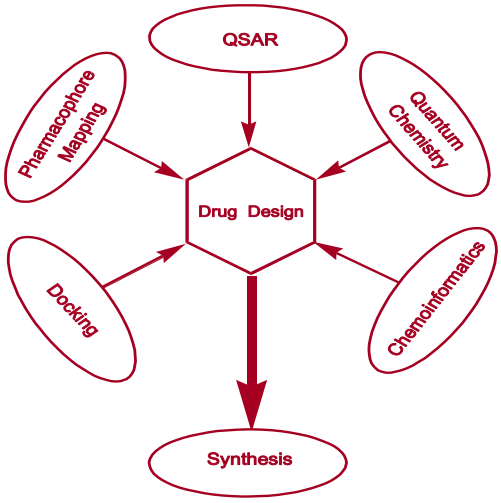
PPARα and PPARγ are well known targets of anti-triglyceridemic and anti-diabetic activities respectively and dual activators of these targets are being designed as synergistically acting agents. Designing the dual activators using 3D-QSAR, Pharmacophore mapping, Molecular docking, Virtual screening, Pharmacoinformatics methods is being practiced in our laboratory [1-20]. Understanding the chemistry, biochemistry and basics of drug action of the glitazone series of compounds and applying the basics to design new molecules is also the major activity in our institute. For example studies on the rapid racemization, sulfur oxidation, of rosiglitazone, pioglitazone was taken up at our laboratory using quantum chemical methods [12]. 3D QSAR methods have been employed to design [10] several new leads. The designed molecules have been synthesized and biologically evaluated [3]. The pharmacophoric features of metformin and other related drugs have been explored [7,9]. The design of GSK3 inhibitors also was taken up [4,5]. The chemistry and biochemistry of several of the anti-diabetic agents was explored using quantum chemical methods [1,6,8,11,13,14-20]. The results of computer aided design, synthesis and biological evaluation of PPARγ activators will be presented in this lecture.



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Activated aziridines and Azetidines: Synthetic and Biological Perspectives

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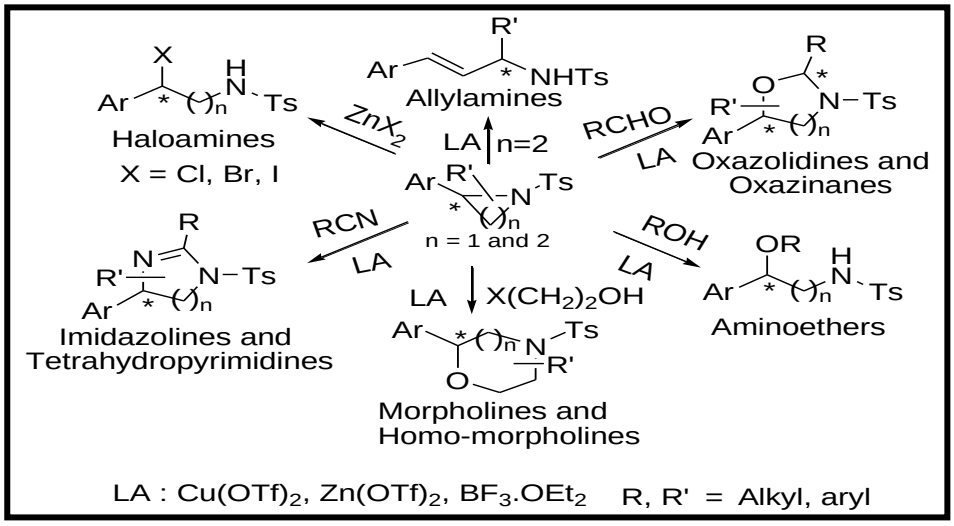
Aziridines and azetidines, the 3- and 4-membered saturated aza-heterocycles are found in many naturally occurring and synthetically important organic compounds which exhibit interesting biological and pharmacological properties. Besides the biological importance of these heterocycles, their utility mainly lies in exhibiting versatile chemistry via their nucleophilic ring opening processes. A part of our research activities [1-9] is devoted in developing synthetic routes for a variety of functionalized aziridines and azetidines and further to utilize them for interesting transformations targeting synthetically important molecules. Recently, we have developed new routes for the synthesis of enantiomerically enriched haloamines, imidazolines, oxazolidines, tetrahydropyrimidines, oxazinanes, aminoethers, morpholines, homo-morpholines and allylamines starting from properly substituted aziridines/azetidines and appropriate nucleophiles in the presence of Lewis acid. All these compounds are of immense synthetic and biological importance. Interestingly, for 2-aryl-N-tosylaziridines and azetidines, all Lewis acid mediated nucleophilic ring-opening processes were found to be stereoselective and proceed via an S_N2-type pathway, which enhanced the scope of this type of chemistry towards enantiomerically enriched compounds.



Scheme 1

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Intellectual Property in Global Pharma Industry

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In recent years the Indian Pharma companies have contributed significantly towards the global economy. They are competing with multi-national giants by supplying life-saving drugs to third world countries, at affordable prices, at the same time showing respect for others' Intellectual Property rights. As these companies explore newer markets around the globe and move from a process to a product regime, Intellectual property assumes a different meaning. Companies need to strategically handle their IP to maximize benefits, gain strength and grow. Research and development should be steered towards innovation and appropriately leveraged, where IP plays a key role. Thus, Patent Portfolio Management is an important tool in the hands of Patent Experts and Business Mangers today.

Novel NXO-Building Blocks for Peptide Backbone Modification and Preparation of New Class Pseudopeptides

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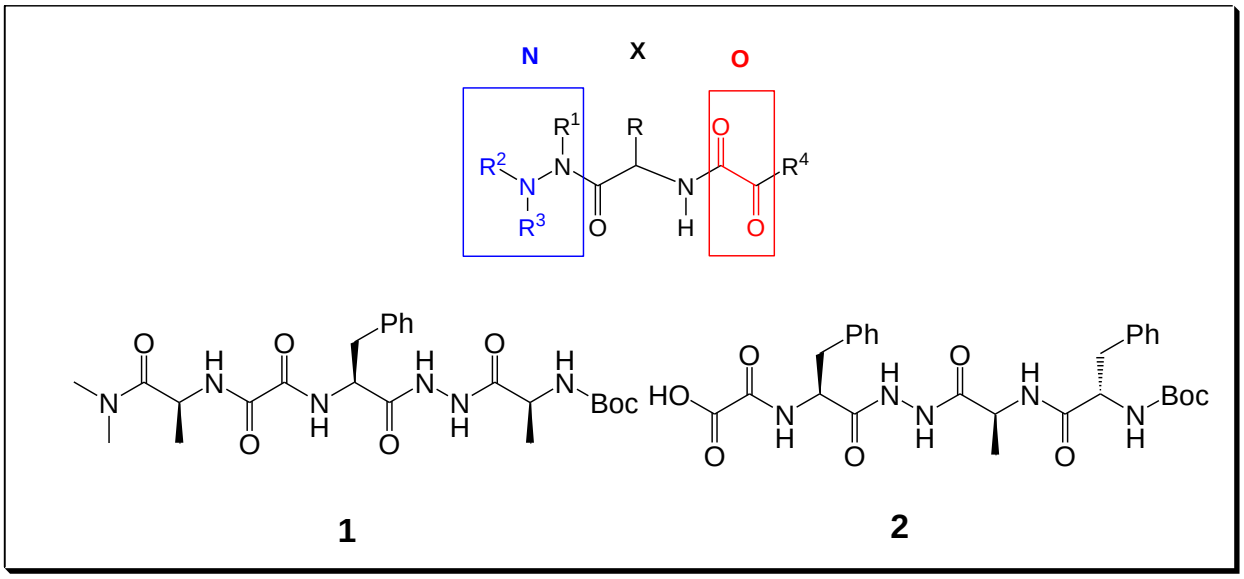
Though naturally occurring and synthetic peptides are promising leads for drug discovery, their therapeutic applications are limited. This fact arises from rapid metabolism, poor bioavailability, and short duration of action. Many peptide analogs have been synthesized to the date through the modification not only of the amino acid side chain, but also of the backbone structure.

In this lecture we present for the very first time the design and synthesis of novel NXO-building blocks for the peptide modification.

The utility of these building blocks in the construction of new pseudo and oligopeptides is demonstrated by the synthesis of model tetrapeptides (e.g. **1** and **2**) using both a conventional liquid phase peptide synthesis protocol and solid supported syntheses.



Synthesis of Azaheterocycles by Ring Transformation

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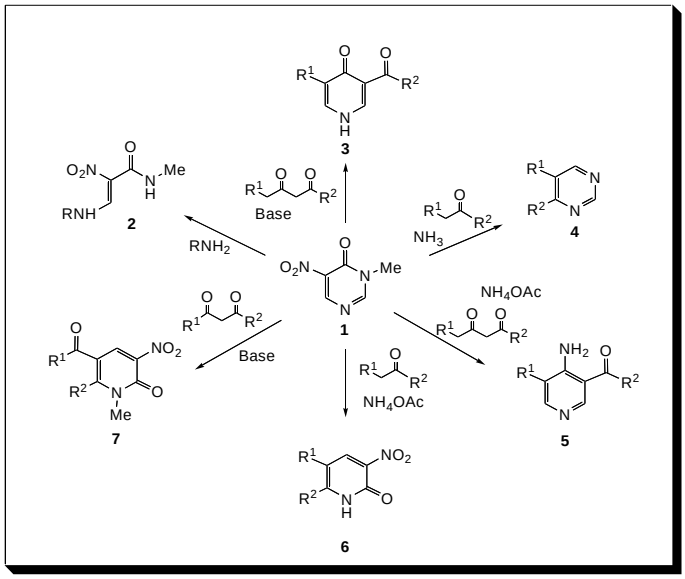
The ring transformation is one of the powerful methods for construction of polyfunctionalized compounds that are not readily available by alternative procedures. We have studied the nucleophilic ring transformation. Electron-deficient heterocyclic compounds are suitable substrates for the present reaction when they have a good leaving group as the partial structure. Among them, 3-methyl-5-nitropyrimidin-4(3H)-one (1) easily causes the aminolysis leading to nitroenamine 2 [1], and serves as an excellent substrate for the ring transformation to afford polyfunctionalized compounds 3-7.

When nitropyrimidinone 1 was allowed to react with 1,3-dicarbonyl compounds under basic conditions, 3,5- difunctionalized 4-pyridones 3 were formed [2]. In this reaction, pyrimidinone 1 behaves as the synthetic equivalent of activated diformylamine. A combination of ketones and ammonia was also usable to give disubstituted pyrimidines 4, which is called three component ring transformation (TCRT) [3,4]. The different types of TCRTs proceeded to give 4-aminopyridines 5 [3,4] and nitropyridones 6 [5] when ammonium acetate was employed as the nitrogen source instead of ammonia. In the latter case, pyrimidinone 1 behaves as the synthetic equivalent of α-nitroformylacetic acid. On the other hand, the reaction of pyrimidinone 1 with 1,3-dicarbonyl compounds in the presence of base such as piperidine, polyfunctionalized pyridones 7 were formed, in which pyrimidinone 1 behaves as the synthetic equivalent of α -nitroacrylamide [6].



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Design and Synthesis of Adenosine A_{2a} Receptor Antagonists to Recuperate Parkinson's disease

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Adenosine A_{2a} receptors have a localized distribution and have emerged as a promising drug target for treating many neurological and psychiatric disorders such as Parkinson's disease [4,5,6,7], schizophrenia and affective disorders [8,9,10]. The adenosine A_{2a} receptors ($A_{2a}R$) belong to the G-protein coupled receptor (GPCR) super family characterized by seven transmembrane (TM) helices arbitrating a surfeit of signals across the plasma membrane in the cell modulating many physiological processes [11,12,13]. The essential residues required for recognition of adenosine receptor agonists and/or antagonists binding within the transmembrane helical domains (TMs) 3, 5, 6, and 7, coincide largely with the corresponding amino acids of the binding site of *cis*-retinal in rhodopsin, although there are additional interaction sites within TMs 6 and 7 of the adenosine receptors in comparison with the binding site of rhodopsin [21]. Stimulation of striatonigral pathway comprising striatal and globus pallidal neurons releasing dopamine, mediated through $A_{2a}R$ in striopallidal region ameliorates to Parkinson's symptoms. Three-dimensional structure of the human $A_{2a}R$ model was constructed by homology modeling, using bovine rhodopsin 1F88 and 1HZX as a template. Both xanthine and non-xanthine known antagonists were selected as reference for generation of docking site and binding parameters with human adenosine $A_{2a}R$ to carry the comparative study of potential antagonists.

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Radiation- and Photo-induced Chemical Reactions of Nucleic Acid Bases under Anoxic Conditions: Mechanistic Studies and Applications

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Ionizing radiation causes harmful effects on living organisms by damaging biomolecules such as DNA, RNA, proteins, lipids, etc. Exposure of cellular DNA to high energy radiation generates electrons and radical ions as highly reactive species, which could lead to wide varieties of damaged base structures including 5,6-dihydrothymine (DHT), 5,6-dihydroxy-5,6-dihydrothymine (Tg), and 7,8-dihydro-8-oxoguanine. Recent studies on interactions between DNA and reductive electrons have demonstrated that the excess electrons migrate along the DNA duplex more than a few base pairs [1] and, the electrons could be eventually trapped by nucleic acid bases, or otherwise quenched by dissolved oxygen molecules. From a viewpoint of cancer radiotherapy, such reductive electron generated in the radiolysis is operative as a reactive species under hypoxic conditions in solid tumor tissues, and thus, in-depth investigation into chemical events which occur at the earliest stage of radiation-induced DNA damage processes under hypoxia helps us develop radiosensitizers for cancer radiotherapy.

Pyrimidine bases, thymine (T) and cytosine (C), are considered to be with higher electron affinities than purine bases, guanine (G) and adenine (A), and indeed, reductive radiolysis of T in aqueous solution affords some reduction products, such as DHT and dimeric products [2]. We have focused our research toward chemical reactions induced by the attachment of reductive electron on DNA containing modified bases. Tg is a major DNA damage structure formed by oxidative stresses, and is a significant block to transcription by T7 RNA polymerase. We have found that photo-excited reduced form of flavin adenine dinucleotide repairs Tg into T under reductive atmosphere [3, 4]. Laser flash photolysis study to identify the radical intermediates during the reductive repair of Tg showed that the electron adduct of Tg loses a hydroxyl ion and generates 6-hydroxy-5,6-dihydrothymin-5-yl radical, which is further reduced to T. On the other hand, photo-induced electron injection into DNA strands containing Tg from an internally tethered phenothiazine (PTZ) did not lead to the repair of Tg, suggesting that excess electron transfer along the duplex is competitive with the irreversible capture of the electron by Tg [2, 3].

5-Fluorouracil (5-FU), an analog of thymine, is used as a chemotherapeutic agent in the treatment of varieties of tumors. We have found that dimeric structured pyrimidines including 5-FU undergoes radiation-induced one-electron reduction under hypoxic conditions to regenerate the corresponding monomers [2, 5], suggesting such pyrimidine derivatives with high electron affinity could be a prototype of radiation-activating antitumor prodrug. Details of mechanistic investigation by time-resolved spectroscopy to understand the reductive regeneration of monomeric pyrimidines will be described.

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Specific Induction of Apoptosis in Cancer Cells by Pancratistatin: Evaluation of its Efficacy as a Non-toxic Anticancer Reagent and Investigation of its Mechanism of Action

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Despite the aggressive research efforts to find selective anti-cancer chemotherapeutics, cancer remains unconquered. The major difficulty with the treatment of cancer is the non-specificity, with which chemotherapy kills cells. Many current treatments, including drugs and radiotherapy are damaging to both normal cells and cancerous cells. Such damage to normal cells causes harsh side effects and mutations that increase the possibility of these cells becoming cancerous.

Pancratistatin is a natural compound that was isolated from the spider lily in 1992 and has been shown to have anti-cancer ability. We have recently demonstrated that while Pancratistatin induces the apoptosis (cell suicide) in cancer cells it does not affect non-cancerous cells. We have also demonstrated the non-genotoxic behaviour of Pancratistatin, that is, its ability to kill cancerous cells without targeting their DNA. We investigated the specificity and biochemical mechanism of action of Pancratistatin; our results indicated that Pancratistatin specifically and effectively induced apoptosis in human prostate, breast cancer, neuroblastoma and leukemia cells. Interestingly, we have demonstrated that Pancratistatin targets mitochondria in the cancer cells. Mitochondria from non-cancerous cells are not affected by this treatment, indicating the vulnerability of only cancer cell mitochondria to these compounds. Our initial *in vivo* results with human colon and prostate cancer xenotransplants in immuno-compromized mice have indicated that Pancratistatin is well tolerated at effective doses that inhibit tumor growth. These results open a new opportunity for development of chemotherapy targeting cancer cell mitochondria, and advance our knowledge of a novel mechanism of action for Pancratistatin.

Molecular Modeling Studies on AChE Inhibitor Carbamates to Design and Synthesize Antialzheimer Agents

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Virtual screening is gaining importance in the current scenario of drug discovery research. The development of new predictive models is the most important step in the process. In an attempt to develop a model for designing novel antialzheimer agents using AChE as the target, the systematic QSAR studies (CoMFA, advance CoMFA and CoMSIA) have been carried out on a series of carbamates as AChE inhibitors. The total set of 78 molecules was divided into training and test sets of 52 and 26 molecules, respectively.

Statistically significant 3D QSAR models were developed on training set molecules using CoMFA and CoMSIA and validated against test set compounds. The highly predictive models (CoMFA q^2=0.733, r^2=0.967, predictive r^2=0.732, CoMSIA q^2=0.641, r^2=0.936, predictive r^2=0.812) well explained the variance in binding affinities both for the training and the test set compounds. The generated models suggest that steric, electrostatic and hydrophobic interactions play an important role in describing the variation in binding affinity. In particular the carbamoyl nitrogen should be more electropositive, substitutions on this nitrogen should have high steric bulk and hydrophobicity while the amino nitrogen should be electronegative in order to have better activity. These studies have provided important insights into structural variations leading to the development of novel AChE inhibitors which may be useful in the development of novel molecules for the treatment of Alzheimer's disease.

Synthesis of (N)-(S)-Butoxycarbonylalaninyl)-(S)-1-amino-3-methyl-4,5,6,7-tetrahydro-2H-3-benzazepin-2-one and Role of 1-Hydroxy benzotriazole in Peptide Bond Formation using N-(3-Dimethylamino propyl)-N-ethyl-carbodiimide hydrochloride in Ethanol

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The efficiency and selectivity of peptide coupling reactions have improved significantly in accord with the development of new coupling agents in organic synthesis. The carboxamide group is an important functionality which occurs in many natural products, and pharmaceutical active compounds. For compounds containing chiral centers, significant attention has been focused on developing amide bond-forming methods which minimize loss of optical purity. Aqueous mediated reactions are gaining importance due to the negative impact of organic waste on the environment (green chemistry). In our early development of the drug candidate for treating Alzheimer's disease, the synthesis involved a classical resolution of a key amine intermediate followed by two peptide forming transformations in methylene chloride. We have developed a dynamic resolution of the required amine, a method for peptide bond formation utilizing N-(3-dimethylamino- propyl)-N-ethylcarbodiimide hydrochloride (EDC), catalytic 1-hydroxy benzotriazole (HOBT) and water or ethanol as the reaction solvent for the synthesis of (N)-(S)-Butoxycarbonylalaninyl)-(S)-1-amino-3-methyl-4,5,6,7-tetrahydro-2H-3-benzazepin-2-one.

This presentation will discuss the process development for the title compound, our studies on the role of N-hydroxy benzotriazole in amide bond forming reactions utilizing EDC as the coupling agent, and the application of this process to other amide containing molecules.

A Journey from Natural Products to Synthesis in Search of a Drug Candidate

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Recently there has been a renewed interest in the beneficial effects of natural products for the prevention of various diseases like, heart disease, diabetes, arthritis, leukemia, Alheimers, Parkinsons and dozens of others. It has been estimated that 80% of the world population still rely on natural plant products, of which some are sold as herbal / food supplement or drugs. Half of the top 50 drugs sold in European Pharmacies are based on or derived from natural products. Thus, the best strategy to discover a new drug candidate is to investigate the natural resources which have been used by different ethnic cultures, for medicinal purposes all over the world. Study of biologically active compounds present in natural resources, normally serve as the lead compounds for the discovery of new drugs.

Keeping the above philosophy in mind we have studied the active principles of various plants and marine sponges and have synthesized over fifteen natural products. These compounds are known to possess strong antimicrobial, molluscicidal and cytotoxic activity specially against p-388 murine leukemia cells. Taking lead from these natural products, we have synthesized number of related compounds, in order to find a potential drug candidate for the future.

An over view of our journey, from the natural products to synthesis of new molecules, in research of a suitable drug candidate, will be presented at the conference.

Chemical Manipulation for New Antitubercular Drug Development Path: A Mini Review

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Mycobacterium tuberculosis, the leading causative agent of tuberculosis (TB), is responsible for the morbidity and mortality of a large population worldwide. According to WHO report, by 2020 AD nearly one billion more people will be infected, 200 million people will get sick, and 70 million will die from tuberculosis if proper steps are not taken to control it. TB is the world's second cause of death from infectious disease, after acquired immune deficiency syndrome (AIDS). No new antibiotics against TB have been developed in the past 30 years. There are three front line antibiotics, isoniazide, rifampin and pyrazinamide and several second-tier antibiotics including ethionamide, streptomycin and *para*-aminosalicylic acid. The current treatment of TB requires an exceedingly lengthy therapy of 6-9 months, often involving a cocktail of three or four different drugs *viz* isoniazide, rifampin, ethambutol and pyrazinamide are prescribed for two months followed by a continuation phase in which isoniazide and rifampin are taken. In light of this, the author's laboratory has synthesized more than 3500 compounds of diversed heterocyclic skeletons including of more than 50 structure and substructure types. A fair highlight of this entire work will be presented along synthetic strategies and biological profile with latest developmental work.

Efficient Synthesis of Structurally Diverse Substituted Taurines

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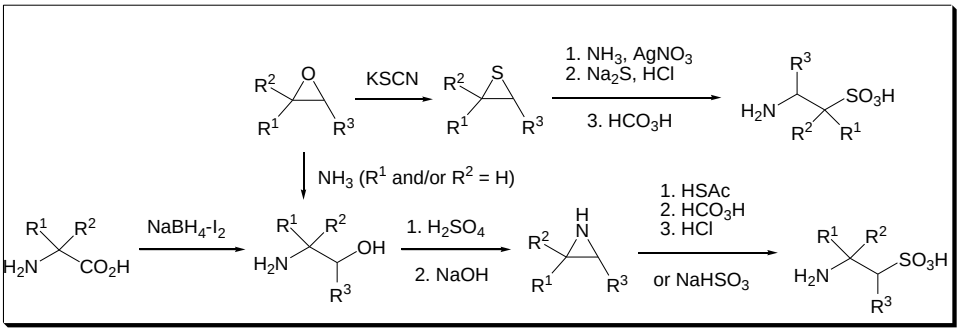
Taurine and some substituted taurines (β-aminoalkanesulfonic acids) are a class of naturally occurring amino acids [1]. They are also significant sulfur analogues of naturally occurring aminocarboxylic acids [1] and involved in various physiological processes [2]. In addition, their derivatives, such as sulfonopeptides, have been widely used as enzyme inhibitors during the last two decades because of their tetrahedrally structural properties [1]. Several synthetic methods of substituted taurines have been reported till now [1]. As increasing attention was paid to substituted taurines in both biological chemistry and pharmaceutical chemistry field [3], we were dedicated to develop efficient method to synthesize structurally diverse substituted taruines.

Recently, our working group developed some novel methods to synthesize substituted taurines from three-membered heterocyclic compounds: ring-opening reaction of episulfides with nitrogen nucleophiles and subsequent reactions gave 1-substituted, 1,1- and 1,2-disubstituted taurines; ring-opening reaction of aziridines with sulfur nucleophiles (and subsequent reactions) led to 2-substituted, 1,2- and 2,2-disubstituted taurines [4]. The methods are efficient and practical for preparation of various substituted taurines.



Scheme 1. Efficient Synthesis of Structurally Diverse Substituted Taurines

Acknowledgments: This work was supported in part by NSFC (Nos. 20772005 and 20472005).

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Polypeptides and Peptidomimetics in Diabetes Therapy

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Type 2 diabetes is a multifaceted disease manifested by hyperglycemia that results from several dysregulated biologic mechanisms. The critical pathophysiological factors are insulin resistance, impaired insulin secretion, and increased glucose production. Most patients with type 2 diabetes have insulin resistance, while others are associated with in sufficient insulin secretion. These pathophysiological conditions, if sustained for longer time may lead to Type 1 diabetes. The treatment of Type 2 diabetes is generally comprises either insulinogenic substances or agents that augment insulin action. In certain cases a combination therapy is also recommended. However, Type 1 diabetes is controlled only by exogenous insulin supply. In recent years several new targets are under extensive research, which may lead to complete cure to both type 1 and Type 2 diabetes. Beside, insulin other polypeptides and peptidomimetics have taken center stage for the development of new paradigm of diabetes therapy. Development of these new targets based antidiabetic therapy will be presented.

Molecular Analyses of *Plasmodium vivax* parasites showing severe manifestations in Bikaner, Rajasthan

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Plasmodium vivax malaria is prevalent in many regions of the world. Recently, we have reported some severe *Plasmodium vivax* cases from Bikaner, Rajasthan (Western India). Patients exhibited severe manifestations including cerebral malaria, renal failure, circulatory collapse, severe anemia, hemoglobinurea, abnormal bleeding, acute respiratory distress syndrome, and jaundice. The pathogenesis of severe *P. vivax* malaria is not clear, but is believed to be multi-factorial, due to its diverse clinical nature. We have analyzed some major vaccine candidate and drug resistance genes with genes from Mitochondrial and Apicoplast genome from Indian *P. vivax* isolates showing severe and non – severe manifestations. Analyses of Circumsporozoite Protein (CSP) sequence from these isolates showed *P. vivax* Type 1 (VK210) repeats. Detailed analyses revealed a mixture of strains similar to North Korean and Belem strains but with some other differences. Analyses were also performed using specific nuclear (*dhfr*, *dhps*, *cdc2* and *ama-1*), mitochondrial (*cytochrome b*) and Apicoplast (*tufA*) genes. All these genes showed different degrees of sequence variations with gene taken from reported uncomplicated Indian and non – Indian isolates. A preliminary phylogenetic analysis has been also performed to understand the variations between severe and non – severe isolates.

Plant Science Learning from Drug Discovery: Chemical Interrogation of Starch Metabolism in Germinating Barley

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Starch is a bulk renewable commodity, generating trade in the EU worth Euros 1.7Bn annually. It has many industrial uses, ranging from thickeners for food and paint to bulking agents for pharmaceutical and animal feed tabletting, pelletting and packaging. Starch in cereal seeds is also central to the baking and brewing industries. Increases in activities of starch-degrading enzymes prior to harvest have a detrimental effect on flour quality for baking, whereas increases in these enzyme activities during the early stages of germination are vital for malting for the brewing and distilling industries. Understanding the nature and control of starch degradation in cereal seeds will help to improve the flour and malting quality of grain, impacting directly on bread, beer and whisky production. We have employed techniques typically used in drug discovery in a focused search for specific inhibitors of plant enzymes regulating starch metabolism during germination. Specifically, structure- and mechanism-based design and high throughput screening of compound libraries (drugs and natural products) have been applied in combination with protein crystallography and molecular modelling as a means of identifying inhibitors of barley glycosylhydrolases GHs). Evaluation of these inhibitors *in vivo* using whole seed screening has revealed changes in morphology and in the endosperm carbohydrate profiles when compared to untreated seeds. Irreversible inhibitors of barley GHs have also provided further insight into mode of action and have helped in defining key active site residues involved in the enzyme-mediated starch hydrolysis.

Synthesis, Thermal Stability and Antimalarial Activity of Symmetrically/ Asymmetrically Substituted Tetraoxanes

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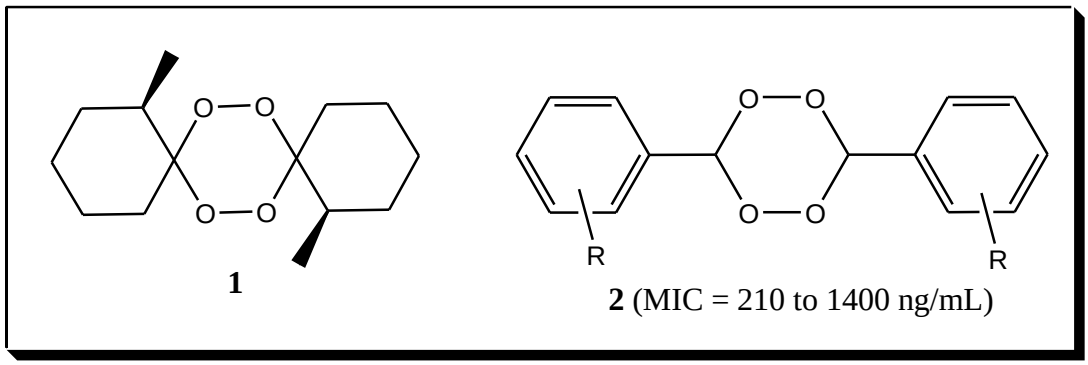
Malaria has remained one of the major diseases that causes 1-3 million deaths annually. Children under age five and pregnant women are the most vulnerable to the disease [1]. Despite efforts to reduce transmission and increase treatment, there has been little change in the statical data of this disease since 1992 [2]. Indeed, if the prevalence of malaria stays on its present form, the death rate could double in next twenty years. The unfortunate fact is that no new drug has been introduced in the market since last thirty years. Artemisinin and its semi synthetic derivatives represent the endoperoxide class of compounds, which shows antimalarial activity against chloroquine-resistant strain of *Plasmodium falciparum* [3]. The impact of drug resistance is very acute for malaria chemotherapy because of the availability of limited number of clinically useful antimalarial drugs. Thus synthesis of new chemical entities for the antimalarial therapy remains a challenging task for the scientists involved in the malaria research [4]. Tetraoxanes (**1**) represent a new class of antimalarials that is equally potent as artemisinin. In spite of huge medicinal potential there are about 250 tetraoxanes reported todate[5]. To this end, synthesis, characterization, thermal stability and antimalarial activity of symmetrically, and asymmetrically substituted tetraoxanes will be presented (**2**) [6].



Scheme 1

References :

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Aberrant Crypt Foci, a Biological System to Investigate Role of Bioactive Compounds as Modifiers of Colon Carcinogenesis

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There is considerable interest in exploring the role of environmental factors in the etiology and prevention of human cancers. Several model systems are being employed to identify cancer modulating factors and their biological effects at the cellular and molecular levels. Carcinogenesis is a complex and multistep process and may remain active in an organism without expressing itself as a disease for several years. To prevent the appearance of cancer it is important to impede, eliminate or retard the growth of precancerous lesions. Several biomarkers are proposed to assess the risk of developing cancer. An ideal marker should be sensitive and specific to the disease state. Precancerous lesions are ideal biomarkers for assessing the risk of developing cancer.

Colon cancer is an important cancer in affluent society and it is generally accepted that environmental factors significantly influence the development of the disease. Aberrant crypt foci (ACF) were identified in a carcinogen treated rodent colons and are being used extensively to identify colon cancer preventive and promoting agents. The biology and growth features of ACF have supported the concept that they are preneoplastic lesions. Experimental evidence from our laboratory suggests that ACF system can be employed to identify cancer preventive agents specific to metabolic states associated with high risk for developing colon cancer such as obesity and insulin resistance. Using the ACF system in pre-clinical model of obesity, Vitamin B6 was identified to have a therapeutic efficacy in alleviating the risk of developing colon cancer and abnormal haematological indices(Supported by the Natural Sciences and Engineering Research Council of Canada).

Nanoparticulate Delivery of Selected Anticancer Drugs

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Nanotechnolgy is unique in that it covers a vast variety of disciplines ranging from basic material science, engineering to personal care applications. This led to tremendous development occurred in computer science, information technology, electronics and in other areas. It has also opened up lots of new opportunities in biotechnology and pharmacy areas. One of important areas of nanotechnology is 'Nanomedicine' which refers to highly specific medical intervention at the molecular scale for diagnosis, prevention and treatment of diseases. Nanoparticulate systems represent very promising delivery systems for poorly soluble and poorly available drugs. Nanoparticles systems can be used for better availability, selective distribution and better therapy, specifically for anticancer drugs.

As anticancer drugs have mostly non-specific distribution in body causing severe side effects. Nanoparticulate delivery systems can have better absorption and selective distribution with no or lesser side effects. Enhanced permeation and retention (EPR) effect and other studies suggested suitability of 200 –300 nm particles for selective delivery to cancer tissues. Nanoparticulate delivery systems of etoposide and imatinib mesylate, two important anticancer drugs, were prepared using biocompatible and biodegradable polymers. The nanoparticles were characterized for particle size, zeta potential, polydispersity index using Transmission Electron Microscope, Atomic Force Microscope and Zeta Sizer. Particle size found to be between 50 μm to 500 μm depending on nature and amount of polymer(s), drug and its amount, proportion and nature of stabilizer and other process conditions. In vitro release studies were done to find extension of release of drug from nanoparticles using selected dissolution media, which varied from 6 hrs to more than 50 hrs.

Using radiolabeled (with Technitium, Tc^{99m}) nanoparticles and free drug of etoposide, biodistribution and pharmacokinetics studies were carried out in mice and rabbit. The uptake and distribution of free etoposide and nanoparticles to various organs/tissues were found to be different. Distribution of drugs was found to more to blood, lungs and bone and less to heart, kidney in nanoparticulate systems. Tumor uptake of nanoparticles in Dalton's lymphoma solid tumor bearing mice was found to be more. Nanoparticulate systems produced more AUC, mean residence time (MRT) and lower clearance on iv as well as oral administration suggesting better availability.

Bioavailability and distribution profile of PLGA based imatinib mesylate nanoparticles were found to be different from pure drug. Bioavailability increased and distribution to brain enhanced with change in distribution in other organs and tissues. AUC and MRT found to be more without much change in C_{max}.

Improved bioavailability and selective biodistribution of nanoparticulate delivery systems may help to lower the drug dose and overcome several problems like side effects and non-specific distributions associated with anticancer treatment leading to better therapy and patient compliance.

Pyrazol[3,4-*d*]pyrimidine Based 'propylene/Leonard linker' Compounds as Models for Studying *arene interactions* in Flexible Molecules

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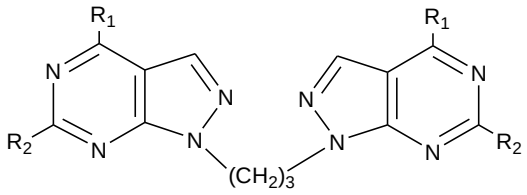
Since the discovery of DNA structure in 1953 stacking among nucleic acid bases has been subject of much curiosity and intense study. Browne *et al.* in 1968 showed that intramolecular interactions between different nucleic acid bases connected by 'propylene linker' can be demonstrated in solution. In addition to stabilization of DNA/RNA structures, arene interactions are known to play an important role in chemistry and biology particularly in molecular recognition, crystal engineering, foldamers, molecular tweezers/clips and drug development. Since Hunter and Sanders' seminal paper (1990) this area has witnessed increased activity, however, the nature of π–π interactions is still not well understood. Interestingly, the offset stacked geometry is the most common geometry for arene interactions, but the least well studied. Apparently, one of the main problems for better understanding of the offset stacked geometry in arene interactions is the lack of good easy to make flexible models. Our work on pyrazol[3,4-*d*]pyrimidine based 'propylene/Leonard linker' compounds (**1**) as models for studying arene interactions in flexible molecules will be presented [1].



1

1a: $R_1 = R_2$ = SMe; **1b**: $R_1 = R_2$ = SEt;
1c: $R_1 = R_2$ = S-iso-Pr;
1d: R_1 = OEt, R_2 = SMe;
1e: R_1 = O-isoPr, R_2 = SMe;
1f: R_1 = OMe, $R_2 = SO_2Me$;
1g: R_1 = OEt, $R_2 = SO_2Me$;
1h: R_1 = O-isoPr, $R_2 = SO_2Me$;
1i: R_1 = O-isoPr, $R_2 = SO_2Et$;

References:

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Stereoselective Syntheses of Densely Subsituted Tetrahydrofurans and their Applications

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The stereoselective synthesis of densely substituted tetrahydrofuran (THF) derivatives have received much attention in recent years owing to their widespread occurrence in various natural products as structural units and also their presence in many biologically active compounds, such as renealtins A and B, asitrocin, 2,4-cis- and trans asitrocinones, and donnaienin. The highly functionalized enantiomerically pure THFs can offer a high degree of structural diversity and may be used as intermediates for the synthesis of various biodynamic compounds. Therefore, an easy access to a synthetic approach capable of targeting chiral substituted THFs is required.

With this in mind, recently we have developed convenient strategies for the stereoselective synthesis of enantiopure tetrahydrofurans starting from glycals, the detailed account of which will be presented therein.

Synthetic Utilization Of Pentafulvenes Towards Fused Oxa-Bridged Cyclooctanoids

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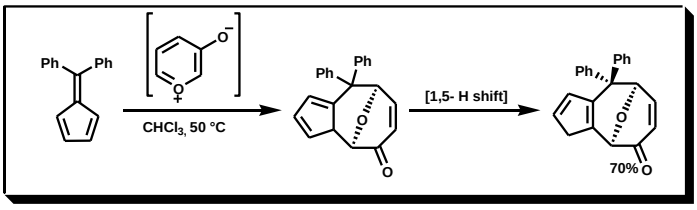
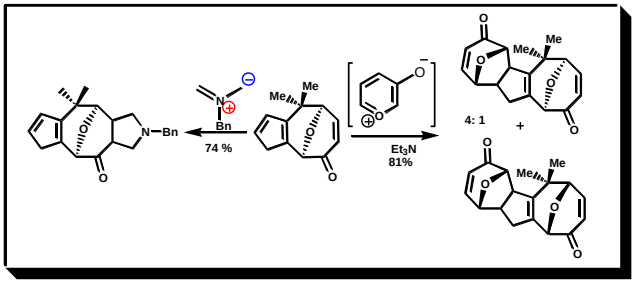
Medium sized carbocycles represent a fabulous collection of synthetically challenging molecules which form the structural motif of numerous bio-medically important natural products. Cyclooctanoids belong to the family of medium sized carbocycles and form the core of numerous natural products displaying intriguing structures as well as potent and selective biological activities [1]. We have unraveled a novel and efficient methodology for the synthesis of 5-8 fused oxabridged cyclooctanoids *via* a [6+3] cycloaddition involving pentafulvenes and 3-oxidopyrylium betaines [2].



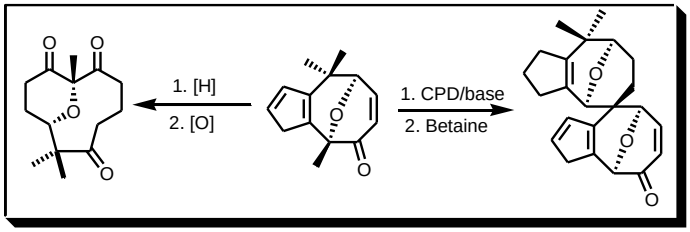
Scheme 1

The products are versatile molecules having multiple points for functionalization and can be synthetically manipulated easily and the feasibility of using the new methodology towards the synthesis of fused oxabridged cyclooctanoids and cyclooctanoids of biological importance was carried out (scheme 2) [3].



Scheme 2

Utilizing the above methodology, we have developed a novel route towards eleven membered carbocycles. The strategy takes the advantage of a selective reduction followed by a ruthenium based oxidative cleavage in the 5-8 fused cyclooctanoid. An efficient spiroannulation strategy towards the synthesis of spirocyclic cyclooctanoids was also developed and is shown in scheme 3. The results of our studies will be presented.



Scheme 3

References:

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Nanotechnology and Medical Science: Challenges Ahead

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One nanometer (nm) is one billionth, or 10^{-9} of a meter. Materials reduced to the nanoscale can suddenly show very different properties compared to what they exhibit on a macroscale, enabling unique applications. For instance, opaque substances become transparent (copper); inert materials become catalysts (platinum); stable materials turn combustible (aluminum); solids turn into liquids at room temperature (gold); insulators become conductors (silicon). Materials such as gold which is chemically inert at normal scales, can serve as a potent chemical catalystat at nanoscales. Nanotechnology could prove to be a "transformative" technology comparable in its impact to the steam engine in the 18th century, electricity in the 20th century, and the Internet in contemporary society. Nanotechnology is a field of applied science and technology covering a broad range of topics. The main unifying theme is the control of matter on a scale below 100 nanometers, as well as the fabrication of devices on this same length scale. Richard Feynman, described the concept of 'building machines" atom by atom in his talk titled "There is plenty of room at the bottom". Top 10 use of nanotechnology include energy, water treatment, diagnosis of diseases, drug delivery, air pollution, construction material, health monitoring, pest control, agriculture and food processing. Microscopes have offered scientists a window inside cells. Yet, what scientists have not been able to do is to exhaustively inventory cells, cell parts, and molecules within cell parts to answer questions such as, "How many?" "How big?" and "How fast?" Obtaining thorough, reliable measures of quantity is the vital first step of this a lab will be established a handful of nanomedicine centers. These centers will be staffed by a highly interdisciplinary scientific crew including biologists, physicians, mathematicians, engineers and computer scientists to design a particular strategy in fighting against diseases.

What is most important today is that people are not aware of the promises nanotechnology holds for the future especially for a country like India. Author who has started a novel concept of science communication called scientoon (a new class of cartoons based on science) and subsequently a new science called Scientoonics, will use this science to create awareness about Nanotechnology as what enormous future nanotechnology holds specially in the area of medical science.

Structural Modifications of Peptidoglycan and Nod Protein Recognition

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The innate immune system consists of a host of pattern recognition receptors (PRRs) like Toll-like receptors, NOD-like receptors, PGRPs etc. that recognizes conserved microbial components called pathogen-associated molecular patterns (PAMPs). Recently NOD-1 and NOD-2 has been implicated in the recognition of breakdown products of peptidoglycan (muropeptides). These muropeptides have been shown to induce TNF-α gene expression without significant TNF-α translation. An apparent synergy between LPS and these muropeptides seems to lift the translational block leading to TNF-α protein production. The compounds that induced synergistic effects were also able to activate NF-κB in a NOD1- or NOD2-dependent manner.

This study exhibits the structure activity relationship of certain modifications of the muropeptides. It was found that a diaminopimelic acid (DAP)-containing muramyl tetrapeptide could activate NF-κB in a NOD1-dependent manner, demonstrating that an exposed DAP is not essential for NOD1 sensing. The activity was lost when the α-carboxylic acid of iso-glutamic acid was modified as an amide. However, agonists of NOD2, such as muramyl dipeptide and lysine-containing muramyl tripeptides, were not affected by amidation of the α-carboxylic acid of iso-glutamic acid. Many pathogens modify the α-carboxylic acid of iso-glutamic acid of PGN. Thus might be a strategy to avoid recognition by the host innate immune system.

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Click Chemistry in the Construction of Kinase-Biased Libraries

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Aminopyrimidine core is widely prevalent in the marketed kinase-inhibiting drugs, which makes it as an attractive scaffold for the design of future kinase inhibitors. However, the chemical space around pyrimidine has extensively been exploited. The appendage of 1,2,3-triazole (modular) building block on pyrimidine core by click chemistry introduces a chemical space, which has never been explored. Click chemistry has been emerging as a powerful approach to accelerate lead identification and optimization by simplifying the compound synthesis with only facile and reliable chemical transformations. The presentation will focus on the generation of 1,2,3-triazole-enabled pyrimidine-derived kinase directed libraries with two-pointed variation and rich diversity. The click compounds were generated by synthesizing first a series of click scaffolds and subsequent generation of libraries from these scaffolds through appropriate functional group interconversion. Alternatively, the click libraries were generated by parallel cycloaddition of azide and alkyne precursors, bearing aminopyrimidine core. The compounds, exceeding 80% of each library, were obtained in >85% purity, resulting in less time, required for purification, and the enhancement of productivity.

Synthesis of Stereodivergent Acyclo-*C*-nucleosides as Drug-like Small Molecules: A Green Chemistry Approach

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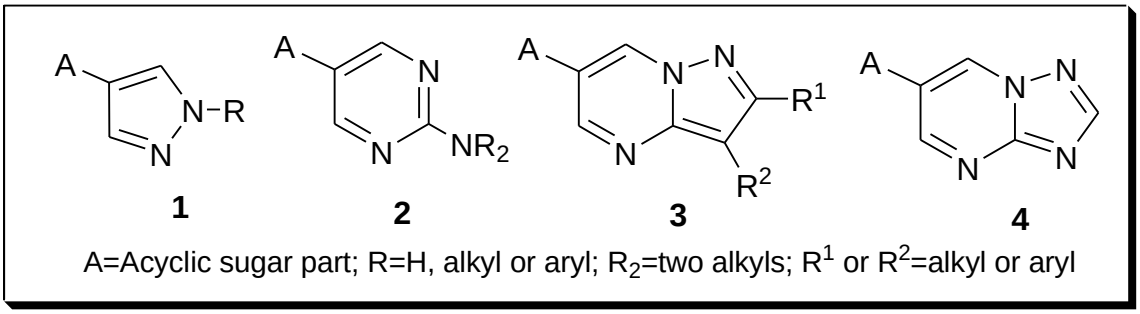
The search of new simple route for the synthesis of drug-like small molecules having structural and stereochemical diversity is an attracting goal for the medicinal chemist and chemical biologist.[1] Diversity Oriented Synthesis (DOS) has been proven to be an essential tool for the discovery of the discovery of bioactive small molecules.[2] Stereochemical diversity (SD) can be achieved by efficient enatio- or diastereoselctive reactions. SD can also be introduced by using sterechemically enriched & naturally abundant carbohydrate synthons. Stereochmically diversified drug-like small molecules can be synthesized by using different epimers of carbohydrates under the identical reaction condition.[3]

Pyrazoles,[4] Pyrimidines,[5] Pyrazolo[1,5-a]pyrimidines[6] and 1,2,4-triazolo[1,5-a]pyrimidines[7] (**1-4**) have been proven as privileged core structures for the synthesis of bioactive small molecules. So we have deigned and synthesized these core structures with acyclic chiral handle, as a acyclo-*C*-nucleoside, from stereochemically enriched starting materials.[8] Further, these privileged core structure linked with open carbohydrate chain can be termed as carbohybrids,[9] an important concept in bioactive small molecule. The details of natural benign, simple and general synthesis of these molecules will be discussed therein.



A=Acyclic sugar part; R=H, alkyl or aryl; R_2=two alkyls; R^1 or R^2=alkyl or aryl

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Synthesis and Biological Screening of Novel Aryloxyacetic Acid Analogs

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Aryloxyacetic acid derivatives are well known for their wide spectrum of pharmacological activities. Keeping in view the biological potency of aryloxyacetic acids as well as taking advantage of biodegradability and biocompatibility of amino acids and peptides, present investigation was aimed at synthesis of two novel series of 2,5-disubstituted and 3,4,5-trisubstituted phenoxyacetic acid derivatives of amino acids and peptides.

2-(5-Bromo-2-formyl-phenoxy)acetic acid and 2-(4-chloro-3,5-dimethylphenoxy) acetic acid were prepared by phenoxylation of corresponding phenols viz. 5-bromosalicylaldehyde and 4-chloro-3,5-dimethylphenol in the presence of chloroacetic acid under alkaline conditions. The free amino group was protected by introducing Boc group and carboxylic end was protected by preparing methyl esters using $EtOH/SOCl_2$. Protected groups were deprotected by using CF_3COOH and LiOH respectively.

In order to synthesize derivatives of the first series, 2-(5-bromo-2-formyl-phenoxy)acetic acid was coupled with several amino acid/dipeptide/tripeptide methyl esters using dicyclohexylcarbodiimide (DCC) as coupling agent and triethylamine (TEA) as base. Selected ester derivatives were subjected to alkaline hydrolysis with lithium hydroxide.

Another series of 2-(4-chloro-3,5-dimethylphenoxy)acetyl amino acids and peptides was prepared by coupling 2-(4-chloro-3,5-dimethylphenoxy)acetic acid with amino acids, dipeptide and tripeptide methyl esters using DCC/NMM (N-methylmorpholine) method. Some of the methyl ester analogs were further hydrolyzed to get corresponding amino acids, dipeptides and tripeptides.

All the synthesized compounds were characterized by spectral and elemental analysis and evaluated for antimicrobial and anthelmintic activities. Some of the compounds showed remarkable bioactivity against gram negative bacterium *P. aeruginosa*, pathogenic fungus *C. albicans* and earthworms *M. konkanensis*, *P. corethruses* and *Eudrilus* sp., as compared to standard drugs - ciprofloxacin/griseofulvin/mebendazole.

Bioloom and CQSAR: Data Mining and Lead Optimization Tools

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One of the approaches to new drug discovery is modification and improvement of existing active molecules i.e. optimization of a lead molecule via QSAR (quantitative structure-activity relationship). CQSAR is a database of QSAR models that has been developed over the past 40 years by Corwin Hansch and his group at Pomona College. The current database has more than 21,900 QSAR models and has come to a point that useful comparisons, and thus predictions, can be made. It relates both biological activities and physicochemical activities of organic chemicals to the different molecular descriptors (physicochemical parameters) available in the system.

Bio-Loom is an extension of ClogP program and master-file database, which was also developed at Pomona College by Al Leo. Bio-Loom consists of a combination of searchable database of bioactive structures (master file), plus a program that calculates the parameters, logP(oct/water), CMR, XMR, NVE.

The utility of the databases to mine information, depending on the user's requirement, is briefly discussed. The two databases, CQSAR and BioLoom, are linked in a manner that serves as a helpful tool to search active molecules that can be used as lead molecules. This followed by comparative QSAR analysis, helps in optimization of a lead molecule that ultimately can become a new drug candidate. Comparative QSAR analysis is very useful for lateral validation of the QSAR models developed. That is, a single QSAR is not strong enough to contribute much towards understanding of drug receptor-interaction, when considered alone, but it becomes significant when bolstered by other similar QSAR.

Drug development strategy for the treatment of Neuropathic pain

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Neuropathic pain can be described as pain associated with damage or permanent alteration of the peripheral or central nervous system. In contrast to acute nociceptive pain, the cascade of events that arise following peripheral nerve injury leads to a maintained abnormality in the sensory system, resulting in an abnormal pain phenomenon that can be grossly debilitating. At present, there are very few effective and well-tolerated therapies for neuropathic pain. The development of animal models and constant progress in the understanding of the basic pathophysiology of neuropathic pain has led to multifarious drug targets and treatment options. The most effective agents are use-dependent inhibitors of Na^+ channels namely phenytoin, lamotrigine and carbamazepine. Owing to an effect of increase in the serotonin and various other biogenic amine levels on the pain modulating system, various classes of antidepressants including selective serotonin re-uptake inhibitors (SSRIs) and selective noradrenaline re-uptake inhibitors (SNRIs) are being used clinically. Modulation of Ca^{2+} channels is another useful approach for the treatment of neuropathic pain. In particular, the modulation of N-type Ca^{2+} channels, which are expressed primarily in central and peripheral nervous tissues, has been the subject of greatest interest. In view of the above, this review discusses the various strategies and approaches to novel drug discovery and pharmacotherapy of neuropathic pain syndromes.

Greener Approaches towards the Synthesis of Pharmaceutically Important Novel 1,5-Benzothiazepine Derivatives and their Analogs

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The synthesis of compounds belonging to 1,5-benzothiazepine series constitutes an important area of research due to their use as well known cardiovascular drugs acting as calcium channel blockers e.g., *Diltiazem*, *Clentiazem*, etc. Literature is also enriched with various biological activities of spiro indoles because this motif is found in numerous natural products and pharmaceutically active compounds. Further, the compactness of heterocyclic system also played an important role in enhancing biological activities.

In our ongoing interest in search of green chemistry routes [1] for the synthesis of potentially bioactive compounds, we schematized here synthesis of novel spiro and annelated 1,5-benzothiazepines incorporating indole and other pharmacophoric moieties using alternative reaction media and non-classical modes of reaction activation, which permits the synthesis of novel systems which are reluctant to be formed under thermal conditions.

Further, to improve the bioactivity and establish the structure activity relationship in 1,5-benzothiazepine derivatives, we have also studied the oxidation and cycloaddition reactions of this motif using non-conventional sources of energy, e.g., microwave, ultrasound and infrared irradiations.

The results obtained from these studied shows that these reactions are highly selective under non classical conditions and selective oxidation to sulfones instead of sulfides occurs exclusively using $Fe(III)NO_3$ impregnated on clay. The chemoselectivity was found in the reaction with chloroacetyl chloride and only one product azeto[2,1-d] benzothiazepines was formed in excellent yield, while thermal reaction gave mixture of products, where, formation of undesirable side products decreases the yield of target adduct and render their purification difficult.

Phototoxicity and Cytotoxic activity of representative compounds were studied against leukemia and adenocarcinoma derived cell lines.

Detailed synthetic methodology and biological activities of these compounds will be presented in the conference.

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Simple and Efficient Synthesis of New α-Aminophosphonates from Imines

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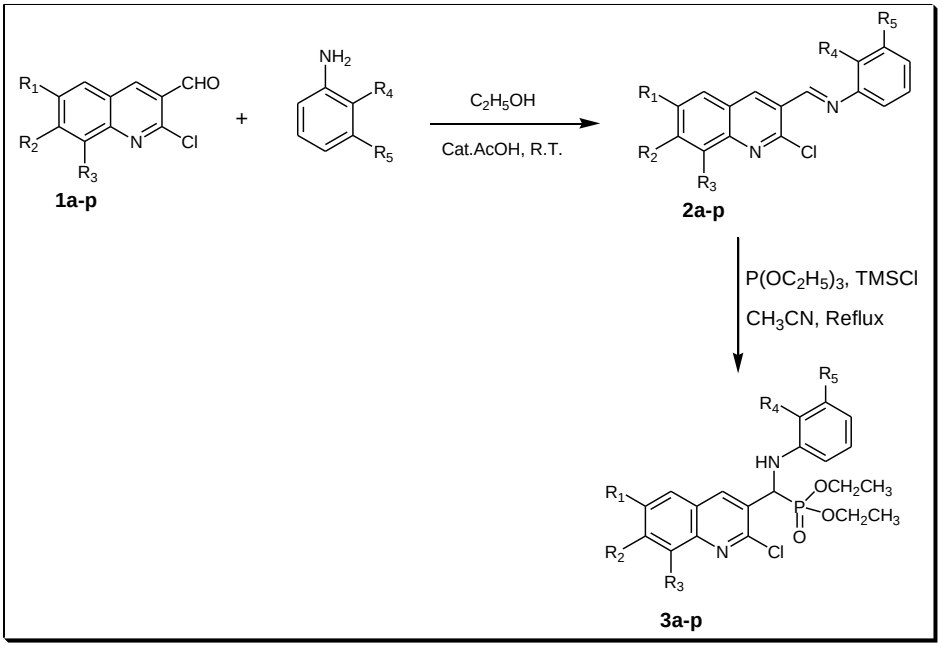
Quinolines are an important class of heterocyclic compounds and have been screened for biological activities such as bactericidal, antitumor, anti-inflammatory, antimalarial activities. α-aminophosphonates are important biologically active compounds due to their structural analogy to amino acids, and has been the subject of considerable current interest. They act as peptide mimics, enzyme inhibitors, antibiotics and pharmacological agents.

Imines were prepared at room temperature from derivatives of 2-chloroquinoline-3-carbaldehyde and 3-fluoroaniline or 2-methylaniline in ethanol using catalytic amount of acetic acid in excellent yields. α-aminophosphonates were then prepared in excellent yields by reacting imines with triethylphosphite in the presence of TMSCl under reflux using acetonitrile as the solvent.



Scheme 1

In conclusion, a new methodology has been developed for the synthesis of new α-aminophosphonate derivatives from imines of 2-chloroquinoline-3-carbaldehydes for first time using TMSCl.

Synthesis of New Sulphamyl thioureas bearing 4-oxo thiazolidinyl moiety and Evaluation of their Antidiabetic Activity

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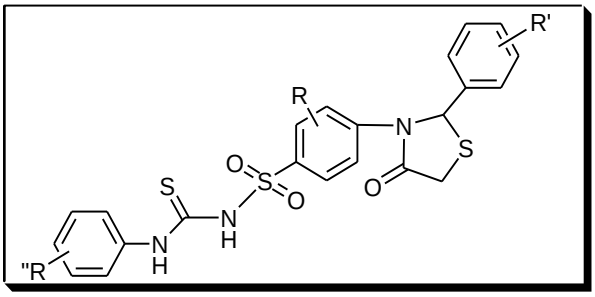
2, 4- Thiazolidinediones[1,2] and sulfonyl ureas [3,5] represents the most promising groups of compounds having a variety of pharmacological features. 2, 4-Thiazolidoinedione (2, 4-TZD) moiety is the generic feature of the glitazone an antidiabetic agent used to treat type-II diabetes [6]. The hypoglycemic action of the sulfonyl ureas is attributed to their ability to stimulate the release of insulin from the pancreatic islets [7].

Considering the clinical efficacy of the sulfonyl ureas, 4-thiazolidineone and our on going interest in developing a new potentially active heteryl nuclei, prompted to undertake the synthesis of new sulfonyl thioureas with 4-thiazolidineonyl moiety. In view of this, the synthesis of new sulfonyl thioureas incorporating 4-thiazolidnonyl moiety has been carried. The details of synthetic route and screening results will be presented.



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The Bioactive C-19 and C-20 Diterpenoid alkaloids of Himalayan *Aconites*

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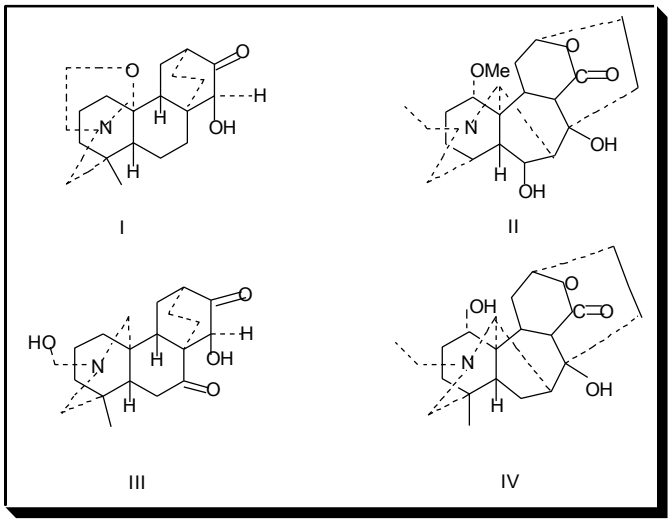
The plants of *Aconitum* genus are highly prized for their use in different Indian Systems of medicine (**ISM**), Unani and Homeopathy. Extracts of *Aconitum* genus of plants are frequently being used [1] for the treatment of **Hypertension**, **Neuralgia, Rheumatism** and **Arthritis**. These extracts are also being used as **Febrifge**, **Antimalarial** and different ***Stomachic*** problems. [2,3]
Aconitum balfourii and *A. heterophyllum* are two different plants growing at an altitude of 1450ft-1550ft in the Indian Himalayan region. Interestingly the former has been found rich in **deadly toxic** class of **C-19 Norditerpenoid** alkaloids [4] while the latter one in less toxic **C-20 diterpenoid** alkaloids . The Extraction , Isolation and Identification of these C-19 (**II.IV**) Norditerpenoid alkaloids and C-20 (**I,II**) diterpenoid alkaloids will be discussed.



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Genetic Polymorphism and Selection in AMA-1 gene of *Plasmodium falciparum*

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A number of stage-specific antigens have been characterized for vaccine development against *Plasmodium falciparum* malaria. This study presents a comprehensive analysis of the sequence polymorphism in *Plasmodium falciparum* Apical Membrane Antigen – 1 (PfAMA-1) in population samples from different parts of India and comparison with other reported sequences from across the world. This is the first study of its kind for the nearly full length PfAMA-1 gene from these regions in India. Our observations confirmed that sequence diversity of PfAMA-1 confines only to point mutations and shows 4 – 8% variation as compared to the prototypes. As opposed to the previous studies on PfAMA-1, our study revealed a greater degree of polymorphism in the Domain II region of PfAMA-1 protein, though signature for diversifying selection is seen throughout the gene. Our present investigation also indicates a very high degree of variation in the reported T and B - cell epitopes of PfAMA-1. Few noteworthy and unique observations made in this study are the substitution of Cysteine residues responsible for the disulphide bond structure of the protein and the presence of premature termination after 595 amino acids in 3 of the 13 isolates under consideration. These crucial findings add new perspectives to the future of AMA-1 research and could have major implications in establishing AMA-1 as a vaccine candidate.

Heterogeneity in α_1-antitrypsin Polymerization: Single Molecule Perspective

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α_1-Antitrypsin (AT) is the most abundantly circulating human proteinase inhibitor in the serpin family. The polymerization of AT, leading to α_1-antitrypsin deficiency, has been studied extensively in vitro by a variety of ensemble methods. Here we report the use of fluorescence correlation spectroscopy to gain further insight into this process. Measurements of the distributions of diffusion times of polymerizing AT, carried out at 45, 50, and 55 °C, clearly show the existence of a kinetic lag phase, during which short oligomers are formed, prior to the formation of heterogeneous mixtures of longer polymers, and suggest that long polymers, which appear to be metastable, are produced through the condensation of shorter oligomers.

Molecular Modeling Study on Chemically Diverse Series of Cyclogenase-2 Selective Inhibitors: Generation of Predictive Pharmacophore Model using Catalyst

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Cycloxygenase (COX) enzymes catalyse the biosynthesis of prostaglandins and thromboxane from arachidonic acid (AA). Currently, there is an ongoing research to design a new COX-2 inhibitors structurally different from the current ones .Indeed, recently Rofecoxib, from the diarylheterocycle family, was withdrawn from the market because of cardiotoxicity [1] which justifies that a constant effort is devoted to identify new scaffolds for the COX-2 inhibition. The present work applies pharmacophore development method on six chemically diverse series of compounds to given a hypothesis. We summarize in this paper, the development of pharmacophores of a dataset of inhibitors for COX-2 by using the Catalyst/ Hypogen module using six chemically diverse series of compounds. The training set includes compounds from viz., 1,2 diarylimadazole class, 1,5 diarylpyrazole class, acyclic 2-alkyl-1,2 diaryl (E) olefins, Aryl-substituted methyleneaminoxymethyl (MAOM), analogues of Diarylcyclopentenyl COX-2 inhibitors, 4'-(4-Cycloalkyl/aryl-oxazol-5yl)benzene sulphonamides, heteroaromatic analogues of (2-aryl-1-cyclopentenyl-1-alkylidene)-(arylmethyloxy) amine.

Training set consisting of 34compounds was carefully selected. The activity spread of the training set molecules was from 0.1 to 10000 nM. The most predictive pharmacophore model (hypothesis 1), consisting of four features, namely, one hydrogen bond donors, one hydrogen bond acceptor, one hydrophobic aliphatic and one ring aromatic feature, had a correlation (r) of 0.954 and a root mean square deviation of 0.894. The entropy (configuration cost) value of the hypotheses was 16.79, within the allowed range. The difference between the null hypothesis and the fixed cost and between the null hypothesis and the total cost of the best hypothesis (hypothesis 1) was 88.37 and 78.51, respectively. The model was validated on a test set consisting of six different series of structurally diverse 27 compounds and performed well in classifying active and inactive molecules correctly. This validation approach provides confidence in the utility of the predictive pharmacophore model developed in this work as a 3D query tool in the virtual screening of drug like molecules to retrieve new chemical entities as potent COX-2 inhibitors. The model can also be used to predict the biological activities of compounds prior to their costly and time-consuming synthesis.

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A New Approach Towards Synthesis of Novel *bis*-fluoroheterocycles

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Innovation, discovery and construction of new biologically active molecules has been challenging and is gaining importance in recent years. The most successful approach explored is the molecular modification, in which different active groups are incorporated in a molecular framework using different reactions. Among the various heterocycles, bis heterocyclic compounds containing a suitable spacer constitute an important class of compounds. These have been under study for various types of activities, preferably antitumor and antimicrobial, based on DNA binding affinity and enzyme inhibiting action. Beside, bis heterocycles can also be used as important intermediate for constructing new molecules. Fluorospiroindoles, on the other hand, are of considerable interest due to their pharmacodynamic nature and therapeutic interest.

In view of above and keeping our interest alive in fluoroheterocycles,we have recently developed an elegant and facile synthesis of some novel bis fluorospiroindoles (symmetrical and unsymmetrical) viz. bis spiro[indol-pyrazolinyl-thiazolidines], bis spiro[indol-indazolyl-thiazolidines] and bis spiro[indol-benzoxazine] by exploiting nature of carbonyl groups present in indole-2,3-diones. The synthetic strategy involves synthesis of hitherto unknown bis schiff's bases containing appropriate spacer like alkyl biphenyl, biphenyl ether, piperazine and morpholine. A series of bis heterocyclic compounds using fluorosubstituted indoles containing different linker have been initially synthesized and then converted into novel bis fluorospiroheterocycles. These compounds have been screened for their *in vitro* antibacterial activity against gram-positive bacteria and some of the compounds showed promising activity at low concentration.

Synthetic details and methodology will be presented during the conference.

Immunomodulatory Activity of Analog of Muramyl Dipeptide and their Use as Adjunct to Chemotherapy of *Leishmania Donovani* in Hamster

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Biochemistry Division, Central Drug Research Institute, Lucknow-226001, India

In search of a potent immunomodulator to be used as an immunoprophylactic agent and as adjunct to chemotherapy against Leishmania infection, two analogs of muramyl dipeptide, viz. N.Ac-*nor*Mur-MeVal-D-*iso*Gln (86/448) and N.AcMur-Acc-D-*iso*Gln (89/729) were evaluated for desired activity. Effect of these peptides on cell mediated and humoral immunity was studied by immunizing the peptide treated mouse with sheep red blood cells (SRBC) and determining HA-titer, Plaque forming cells assay and dealyed type of hypersensitivity (DTH) response after 4-5 days. Both the peptides stimulated cell mediated immunity (CMI), humoral response as well as macrophage function in terms of super oxide anion ($O_2^{-)}$ and nitric oxide (NO) generation. Mitogen induced lymphocyte proliferation and production of IL-2 and INF-γ increased while that of IL-4 and IL-10 decreased by both the peptides showing a typical Th1 type response.

After establishing the immunostimulatory activity, these peptides were evaluated for immunoprophylactic efficacy as well as for use as adjunct to chemotherapy with stibanate (SSG) against *Leishmania donovani* infection in golden hamster. These peptides were found quite effective in both the modes. In adjunct use the treatment may require lower dose of SSG and thereby reducing the chances of the drug toxicity.

Carbamate Chemistry using Mitsunobu's Chemistry

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Mitsunobu reaction has been known for more than three decades, mediated by the redox combination of triaryl-phosphine/dialkyl azodicarboxylate.[1] Mitsunobu reaction is popular in organic synthesis and medicinal chemistry because of its scope, stereospecificity and mild reaction conditions. Mitsunobu reaction has extensively been used in the synthesis of various kinds of natural products,[2] peptide chemistry [3] and combinatorial chemistry [4] as well.
In the present talk, I would like to disclose our recent work for the synthesis of carbamates,[5] dithiocarbamates,[6] xanthates,[7] carbonates,[8] *S*-alkyl carbamates[9] and substituted ureas[10] using Mitsunobu's reagent from the various kinds of starting materials using cheap, abundant and safe reagents like CO_2/CS_2 respectively.

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Evaluation of Plant Ointments on Wound Healing in Wistar RAT

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This study was conducted to evaluated about 10 % (w/v) aqueous extracts of *Stachys lavandifolia* (local name: Chaye Kohi or Lolopashmak), *Achillea mellifolium* (local name: Boomadaran or Golberenjas) and *Malva sysestris* (lacal name: panirak) for wound healing properties. Male Wister rats (150-200 g) of 2-3 months were used. A 7*7 mm full thickness excision wound was made in the dorsal area of the rat. The wounds were treated with different preparation. At days 6, 12 and 16 the experiment was terminated. The wound area of each Wister rat was measured under anesthesia on 6 th, 12 th and 16 th days post surgery.
The best wound healing was observed with the extract *Stachys lavandifolia* + simple ointment (base 10 % w/w) and *Malva sysestris* + simple ointment (base 10 % w/w).

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Synthesis and Biological Study of Oxopyrimidines and Thiopyrimidines of 2-(2,4-dichlorophenyl) imidazo [1,2-a] pyridin-3-carbaldehyde

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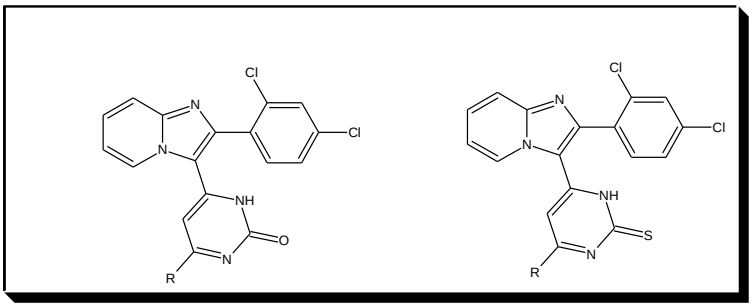
Oxopyrimidines and thiopyrimidines are potential bioactive agents due to their wide spectrum of pharmacological activities like anticonvulsant, fungicidal, antihypertensive, analgesic, antidiabetic, antitumor, antiviral, antibacterial and anti HIV.



3a-l **4a-l**

Where, R = Aryl

We report here in the reaction of different aryl ketones with 2-(2,4-dichlorophenyl) imidazo[1,2-a]pyridine-3-carbaldehyde in the presence of 40 % KOH afforded (*2E*)-3-[2-(2,4-dichlorophenyl)imidazo[1,2-a]pyridin-3-yl]-1-arylprop-2-en-1-ones **(2a-l)**. Compounds **(2a-l)** on cyclization with urea and thiourea in the presence of basic catalyst like KOH afforded 6-[2-(2,4-dichlorophenyl) imidazo [1,2-a] pyridine-3-yl]-4-arylpyrimidin-2 (*1H*)-ones **(3a-l)** and 6-[2-(2,4-dichlorophenyl)imidazo[1,2-a]pyridine-3-yl] -4-arylpyrimidin-2(*1H*)-thiones **(4a-l)**.
Elemental analysis and IR, 1H NMR, and mass spectral data have confirmed the structures of the synthesized compounds 2a-l, 3a-l and 4a-l**.** All the synthesized compounds were screened for their antimicrobial activity against various microbes under identical conditions,

4-(2-Pyridyl)-2H-(1) benzopyrans and 4-(-2-pyridyl) 4-hydroxy 3,4-dihydro benzopyrans: A Novel Class of Potential Anti-cancer Agents

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2-H-1-Benzopyrans, commonly known as 2H-benzopyrans or 2H-chromines, are an important structural motif present in the varieties of biologically active natural and synthetic drugs and lead molecules.[1] Interesting chemistry have been exploited to this structural unit for generating diverse series of compounds, have displayed a wide spectrum of potential biological activities,[2] such as anti-cancer, anti-diabetic, anti-HIV, anti-inflammatory, anti-microbial, anti-bacterial, anti-tubercular, anti-feedant, anti-arrhythmatic, anti-estrogenic, anti-anxiety, anti-leishmanial, anti-biotic, anti-filarial, anti-malarial etc. Moreover, their use in the synthesis of various kinds of dyes [3] and agrochemicals [4] are well known. Their major use in the development of diverse kinds of potassium channel openers have made further interest for benzopyran chemistry. [5] In continuation of our recent work [6] towards the development of various derivatives of benzopyrans, We have invented a novel class of substituted benzopyrans, have displayed potential anti-cancer activity.

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Synthesis of Linker Based Artemisinin Dimers Using Michael Addition Reaction

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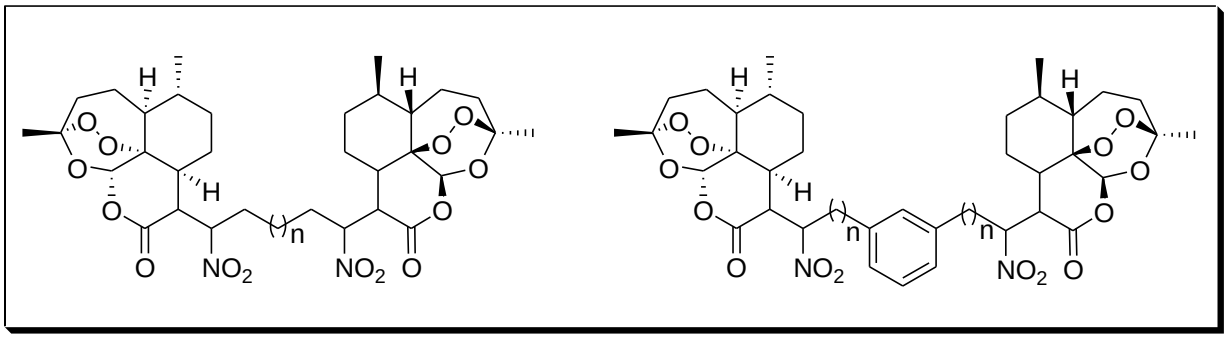
The importance of Artemisinin and related 1,2,4-trioxanes in malaria chemotherapy needs no emphasis [1]. Artemisinin dimers are a new class of semi-synthetic compounds obtained by joining two Artemisinin (or its derivatives) molecules without affecting the 1,2,4-trioxane-ring system. This class of compounds is gaining importance in recent years because of their profound antimalarial and anticancer activity even at very low concentrations [2].



In continuation of our interest on the development of novel Artemisinin derivatives as potent antimalarial agents, we synthesized certain Artemisinin dimmers.The details of this work will be presented.

References:

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DDQ Catalyzed Stereoselective Synthesis of (*E*)-α,β-Unsaturated Aromatic Carbonyl Compounds

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Dehydrogenation of various dihydro aromatic carbonyl compounds to their α, β unsaturated counterparts is an important and frequently desired transformation for the synthesis of various biologically active scaffolds as well as in complex natural product synthesis. For instance, the cinnamic ester moiety is widely represented in various natural products and has also been recognized to possess important medicinal and industrial applications such as plasticizers, graphics, lubricants, flavors, perfumes and cosmetics. There has been a perceptible dearth of convenient protocols for alpha–beta dehydrogenation of aromatic carbonyl compounds as a majority of the prevalent methodologies require prior derivatization of alpha position with various groups followed by their elimination. In this context, a convenient green synthetic protocol for α,β-dehydrogenation leading to the synthesis of (*E*) α, β unsaturated aromatic compounds is developed.

Synthesis and Antibacterial screening of N-[coumarin-6-yl-amino] spiro-indoloazetidin-2-ones/thiazolidin-4-ones

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Coumarins are now a day an important group of organic compounds that are used as bactericides, fungicides, anti-inflammatory, anticoagulant and antitumour agents. There are also many studies on isatin (1H-indole-2, 3-dione) in the literature. The synthetic versatility of isatin has led to the extensive use of this compound in organic synthesis. These pharmacological properties of coumarins and isatin aroused our interest in synthesizing several new spiro compounds featuring different heterocyclic rings fused with the coumarin moiety with the aim of obtaining more potent pharmacologically active compounds.

Coumarin-6-yl-hydrazine hydrate (**1**) on condensation with isatin yields 1, 2-dihydro-3-[coumarin-6-yl-hydrazono]indole-2-one (**2),** which on treatment with thioglycollic acid in dry 1,4-dioxane in presence of catalytic amount of $ZnCl_2$ (anhydrous) affords N-[coumarin-6-yl-amino]spiro-[3H-indole-(1H,2H)-3,2-(4H)-thiazolidin]-2,4-diones (**3**) . Compound (**2**) was also treated with chloroacetylchloride to afford N-[coumarin-6-yl-amino]spiro-[3H-indole-1H,2H-5-chloro-azetidine]-2,4-dione (**4**)**.** The compounds **2**, **3**, and **4** have been conformed on the basis of their spectral and analytic data. The synthesized compounds **2, 3** and **4** were screened for the antibacterial activities against Gram positive and Gram-negative bacteria and have been found to exhibit significant antibacterial activities.

Cyanoethylation of Thioglycollic Acid in the Presence of Antialcoholic Drug and its Determination with Iodine Monochloride

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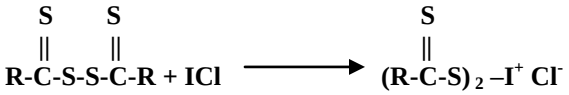
Cyanoethylation is one of the important reactions for the synthesis of drug intermediates, plasticizers, insecticides, emulsifiers, additives for synthetic rubber and physiologically active compounds. [1] A titrimetric and spectrophotometric method has been reported for the cyanoethylation of thioglycollic acid at pH 7.0 by using phosphate buffer on heating at 50^{o} C for 5 mins with the help of acrylonitrile in the presence of antialcoholic drug Disulfiram (tetraethylthiuram disulfide) which act as a deterrent to alcohol consumption in patients. As Disulfiram is sulphur containing drug and can be determined with the help of interhalogens as reported by srivastava et al [2-3]. Iodine monochloride has been used as an oxidant for the determination of Disulfiram alone, in mixture containing thioglycollic acid and for cyanoethylated products.

The quantitative determination of Disulfiram can be done with iodine monochloride by the following reaction.

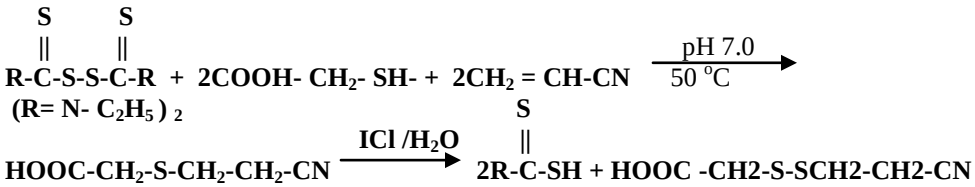


(Disulfiram)
(R= N- C_2H_5) $_2$

A mixture containing thioglycollic acid along with disulfiram can be resolved with iodine monochloride involving the reaction given below.

(R= N- C_2H_5) $_2$ (Thioglycollic acid**)** **(**Diethyldithiocarbamate)

On masking thioglycollic acid with acrylonitrile and then determined by iodine monochloride by the following reaction.



The above products were confirmed by FTIR and ^{1}H NMR study.

References:

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Synthesis and Product Development Studies of Amino Acid Conjugate of Ketoprofen

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The prodrugs designed by classical approach increase lipophilicity of the drug, which decreases the water solubility thus decreasing the concentration gradient, which controls drug absorption. To overcome the limitations of traditional prodrug approach, the solubility behavior of ketoprofen with its L- tryptophan amino acid conjugate in relation to the development of safe and effective oral (solid or liquid) or parenteral formulation(s) for KP. Amino acid conjugate of ketoprofen (KPaa) is of interest due to the poor aqueous solubility of parent drug KP. KPaa was synthesized by conjugation with l-tryptophan by conventional coupling method using N, N-dicyclohexylcarbodiimide and KPaa was characterized by melting point, TLC, photomicrograph, UV, FT-IR, FT-NMR, MS-FAB and DSC. As a part of product development study KPaa was subjected to studies like *in-vitro* KPaa reversion to KP in aqueous buffers of pH 1.21, 2.38. 3.10, 6.22 and 7.41, at a constant concentration (0.05M), ionic strength ($\mu = 0.5$) and at a temperature of 37 ^{0}C ± 0.5 ^{0}C, KPaa showed negligible reversion (1.11 %) up to 24 h study at acidic pH thus suggesting stability in acidic environment of stomach, the rate of reversion increased as pH of medium increased. pH- partition profile, pH- solubility profile and micromeritic studies were also carried out in comparison to pure drug. Both, the solubility and lipophilicity of KPaa exhibited higher values at all pH range as compared to KP. an IQCS value approached zero thus suggesting reducing in the degree of skewness and thus normalization of particle size distribution.

Design and Synthesis of Peptidomimetics as PTP-1B Inhibitors

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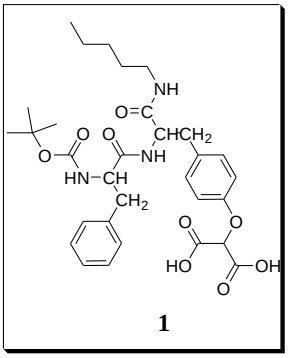
Insulin resistance is the common cause of type 2 diabetes. It is now clear that insulin resistance can result from a defect in the insulin receptor signaling system, at a site where the insulin binds to its receptor. Protein tyrosine phosphatase-1B (PTP-1B) is considered as a negative regulator of insulin signaling which is proved from the PTP-1B knock out mice where the mice lacking the PTB-1B gene have enhanced insulin sensitivity. Low molecular weight peptidomimetic compounds based on O-malonyl tyrosine, derived from tripeptide Ac-Asp-Tyr(SO_3H)-Nle-NH_2 are potent inhibitors of PTP-1B[1]. With this objective we have designed several novel peptidomimetics with surrogate phosphates and phosphate biostears. In an effort to get more potent analogues, we have done various modifications on previously reported O-malonyl analogue [1].On substituting O-malonate with the non-hydrolysable phosphate mimics such as H-Phosphonate, Phenyl phosphonate, Phenyl phosphate, Chloro phenyl phosphates and Methyl phosphonate we did not get the desired results, therefore modifications of the C-terminal pentyl moiety were done in an effort to improve potency. Although pentyl ultimately proved to be the optimal N-terminal group, several viable replacements for the pentyl group were identified, two of which afforded analogues with significant inhibitory activity at 100 µM and IC_{50} values up to 80 µM . In order to increase the stability of amide bond, various peptidomimetic modifications like N-Methylation and substitution with β-amino acid were performed.



1

Substitution with β-amino acid finally resulted in inhibitors with significant IC_{50} values ranging from 10 to 30 µM. Details of synthetic procedure and biological activity will be presented in detail.

References:

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Aromatization of 1, 4-dihydropyridines using Quaternary Ammonium Bromates as the Oxidizing Agent

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Quaternary ammonium bromates have been prepared from the corresponding bromides and used as a mild and efficient oxidizing agent for the aromatization of 1, 4-dihydropyridines to the pyridines.Dialkyl-1, 4-dihydro-2, 6-dimethyl-3, 5-dicarboxylates (1, 4-DHP) are well known compounds having analgesic, curare like properties, antitumour and coronary dilating activities [1,2].They are also reported to have hypotensive activities [3]. Oxidative aromatization of 1, 4-DHP has also attracted considerable attention because metabolism of 1, 4-DHP based drugs involved a cytochrome P-450 catalyzed oxidation in the liver [4]. Due to the biological importance of the oxidation step of 1, 4-DHP, the aromatization reaction reaction has been the subject of elaborate studies in order to mimic the in vivo transformation. 1, 4-DHP and their synthetic analogs are reported to be model compound for oxido-reductase enzymes namely NADPH/NADH. In order to decipher the mechanism of reduction by NADPH/NADH the characteristics of enzyme models are extensively studied.The study on the aromatization of 1, 4-DHP is therefore expected to be of biological importance.

Several methods are reported for aromatization of 1, 4-DHP and notable among them are the use of HNO_3 at 60 ^{0}C [5] , and $NaNO_2$ in acidic media [6], CrO3 in Ac_2O [7], Chloranil in benzene at reflux temperature, $K_2Cr_2O_7$ in H_2SO_4 [8], $KMnO_4$ in acetic acid [9], clay supported metal nitrates [10] and microwave irradiation [11]. Herein is reported a simple and efficient method for the aromatization of 1, 4-DHPs by using the tetra-n-alkylammonium bromates as the oxidizing agent. The oxidant was prepared from easily available tetra-n-alkyl ammonium bromide by a simple process [12].

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Synthesis, Antioxidant Activity and Cytotoxicity of Some 2-amino-4-aryl-3-cyano-7-(dimethylamino)-4*H*-chromenes

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The discovery of 4-aryl-4*H*-chromenes as a new series of potent apoptosis-inducing agents possessing vascular-disrupting activity has been reported. The 4-aryl-4*H*-chromenes inhibit tubulin polymerization and bind at or close to the binding site of colchicine. They are also active in the multidrug resistant MES-SA/DX5 tumor cells and are highly active as single agents and in combination with other anticancer agents in several tumor animal models.
In this study, a new series of 2-amino-4-aryl-3-cyano-7-(dimethylamino)-4*H*-chromenes was synthesized by the condensation of 3-(dimethylamino)phenol, an aromatic aldehyde and malonitrile in ethanol containing piperidine. The assignments of the structure of all the newly synthesized compounds were based on elemental analysis and spectral data (IR, Mass,1H NMR). The antioxidant activity of the synthesized compounds was determined by Ferric Reducing Antioxidant Power (FRAP) and DPPH free radical scavenging methods. Several compounds showed significant antioxidant activity. The cytotoxic activity of the target compounds was also characterized by growth inhibition MTT assay. A panel of four different human cancer cell lines was used for these experiments. Several compounds were found to be highly active in the growth inhibition MTT assay.

^{1}H NMR and X-ray Crystallographic Studies on Robustness of Folded Conformation of pyrazolo[3,4-*d*]pyrimidine Core Based 'Trimethylene Compounds' due to Arene Interaction

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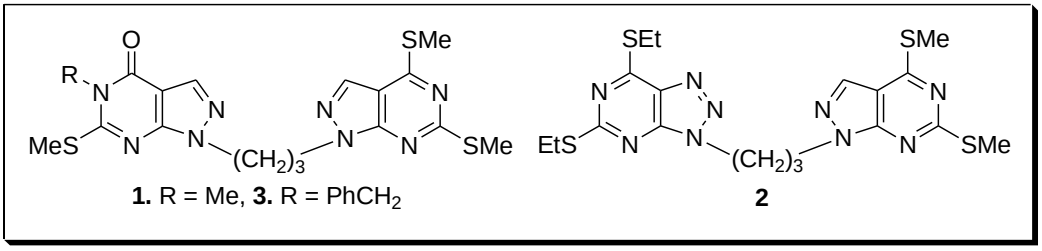
Arene interactions play very important role in structure of DNA, protein folding, drug-receptor binding, stabilization of transition states/intermediates during chemical reactions, stabilization of supramolecular assemblies etc. Since the pioneer work of Leonard, several heteroaromatic core based flexible polymethylene compounds have been used as models to study this interaction. Pyrazolo[3,4-*d*]pyrimidine core (which is isomeric to purine) and polymethylene linker based flexible model is one of them, developed at CDRI, Lucknow. ^{1}H NMR and X-ray crystallographic studies (1995-2007) on many symmetrical pyrazolo[3,4-*d*]pyrimidine core based flexible 'trimethylene linker' compounds showed folded conformation both in solution and solid state, revealing a strong π-π stacking tendency in this nucleus. Compared to symmetrical compounds not much work has been done on related dissymmetric molecules. The first dissymmetric compound (**1**)[1] based on pyrazolo[3,4-*d*]pyrimidine core was reported, recently in 2006, followed by another (**2**)[2] in 2007 showing similar stacking in solution and solid state. Present work reports synthesis, ^{1}H NMR and X-ray crystallographic studies on new dissymmetric molecule (**3**) related to **1** for evaluating its robustness from molecular recognition and crystal engineering point of views.



1. R = Me, **3.** R = $PhCH_2$ **2**

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Studies on Arene Interactions: Synthesis, ^{1}H NMR and Crystallographic Studies on Pyrazolo[3,4-*d*]pyrimidine Core Based Flexible Polymethylene Linker Compounds

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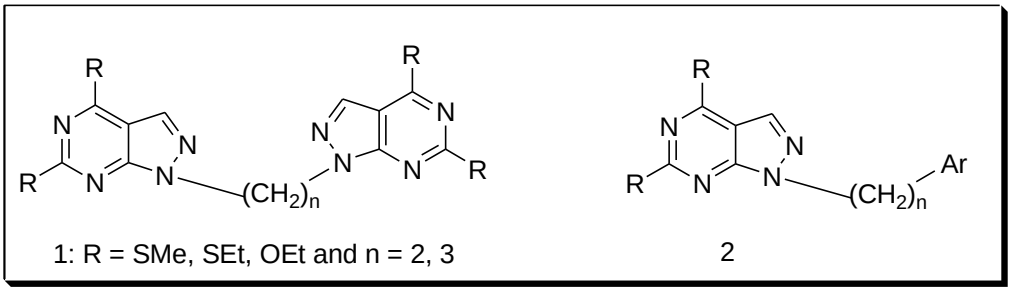
Interactions between aromatic units play a significant role in chemistry, biology and crystal engineering. However, the nature of arene interactions remains unclear. One of the strategies employed to study arene interactions include connecting two aromatic moieties with polymethylene especially 'propylene/Leonard linker' so that arene interactions could be studied by ^{1}H NMR spectroscopy at molecular level.



1: R = SMe, SEt, OEt and n = 2, 3 2

Pyrazolo[3,4-*d*]pyrimidine (PP) which is isomeric with purine provides a good model for studying arene interactions. Studies on this model were done both by analyzing ^{1}H NMR in solution and X-ray crystallography in solid. ^{1}H NMR study in solution showed intramolecular stacking. X-ray crystallography further confirmed intramolecular stacking with formation of an unusual U-motif in case of 'trimethylene linker' compounds. Similar results were also obtained by ^{1}H NMR studies in case of 'ethylene linker' compounds, however, X-ray studies showed open conformation, which highlighted the subtle difference between molecular recognition (solution) and crystal engineering (solid).[1] Robustness of the unusual U-motif has been confirmed in many other related 'trimethylene linker' compounds. Further investigation on dissymmetrical compounds with one pyrazolo[3,4-*d*]pyrimidine nucleus on one side of the linker (ethylene and trimethylene) and other PP moiety replaced by different arene residue also showed intramolecular stacking by ^{1}H NMR and X-ray crystallography (e.g. **2**).[2]
Synthesis, ^{1}H NMR & crystallographic studies of new dissymmetrical polymethylene linker compounds with one pyrazolo[3,4-*d*]pyrimidine core on one side will be discussed.

References:

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QSAR Modeling of N-Aryl- Oxazolidinone-5-carboxamides as HIV-1 Protease Inhibitors

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AIDS (Acquired immune deficiency syndrome) is one of the most frightening infections for which no complete cure has so far been reported. About twenty million people worldwide died of this alarming infection by 2001 and the number is rising steadily till date. HIV-1, which is a cytopathic lentivirus of family *Retroviridae,* causes eventual exhaustion of helper T cells and macrophages and destroys body immune system completely. Protease is an indispensable enzyme for HIV-1 as it gives rise to some important structural and functional proteins like p17, p24, p9 and p7 for the replication of new viral progeny. Being a virus-specific enzyme, protease is considered as a potential target for anti-HIV treatment. N-Aryl-Oxazolidinone-5-carboxamides have been reported to have protease inhibitory action in picomolar level. In order to find out more active and selective compounds, QSAR study was performed using topological indices like E-state and R- state indices along with electronic descriptor like Wang-Ford charges, hydphobic index like partition coefficient, steric descriptor like molar refractivity, geometrical descriptors like principle moment of inertia at X, Y and Z axis and some indicator parameters. Two statistical methods, multiple linear regression and partial least square have been performed to develop QSAR models. Results show that E-state index of atom number 12 and R-state index of atom number 34 are likely to be important because these atoms may confer electronic interaction and van der Wall interaction with the receptors respectively. The study also shows significance of Wang-Ford charges of atom number 5, 9, 20, 23, 26, 27, 29, 32, 35. Three indicator parameters have also been found to be important. One geometric parameter, principle moment of inertia towards X axis is useful for protease inhibitory action. Deletion some of outliers developed statistical quality of the models.

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Ring-opening Rearrangement of 2-Aryl-*N*-tosylazetidines: A Facile Route to Allylamines

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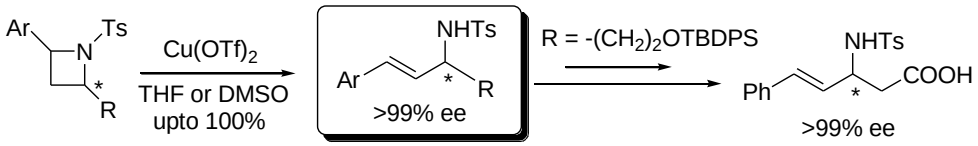
Synthesis of allylamines has been an area of considerable research activity primarily due to their key function as precursors or intermediates in organic synthesis, as well as their presence in several biologically active compounds. Moreover, enantiopure allylamines are the direct precursors for natural and unnatural amino acids. In continuation of our research [1-6] activities in the area of azetidine chemistry, to elucidate the mechanism of nucleophilic ring-opening of 2-aryl-*N*-tosylazetidines, we studied their fate in the presence of Lewis acid in polar solvents and discovered an unprecedented rearrangement of 2-aryl-*N*-tosylazetidines to (*E*)-allylamine. The rearrangement was found to be highly stereoselective towards the formation of (*E*)-isomer exclusively. Further, this methodology has been applied for the synthesis of unnatural olefinic *β*-amino acids.



Ar = Ph, 4-OMeC_6H_4, 4-ClC_6H_4, 2-ClC_6H_4, 3-BrC_6H_4
R = Et, *n*-Pr, *i*-Pr, *n*-Bu, *i*-Bu, -$(CH_2)_2$OTBDPS

Scheme 1

References:

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Computational Allergenicity Prediction of Genetically Engineered Crop Proteins

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According to Codex criteria [1], a novel protein can be classified an allergen, if any of its 80 amino acid protein fragments share at least 35% homology and/ or any 6 amino acid fragment of protein showed 100% homology to a known allergen. To test and validate the Codex criteria for allergenicity prediction, 24 allergenic, non-allergenic and inserted protein sequences each were taken. Studies were performed taking limits of homology to 35, 50, 60 and 70 % to determine suitable percent homology. Proteins were also assessed for their allergenicity using Algpred [2]. Overall homology of 35% was found to be appropriate and increasing above 35% resulted in false negatives. Sequence homology of allergenic proteins gave exact matches for 6, 7 and 8 mer and showed more than 35% homology. Non-allergenic proteins, as expected showed no match in case of 8 mers as well as with 35% homology; however 6 mer match analysis qualified 16 proteins as false positive allergens. Similarly, out of 24 inserted protein sequences, 13 showed positive allergenicity as per 6 mer criteria, however, 7, 8, and 80 mers did not show any match to allergens. Algpred software predicted all the allergenic proteins as allergens. In case of non-allergenic and inserted proteins 6 and 7 false positive results were obtained, respectively, indicating this to a better tool than 100% match with 6 mer criteria. Hence, recommendation of Codex needs to be changed from 6-mer to 8-mer homology along with use of Algpred software for allergenicity prediction.

References:

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[2] www.imtech.res.in/raghava/algepred/

Optimization of Molecular Descriptors Using Machine-learning Approach to Aid Structure Based Drug Designing for Viruses

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Viruses have remained a perplexing enigma for drug designers and scientists ever since their discovery. The main problem has been of limited availability of drug targets because of their tiny proteome and genome size. Available drugs also prove ineffective due to their insignificant binding affinity with viral drug target because of their higher mutation and short generation time in our system. The main concern is to design lead molecules from the available structure information of target molecules. Structure based drug design maps the knowledge of 3D structures of target molecules to the activity. The physiochemical properties of any molecule are numerically represented as descriptors. Descriptors can be derived from parameters such as hydrophobicity, topology, electronic properties, molecular properties and steric effects.In our approach, we focus upon; optimization of molecular descriptors derived from viral drug target-ligand interactions, which are input for effective structure based drug design. [1-3] We consider the variations among the target proteins during optimization of molecular descriptors so that designed drug has significant biological activity in our system. Our approach divided into following steps- 1) Literature mining – Study the viral drug targets for which 3D structures are available, 2) Extraction of molecular descriptors for these 3D structures along with ligand molecules, 3) optimization of these molecular descriptors by machine learning methods 4) Cross-validation of optimized descriptors by known dataset.

QSAR have been used to model the relationships between observed physical, chemical, and biological properties of a compound. These optimized molecular descriptors can be used for selection of suitable lead molecules which have significant binding affinity with viral drug target in our system.

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Green Chemical Approach for the Synthesis of Schiff Bases under Microwave Irradiation

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Schiff bases have a wide range of applications such as corrosion inhibitor, intermediates in various reactions, in perfumery etc. Some are known to be used in many potential drugs and are known to possess broad spectrum of biological activities such as antiviral, antifungal, antiparasitic, antibacterial, anti-inflammatory. It can be synthesized by Microwave irradiation. Reaction of 6-methoxy-1, 3-benzothiazol-2-amine with substituted aldehydes under microwave irradiation (M.W.) gave the corresponding imines (Schiff bases).The structure of all the synthesized compounds was elucidated on the basis of IR, ^{1}H NMR and mass spectral data.

Synthesis of Multiporphyrins and Their Spectral Characterization in Different Conditions

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Multiporphyrins have attracted great attention because of their potential in applications ranging from light harvesting arrays, molecular wires, photovoltaic cells, non-linear optics, to photodynamic therapy. Multiporphyrins with well defined shape and dimensions may be synthesized by covalent linkage than non-covalent bonding. The covalently linked multiporphyrins have been synthesized by carbon-carbon single bonds and polyethylene linkages between two or more porphyrin units by using different reagents and reaction conditions. We report the synthesis of meso-to-meso ethyne and butadiyne bridged multiporphyrins and their spectral and photopysical studies in different reaction conditions.

The synthesis of highly conjugated multiporphyrins involves palladium mediated coupling and Glaser-Hay coupling reaction conditions. The reaction of 5,15-bis-(ethynylphenyl)zinc porphyrin with CuCl in presence of TMEDA under dry air in dichloromethane gave trimer, tetramer and other higher porphyrin oligomers. The products have been characterized by UV-VIS, IR, ^{1}H-NMR and EI-MS spectroscopic analysis in different conditions.

Genomic Signatures of Adaptaion in Different *Prochlorococcus* Strains

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The work is an effort to analyze the nucleotide and amino acid usage patterns in all closely related strains of the marine cyanobacterial species ***Prochlorococcus marinus,*** whose genomes have been fully sequenced. These strains have been isolated from different depths of the ocean, ranging from the turbulent sea surface to the shadowy depths almost beyond the reach of the sun. Although occupying the same hierarchy in the taxonomy table, these strains have been found to adapt to these diverse conditions, which makes the study of their genomes both an interesting and intriguing task.[1,2]

Statistical analysis show a clear segregation in patterns of codon and amino acid usage between the strains adapted to different depths. Especially low light adapted strains (isolated from greater oceanic depths) exhibit a strong asymmetry in usage of codons on their leading and lagging strands of replication. This asymmetry being absent in their high light adapted cousins, which also happens to have smaller genome sizes, suggests an extensive reshuffling of genomic segments and gene loss in course of evolution. The 16S rRNA phylogeny also suggests that the extent of these differences in genomic arrangements and composition between *Prochlorococcus* strains are in some way correlated to their evolutionary distances from the last common ancestor. Gene rearrangement plots between strains representative of different light adaptations were drawn during the analysis which clearly shows the extent of this reshuffling.

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Solvent Free Microwave Assisted Synthesis of 3-(2-methylquinoxalin-3-yl)-2-substitutedphenyl)thiazolidin-4-ones

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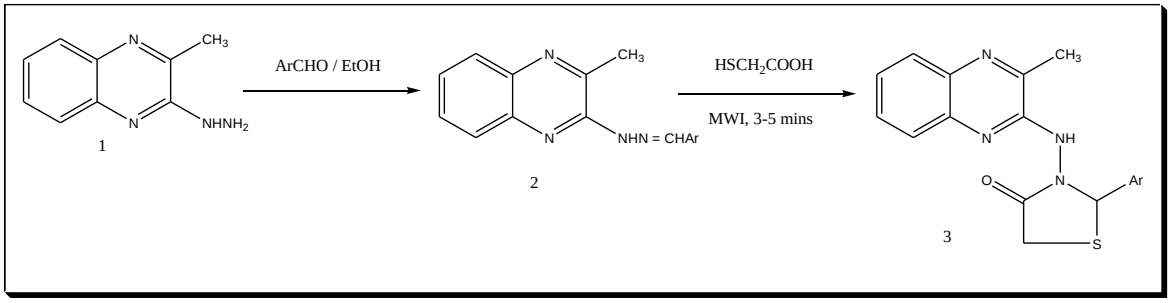
Thiazolidinones are known to have antibacterial, antifungal, anticonvulsant, anti-inflammatory, anti-HIV, anticancer and antimicrobial properties. We here in report, rapid and efficient conversion of arenecarbaldehyde-3-methylquinoxalin-2-yl-hydrazones to the corresponding heterocyclic thiazolidin-4-ones (Scheme 1) using microwave assisted synthesis on silica support under solvent free conditions. These solvent-free microwave assisted reactions provide an opportunity to work with open vessels thus avoiding the risk of high-pressure development and increasing the potential of such reactions to upscale. Equimolar amounts of the appropriate heterocyclic hydrazone, thioglycollic acid was mixed in pestle and mortar homogeneously with 1 g of silica gel (60-120 mesh). This mixture upon subjection to microwave irradiation at 60 % power output (540 watt) for around 3-5 minutes yielded the desired products which were isolated, purified and characterized by various spectroscopic techniques such as IR, ^{1}H-NMR and mass spectrometry. Yields were ranging from 58 to 75 %.



Scheme 1

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QSPR Correlation of Molecular Discriptors and Relaxometric Properties of Novel MRI Contrast Agents

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Magnetic resonance imaging (MRI) is a powerful, non-invasive, and widely applied diagnostic technique, which allows to obtain inside images of the human body. Now adays, more than one-third of the MRI scans are performed by administration of a contrast agent, usually a gadolinium complex. Gadolinium (III) ion is suitable, due to its favorable paramagnetic properties, as it increases the relaxation rate of the surrounding water protons, making the region of interest brighter than the background.

All chemicals used in present study of analytical grade purchased from Sigma, Aldrich and Merck chemical Co. IR spectra were recorded on the FT-IR perking Elmer spectrum BX spectrophotometer. NMRD spectra were obtained by using Brucker NMR instrument 100 MHz. The 2D –QSAR correlation was done with hyperchem software and statistical analysis were done with SYSTAT-7 software. 2D QSAR studies correlate the ligand protonation and relaxometric studies with physio-chemical properties for a series of phosphonic acid derivatives of tetraaza macrocyclic derivatives, using both potentiometric titrations and NMR. The decreased basicity of the backbone nitrogens brought about by amide formation modifies their percent protonations in ways that allow a rationalization of the macroscopic protonation constants. The protonation constants of the ligands and the stability constants of the corresponding 1:1 Gd^{3+} chelates are highly sensitive to the number of phosphonic groups modified but only moderately sensitive to the nature of the side chains of the amide moieties.The correlation facor and predicted mathematical equation gives the idea of most important factors for futher studies.Our results also confirm that QSAR correlation is very important tool for searching novel MRI contrast agent as well as other imaging modalities from bench to clinical trials.

Synthesis and Studies of Mannich Bases of 2-chloro 4-nitro benzamide as Potential Antimicrobial Agent

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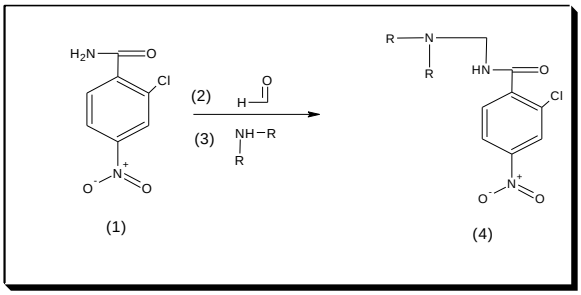
Mannich reaction is a classical method for synthesis of numerous pharmaceutical, bioactive and natural products [1]. Interest in Mannich bases has been quite attractive and wide ranged considering the enormous domain of the applications involving variant nature. While, a large number of Mannich bases continue to be synthesized to explore their biological potential [2], there is an additional effort to look for variations in the execution of Mannich reaction. 2-chloro 4-nitro benzamide is the derivative of benzoic acid and used topically as antiprotozoal agent [3]. Morpholine and piperazine are well known for their physiological activities [4,5] were used as building blockers for making Mannich bases from 2-chloro 4-nitro benzamide. Due to active hydrogen, 2-chloro 4-nitro benzamide undergoes Mannich reaction. The pharmacological effectiveness of 2-chloro 4-nitro benzamide and secondary amines prompted us to introduce these moiety into 2-chloro 4-nitro benzamide, which may furnish products with enhanced therapeutic potency [6]. The Mannich bases of this compound have proved to be more effective and less toxic antibacterial agent [7]. The purity of synthesized novel Mannich bases were checked by thin layer chromatography and the chemical structure of Mannich bases were confirmed using elemental analyses, UV, IR and ^{1}H NMR spectroscopy. All synthesized Mannich bases were evaluated for their antibacterial activity towards pathogenic Gram-negative bacteria (*E.coli and K.pneumoniae*). The results were stastically analyzed.



Scheme 1

References:

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Diversity Oriented Green Approach to Fused-ring 1,3-oxazin-2-ones(thiones) from Carbohydrates as Biorenewable Feedstocks

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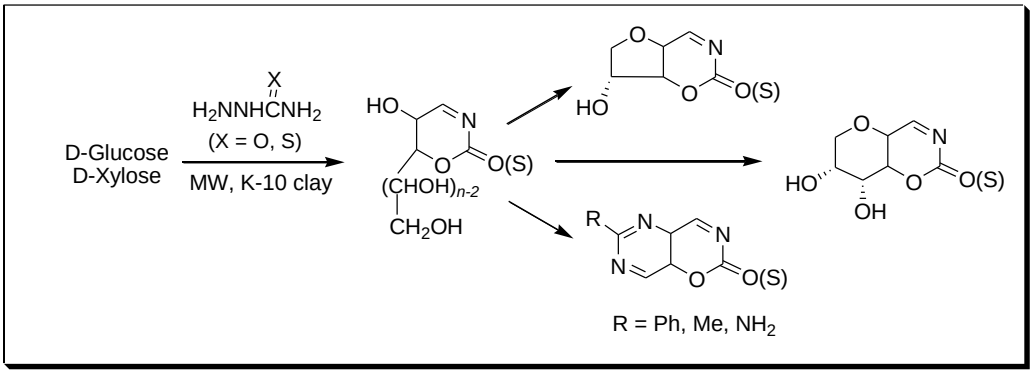
A raw material as feedstock should be renewable rather than depleting wherever technically and economically practicable'. This quotation is one of the 12 principles of green chemistry and thus, a synthetic approach involving the utilization of biorenewable feedstocks is in accordance with the sustainable development. [1] Diversity oriented (DOS) plays an important role in drug discovery processes because it provides attractive scaffolds that can be utilized for exploiting chemical diversity and generating drug-like screening libraries to screen for lead candidates. A benzoxazine derivative, Efavirenz (Sustiva), has been approved by the FDA in 1998, and is presently in clinical use for the treatment of AIDS. This has stimulated continued interest of synthetic chemists in fused-ring oxazines [2] and encouraged us to devise the present diversity oriented green synthesis of fused-rings 1,3-oxazin-2-ones(thiones) using biorenewable feedstocks. D-glucose/D-xylose 4-phenylsemicarbazone/thiosemicarbazone-derived 1,3-oxazin-2-ones(thiones) afforded:

1. Perhydrofuro/pyrano-1,3-oxazin-2-ones(thiones) on microwave (MW) irradiation under acidic condition.
2. Pyrimidino-1,3-oxazin-2-ones/(thiones) on Melaparade reaction followed by treatment with amidines/ guanidine under solvent-free MW irradiation conditions.



Scheme1

References:

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Scope of Coordination Compounds of Lanthanon (III) Ions with Some Bioactive Ligands in Biomedical Science

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Coordination compounds are widely present in minerals, plants & animals world. They have extensive application in Biological & Medicinal field. This prompts us to synthesize the Coordination compounds of lanthanon (III) ion, which are used as a structural probe in the biological system. In the present work thermodynamic and spectrophotometric studies of lanthanon compounds with Schiff base derived from β-diketones & amino acid have been carried out. The presence of active –NH– group in ligand has been regarded as a useful building block in supramolecular chemistry and show antimicrobial, antifungal, antibacterial & antidepressant activity. In the thermodynamic study dissociation constant of ligands and stability constant of their chelates have been determined potentiometrically using Calvin's extension of Bjerrum's method in 20% dioxane-water medium at 25^0, 35^0 & $45^0 \pm 0.1^0$C and at (□ = 0.01M, 0.05M & 0.1M $NaClO_4$). The values of stability constants follow the Stagg & Powell rule. Free energy change, enthalpy change, entropy change have also been calculated. In the spectrophotometric study various energy & intensity parameters such as Slator Condon, Racah, Lande, Judd-Ofelt, nephelauxetic ratio & bonding parameter have been evaluated for different metal to ligand ratio in aqueous medium.

De Novo Design of Antimicrobial Peptides with Simultaneous Modulation of Toxicity based on Amphipathic Leucine Zipper Sequence

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Toxicity of the naturally occurring or designed antimicrobial peptides is one of the major barriers to convert them into drugs. In order to synthesize antimicrobial peptides with reduced toxicity several amphipathic peptides were designed on the basis of leucine zipper sequence and characterized structurally and functionally. The first one was a leucine zipper peptide (LZP) and in others leucine residues at 'a' and/or'd' position were substituted by single or double alanine. The results showed that the LZP and its analogs exhibited appreciable and similar antibacterial activity against the tested Gram-positive and -negative bacteria. However, the single alanine-substituted analogs showed lower toxicity against the human red blood cells (hRBCs) than the LZP and the double alanine substituted analogs were the least toxic. The reduction in toxicity of the alanine substituted analogs compared to the LZP could be related to their impaired assembly in aqueous environment, decrease in helical structure and membrane permeability and altered localization in zwitterionic membrane or hRBCs. Similar secondary structures, localization and permeability in the negatively charged membrane may be attributed to the similar antibacterial activity of the LZP and its analogs. Furthermore in gel electrophoresis in hRBCs and E. coli spheroplast, the structural features of the oligomer remained significantly different and almost comparable in respective cells. These findings disclose that assembly of these peptides is pivotal in determining their antibacterial and toxic activity. Moreover it lends a new dimension to the designing of peptides with desired activity by altering/modulating their assembly in a particular cells. The results suggest a novel approach of designing antibacterial peptides with modulation of toxicity against hRBCs by employing the leucine zipper sequence. Also, the results demonstrated that this sequence could be utilized for designing novel cell-selective molecules for the first time to the best of our knowledge.

QSAR Study on Oxadiazones and Oxadiazinethiones : Selective Monoamine Oxidase type B Inhibitors

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Oxadiazinones and Oxadiazinethiones are of pharmacological interest because of their key role in neurotransmitter and in many neuropsychiatric disorders. QSAR study were performed on a series of 11 derivatives of Oxadiazinones and Oxadiazinethiones using vander Waal,s volume(V_w), equalized electronegativeity (X_{eq}) and topological index(Ґ) parameters.

QSAR studies through MRA led to the conclusion that both electronic and steric factors are important and the size of the substituent seems to cause hinderance in the binding of the drug with receptor site, as shown by (-)ve coefficient of Ґ, whereas (+)ve coefficient of X_{eq} reveals that electronic groups are favourable for the drug to become more potent and (+)ive coefficient of indicator consider for the most active reference compound clogyline also indicates that drug structure should be similar to the reference compound, having electronegative and small substituents.

Structural Analysis of Purine Nucleoside Phosphorylase of *Schistosoma Mansoni.*

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Schistosomiasis is a chronic, debilitating, major human parasitic disease caused by trematode parasites of the genus Schistosoma infecting over 200 million people in more than 74 countries throughout the world. Purine Nucleoside Phosphorylase (PNP) [EC 2.4.2.1] of nucleotide salvage pathway is reported to be a good drug target for Schistosomiasis. The complex of human PNP with guanosine where guanosine is a natural substrate of *S. mansoni* PNP as well, retrieved from PDB, was analysed using HyperChem 7.5 for the identification of its substrate-binding residues. The corresponding amino acid residues in the *S. mansoni* PNP were identified by manual inspection of the sequence alignment of human & *S. mansoni* PNP. The amino acid residues of *S. mansoni* PNP with a potential for hydrogen bond formation with guanosine were identified by calculating the inter-atomic distances between the guanosine & amino acid residues using HyperChem 7.5. Computed Atlas of Surface Topography of Proteins (CASTp) was used to identify the substrate-binding pocket of *S. mansoni* PNP. Structure alignment of *S. mansoni* PNP and Human PNP was carried out using Combinatorial Extension (CE) algorithm which indicated an average RMS deviation of 1.20 Å. However, some of the amino acid residues involved in substrate-binding have *significantly different spatial orientations*. These residues are His 88, Tyr 90, Val 217, Thr 244, Asn 245, His 259. This observation higlights the significance of PNP as a drug target for *Schistosoma mansoni*.

Comparative Study of Schiff's Bases Synthesis Under Classical Heating and Microwave Irradiation

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Among the challenges for chemists include discovery and development of novel and simple environmentally safe chemical processes for selective synthesis by identifying alternative reaction conditions and solvents for much improved selectivity, energy conservation and less or no toxic waste generation and inherently safer chemical products. Therefore, to address depletion of natural resources and preservation of ecosystem it is just urgent to adopt so called "greener technologies" to make chemical agents for well being of human health. Schiff's bases are reported to show characteristic biological activities including antibacterial, antifungal, anticancer and herbicidal properties. Other application of Schiff's bases includes industrial synthesis of high value life saving beta lactam antibiotics from class of penicillins and cephalosporins.

The number of useful properties prompted us to synthesize these Schiff bases and develop cleaner methods to scale up. We have synthesized Schiff's bases using classical organic chemistry methods as well as by heating key raw materials using microwave irradiations. In our experiments we have studied number of reaction parameters such as duration of reaction, yield of products and ease of work up procedure. As expected we have observed significant advantages while using microwave radiations for heating the reactants. Elemental analysis, IR, 1H-NMR and Mass spectroscopy did the structural determination and their confirmation using both technologies. Comparative study and advantages of microwave irradiation for Schiff's bases synthesis over conventional methods will be presented.

Drug Development for the Treatment of Neuropathic Pain: 1, 2, 4-Triazole GABA Derivatives

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Neuropathic pain syndromes are chronic pain disorders associated with damage or permanent alteration of the peripheral or central nervous system. It has been estimated that 1–1.5% of the general population is affected with neuropathic pain. Till date there is no single 'gold standard' medication for neuropathic pain and it is managed with few effective therapeutic options like anticonvulsants, antidepressants, opioids and topical local anesthetics. γ-Aminobutyric acid (GABA) is the principal inhibitory neurotransmitter in the mammalian brain. It has been well documented that the reduction of GABAergic neuronal activity plays an important role in the pathophysiology of a number of neurological disorders, including epilepsy, anxiety and pain [1]. Various chemical analogues of GABA like gabapentin and pregabalin have been shown to attenuate neuropathic pain in both animal and human studies [1]. In the present study, various GABA analogues with 1, 2, 4-triazole-2H-3 one nucleus were synthesized and evaluated for their antiallodynic and antihyperalgesic activities in two rat models of neuropathic pain namely the sciatic nerve ligation and L5 spinal nerve ligation models. The titled compounds were synthesized by the medicinal chemistry research laboratory of our institute. The 4-aryl substituted triazole derivatives of GABA were named from **SP1** to **SP5**, while the 5-aryl substituted derivatives were named from **TN1** to **TN5**. For antinociceptive screening, the rats were anesthetized with ketamine (75 mg/kg, i.p.) and xylazine (5 mg/kg, i.p.) and four loose ligatures with a 4-0 silk thread along the sciatic nerve were made for the chronic constriction injury (CCI) model and a single tight ligation of the L5 spinal nerve was made for the spinal nerve ligation (SNL) model as previously described [2,3]. Compounds were administered intraperitoneally at 100mg/kg dose level on day 9 post-surgery. The control group rats received the vehicle (30% PEG 400). Behavioral signs of different components of neuropathic pain namely spontaneous pain, dynamic allodynia, cold allodynia and mechanical hyperalgesia were measured. The pre-dose screening values were used as the animal's baseline scores. In SP series **SP3** and **SP-4** were active in both CCI and SNL models. **SP1** and **SP2** had non-uniform responses among various behavioral tests, while SP5 was totally inactive in both of the models. In TN series **TN1** was the most active throughout the period of 2.5 hours in both the models. TN-5 was active in all behavioral studies of SNL model but active only against spontaneous pain and dynamic allodynia in CCI model. **TN-2** and **TN-4** showed a non-uniform reduction of pain in various behavioral studies of both CCI and SNL models. **TN-3** was inactive in both of the models. In conclusion, we have shown that aryl substituted triazole derivatives of GABA produce antinociceptive action in the peripheral nerve injury (CCI and SNL) models of neuropathic pain.

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Design and Synthesis of Novel Inhibitors for *Plasmodium Falciparum* Lactate Dehydrogenase (*Pf*ldh)

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Malaria is claiming around 2.7 million lives annually. Resistance against first line antimalarials like chloroquine, quinine, amodiaquine, and halofantrine is alarming, thus calling in for the identification of novel antimalarial agents. The absence of a functional TCA cycle makes glycolysis the main source of ATP generation during the asexual erythrocytic stage. Glycolysis requires a continued supply of NADH which is generated through the conversion of pyruvate to lactate which is catalyzed by the lactate dehydrogenase (LDH) enzyme. Hence, inhibition of *pf*LDH stops NADH regeneration leading to the cessation of the glycolysis pathway of ATP generation; which subsequently results in parasite death. Selective inhibitors for the *pf*LDH provide an important route to novel hits that could prove to be potent antimalarials agents.

Computational studies were carried out on a series of 3,4-di-substituted azole based compounds using *InsightII v2005L* (Accelrys Inc., USA), *Sybyl v7.1*, (Tripos Inc., USA), and *Gold v3.2* (CCDC, UK). The crystal structure of *pf*LDH (PDB code 1T24) and *hs*LDH (PDB code 1T2F) were subjected to docking validation studies to establish the virtual screening protocol using the oxadiazole (OXD-1) as the ligand. The crystal structure validation was followed by the virtual screening of the *iResearch* molecular database for searching precise hits. Top-scoring hits were modified iteratively based on docking scores and binding poses, which were then subsequently taken up for synthesis. Literature revealed important kinetic differences in the activities of *pf*LDH and *hs*LDH. To check for the specificity, docking studies were carried out on the synthesized molecules for the *pf*LDH and *hs*LDH enzymes which revealed important structural differences in the substrate binding site.

A new set of structurally diverse substituted pyrans, and pyridines has been synthesized and characterized by IR, NMR and MS.

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Synthesis and Biological Evaluation of Quinoline-Based Piperazine Derivatives as a Antimalarial Agents

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In terms of human suffering, malaria is clearly the most important parasitic disease. Furthermore, the worldwide burden of malaria is increasing in part due to the unfortunate spread of resistance to most, if not all, of the drugs that were once effective and safe.Among these drugs, Chloroquine (CQ) had been the primary therapy for nearly half a century, CQ was safe, effective, widely available and remarkably inexpensive and could be administered to pregnant women and infants but Plasomdium falciparum , the cause of the most deadly variety of malaria is now CQ-resistant in nearly all malarious regions of the globe. The mechanism of action of CQ-resistance is compound specific.So there is still scope to develop new quinoline baesd derivatives as antimalarial agents by doing modification in the side chain. Keeping this fact in view, we have synthesized a small series of quinolin-based piperazine derivatives.All the compound have been evaluated In Vitro against plasmodium falciparum strain NF54 exhibiting activity in the range 1.00 to 0.125 μg/ml (MIC).

Synthesis and Biological Activity of Tetrapyrrole Ethanolamides as Novel Anticancer Agents

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Photodynamic therapy (PDT) which involves irradiation of a photosensitizer with a light source in the visible or near IR is a mean to treat cancer cells.[1] The photosensitizers are usually non-toxic without appropriate light exposure but produce reactive oxygen species (singlet oxygen) when exposed to a light source in the presence of oxygen which leads to tumour damage.[2] In cancer treatment, the efficacy of a PTD dye lies in its capacity to accumulate selectively in tumor tissues as well as its overall good drug clearance ability. Thus, a clinically useful PDT drug should demonstrates, not only selective retention in tumour tissue but also, rapid clearance in healthy tissues. Skin photosensitivity is a major impediment in PDT treatment. In our continuous efforts towards the synthesis of original anticancer agents, we have recently reported two tetrapyrrole ethanolamide derivatives (**1** and **2**) showing dual action properties: chemotherapeutic and photodynamic activities (**Figure 1**).[3] The *in vitro* cytotoxic and photohaemolytic activity results confirmed their potential as anticancer agents. This prompted us to further evaluate these ethanolamide derivatives for their *in vivo* anticancer activity, toxicity and pharmacokinetic properties in order to assess their efficacy as tissue selective anticancer chemotherapeutics and photodynamic therapeutics. We have found that ethanolamide derivatives effectively prevented the secondary growth of tumours without any apparent toxicity and good tissues clearance. The prevention of secondary tumours suggests that these novel molecules may possess some antimetastatic effects. Taken together, the results obtained from these studies suggest that the ethanolamide derivatives may be effective as a dual action drug for cancer treatment.

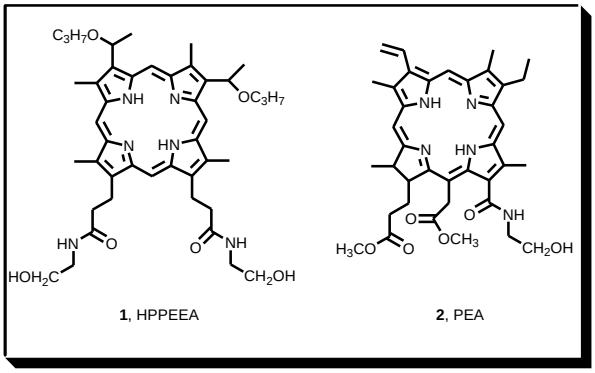

Figure-1

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Production, Purification and Structure Determination of Glucan from *Leuconostoc Dextranicum*

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Polysaccharides are a highly diverse group of polymers, the functional features of which are determined by structural characteristics that may differ in molecular mass, type of osidic linkages, degree of branching and chemical composition. As a result of the unmatched variety of possible chemical linkages, the polysaccharides are the most versatile compounds. This diversity offers broad applications of these polymers in industry. Several polysaccharides have been reported to exhibit a variety of biological activities such as, anti-tumor and immunostimulation. Lactic acid bacteria produce a wide variety of exopolysaccharides. Homopolysaccharide synthesis in lactic acid bacteria has been mainly studied in oral *Streptococci*, *Leuconostoc* species and *Lactobacillus* species. *Leuconostoc* species are commercially exploited for the production of homopolysaccharide glucan.

The production of glucan from *Leuconostoc dextranicum* NRRL B-1146 was carried out in 100ml medium as designed by response surface methodology at 28°C for 48h for obtaining the maximum yield. Glucan from the culture supernatant was recovered by alcohol precipitation and its concentration was determined by phenol-sulfuric acid method in a microtitre plate. The precipitate of glucan was dissolved in 50mM sodium phosphate buffer (pH 7.0) and loaded onto a Sephacryl G-200 column for further purification. The glucan was eluted from the column using the same buffer and the fractions containing glucan were pooled and lyophilized for further analysis. The polysaccharide was characterized using FTIR. Optical rotation was measured at 27°C using a polarimeter. ^{1}H and ^{13}C-NMR spectra for glucan were recorded at 30°C. *Leuconostoc dextranicum* NRRL B-1146 elaborated a glucan comprising α-(1→6) and α-(1→4) linkages. GLC-MS analysis of the glucan was carried out to determine the percentage of linkages. The surface morphology of glucan was studied by SEM (Fig. 1).

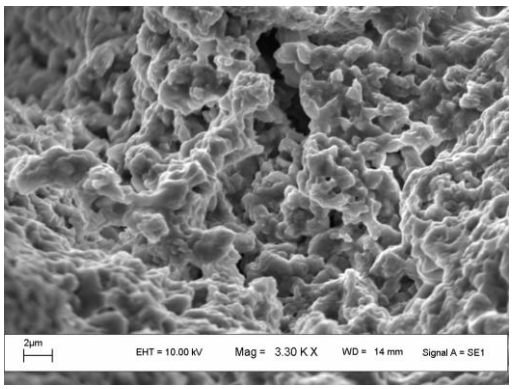

Fig.1 Scanning Electron Micrograph of glucan

Direct Synthesis of 8-Fluoro Purine Nucleosides

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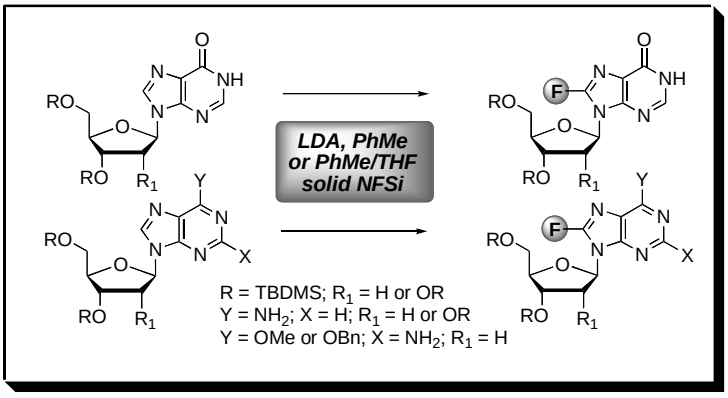
Introduction of fluorine can alter properties of molecules in interesting ways. Nucleosides as a family of compounds are of chemical, biochemical and biological importance, and fluoro nucleosides have stimulated interest in these contexts.[1] Substitution by fluorine atom at the C-8 position has been accomplished through direct reaction with F_2/N_2,[2] the halex reaction with C8 bromo[3] or chloro[4] substituted nucleosides, as well as by electrochemical oxidation in $CH_3CN/Et_3N.3HF$.[5] Recently, we discovered that fluorination of carbanions by *N*-fluorobenzenesulfonimide under homogeneous conditions led to recovered starting material only, whereas under *heterogeneous conditions*, high yields of fluorinated products were obtained.[6] We have therefore explored the direct metalation-fluorination of a series of purine nucleosides. The results of this approach for nucleoside fluorination, leading to the first synthesis of 8-fluoropurine 2'-deoxyribonucleosides and that of fully deprotected 8-fluoro-2'-deoxyadenosine, are presented.



Scheme1

References:

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Rapid Synthesis of Fused Bicyclic Thiazolo-Pyrimidine and Pyrimido-Thiazine Derivatives Devoid of Use of Catalyst by Microwave Assisted Method

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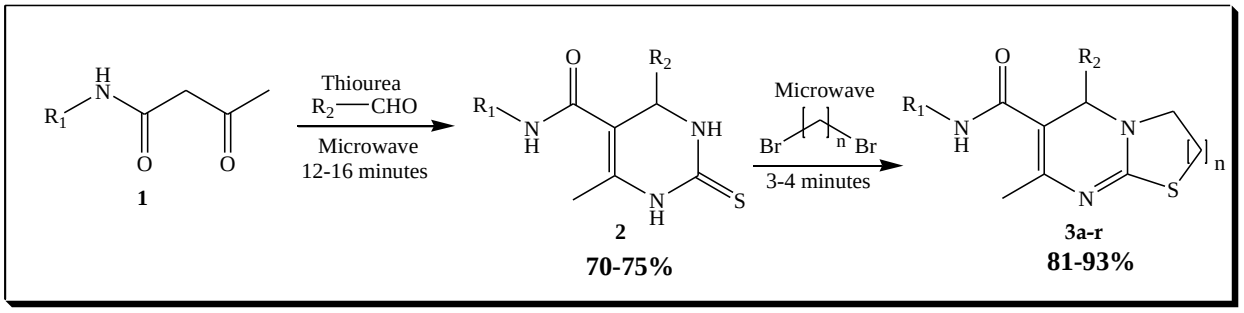
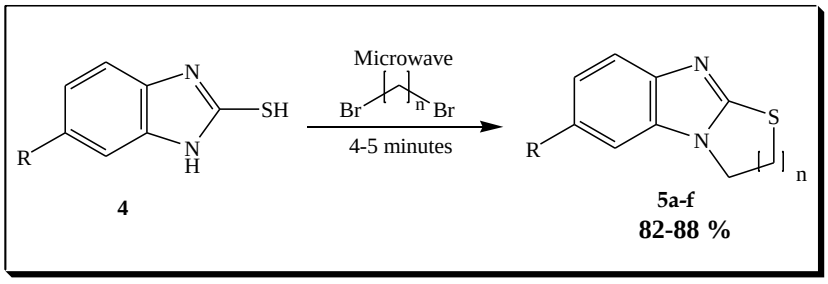
Current paper reports the rapid microwave assisted synthesis of compounds containing fused bicyclic systems. Dihydropyrimidines obtained via microwave assisted Biginelli reaction were treated with dibromo alkanes under microwave conditions to yield thiazolo-pyrimidine and pyrimido-thiazine systems. The usefulness of method lies in carrying out reaction without catalyst and solvent in shorter time.(3a-r & 5a-f) The reaction was successfully extended to develop fused systems from benzimidazole-2-thiol.



Scheme 1



Scheme 2

Microwave-Assisted And Zn[L-Proline]$_2$ Catalyzed Tandem Cyclization Under Solvent Free Conditions: Rapid Synthesis of Chromeno[4,3-*c*]-Pyrazol-4-Ones

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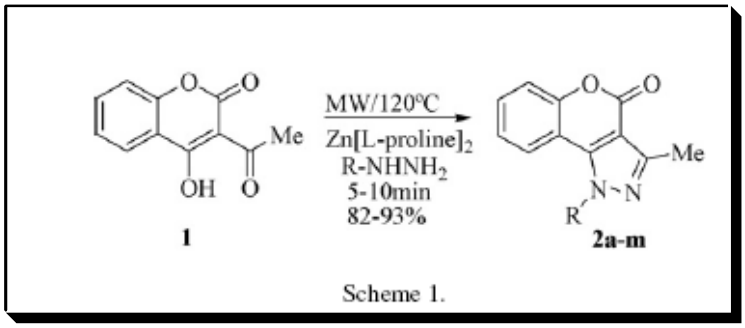
Present study and investigations reveals that, the hydrazones of 3-acetyl-4-hydroxycoumarin undergo ring cyclization to give, 3-methyl-1-substituted phenyl-1*H*-chromeno[4,3-*c*]pyrazol-4-ones (2a–m) under the influence of microwave irradiation and by using Zn[L-proline]$_2$, a Lewis acid catalyst first time for title products. The overall yields of the products were found to be 82–93%. Without use of the catalyst, no reaction progress was observed. No significant changes in the overall yields of the products were observed at high microwave power and at high temperatures. The reusability of the catalyst was also checked and found up to seven cycles successively.



Scheme 1.

Prediction of Binding Affinity of TAP Binders From C-Terminal Domain Human Papillomavirus Oncoprotein E7

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Human papillomavirus (HPV) is one of the most common causes of sexually transmitted disease (STD). Human papillomavirus viral peptides are most suitable for subunit vaccine development because with single epitope, the immune response can be generated in large population [1]. TAP is a transporter associated with MHC class I restricted antigen processing. The TAP is heterodimeric transporter belong to the family of ABC transporter, that uses the energy provided by ATP to translocate the peptides across the membrane [2]. The subset of this transported peptide will bind MHC class I molecules and stabilize them.These MHC-peptide complexes will be translocated on the surface of antigen presenting cells (APCs) [3, 4]. In this assay we predicted the binding affinity of Human papillomavirus oncoprotein e7 having 56 amino acids, which shows 49 nonamers. Small peptide regions found as 9-RHKILCVCC (score 6.186), 34-LRTLQQLFL (Score- 6.091), 31-AEDLRTLQQ (Score- 5.979), 8-QRHKILCVC (Score- 5.960), 45-LSFVCPWCA (Score-5.604), known as oncoprotein e7TAP transporter. Adducts of MHC and peptide complexes are the ligands for T cell receptors (TCR). These complexes elicit the immune response for clearing various intracellular infections. Prediction methods based on the specificity of TAP transporter will complement the wet lab experiments and speed up the knowledge discoveries on the basis of these two computational algorithms [5,6].

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Novel and Efficient Synthesis of Indolylazoles

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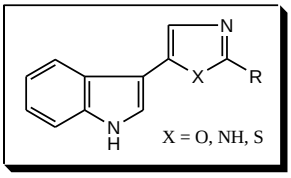
A number of indole alkaloids produced by many species of Streptomyces are known to display anticancer, antibacterial and antiviral activities [1]. Some of the naturally occurring indole alkaloids containing 2,5-disubstituted oxazoles are pimprinine, pimprinethine, pimprinaphine etc. Recently, indolylazole, Labradorin 1 is reported to display GI_{50} value of 9.8 μg/mL against human cancer cell line for NCI-H 460 [2]. Although, there are many procedures reported for the synthesis of indolylazoles, but most of them suffers from lack of generality, rare availability of starting materials, rigorous reaction conditions, lengthy and complicated procedures [3]. In continuation of our programme to develop a novel and biologically potent heterocyclic compounds, we have discovered a short and high yelding method for the synthesis of various indolyloxazoles and its analogues. The key steps in this protocol involve formation of β-hydroxynitro compounds and α-acylaminoketones. The intermediate α-acylaminoketones have been further utilized for the synthesis of indolyl thiazoles and indolylimidazoles in very good yields. The details about this synthesis will be presented in the conference.



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A Facile Synthesis of 6,12-Disubstituted 5,7-Dihydroindolo[2,3-*B*]Carbazoles from the Reaction of Indole and Aldehyde Catalysed by Molecular Iodine

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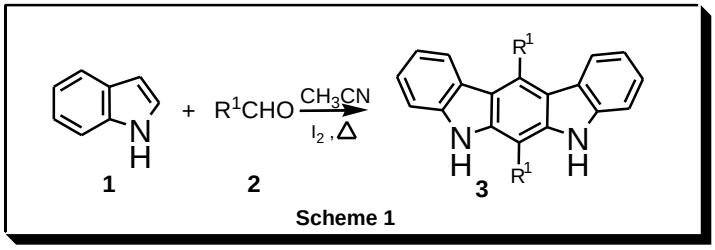
Since the first isolation [1] of an indolocarbazole (ICZ) alkaloid in 1977, the importance of this family of natural products is well recognized by chemists, biologists, physicians and pharmaceutical companies. Compounds with this ring system possess significant biological activities. Therefore, considerable efforts have been made for the preparation and synthetic manipulation of these molecules to find useful compounds [2]. As a result of this effort a number of ICZ analogs have been obtained with diverse biological activities some of which are currently used as potential drugs [3] and some other being tested in clinic for their future use against cancer and other diseases. Indolo[2,3-*b*]carbazole is one of the five possible isomeric indolocarbazoles that possesses anti tumor, anticancer activity [4]. But interestingly, a literature survey reveals only a few reports for the synthesis of it. The use of molecular iodine in organic synthesis has been known for a long time and in the recent years it has received considerable attention as an inexpensive, nontoxic, readily available and mild Lewis acid catalyst property. As a part of our continued [5] work on indoles and synthesis of diverse heterocyclic compounds of biological significance we are reporting here a very simple, highly efficient and cost effective procedure for the synthesis of 6,12-disubstituted 5,7-dihydroindolo[2,3-*b*]carbazoles (**3**) from the reaction of indole (**1**) with aldehyde (**2**) using molelcular iodine (I_2) as catalyst.



Scheme 1

The details of the work will be presented.

References:

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Antioxidant and Antithyroid Activity of *Bauhinia Variegata* Bark

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Bauhinia variegata Linn. (Leguminaceae) is commonly known as 'Kachnar' in Hindi. It is distributed almost through out India. Its powdered bark is traditionally used in bronchitis, leprosy, tumours [1] and ulcers and its extracts have been found to have antibacterial and antifungal activity. [2,3,4] The roots are used as antidote to snake poisoning. The objective of the present work was to evaluate its antioxidant and antithyroid activity.

The antioxidant and antithyroid activity of Bauhinia variegata bark was evaluated in albino rats as per the protocol sanctioned by CPCSEA and IAEC. The results revealed that extracts of Bauhinia variegata bark had significant effect on the markers of oxidative stress (i.e. LPO, SOD, GSH and CAT). These extracts reduced oxidative stress as indicated by the changes observed in markers of oxidative stress in control, hypothyroid, hyperthyroid and stressed group as compared to their respective normal. The results were comparable with standard antioxidant (vitamin-E) treatment. This showed that the Bauhinia variegata bark has antioxidant property.

The extract of Bauhinia variegata bark also showed significant changes in thyroid function tests. The treatment of the extracts exhibited decrease in the levels of T_3 and T_4 as compared to their respective normal in different thyroid states as well as in stressed state. This indicated antithyroid effect of Bauhinia variegata extracts. Thus Bauhinia variegata bark showed significant antioxidant and antithyroid activity.

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Microwave Assisted Synthesis and Pharmacological Screening of Fluorinated Spiro Heterocycles

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Green Chemistry is an imported area for the Science and technology to pursue for the benefit use of solvents that have carcinogenic properties is an attempt towards greening of chemistry and thereby protecting the environment. Multi-component reactions leading to interesting heterocyclic scaffolds are particularly useful for the creation of diverse chemical libraries of 'drug-like' molecules for biological screening, since the combination of three or more small molecular weight building blocks in a single operation leads to high combinatorial efficacy. The chemistry of Spiro indoles in which an indole ring is joined to sulfur and nitrogen containing heterocycles at the C-3 position through a Spiro carbon atom is of great interest due to their physiological and biological activities. Spiro Indolo-thia compounds are known to possess various biological activities.

Reaction of fluorine containing Indole-2,3-dione with substituted anilines and different mercapto acids under varying reaction conditions such as temperature, reaction period and molar ratio of the two reactants, have been investigated. The reaction of 3-indolylimines with a slight excess of acid at room temperature, resulted in the formation of an acidic compound, instead of expected Spiro product, which has been further subjected to acetylation and chloroacetylation. The Spiro compounds were converted into corresponding thiones.

Representative compounds were screened from antifungal and antibacterial activities. The compounds have been characterized on the basis of elemental and spectral studies.

A Novel Eco-friendly Approach for the Functionalized Dihydropyrimidines from Biorenewable Resources

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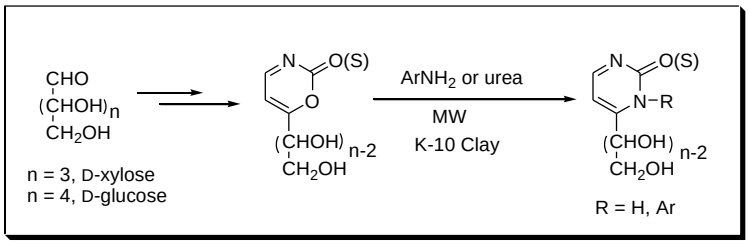
Functionalized dihydropyrimidines (DHPMs) represent a heterocyclic system of remarkable pharmacological efficiency. For example, appropriately functionalized DHPMs are orally active hypertensive agents, α_{1a} adrenoceptor selective antagonists as well as valuable new leads for anticancer and AIDS therapy [1]. Biorenewable resources are new and rapidly developing concept in the environmental and chemical sciences that concerns the wide use of biorenewable materials for industries. Carbohydrates are the major biorenewable feedstocks for synthesizing various industrially and biologically important compounds. In pursuing our work on functionalized pyrimidines [2-4], we have developed a green strategy for a novel synthesis of functionalized DHPMs using carbohydrates as biorenewable resources.

The synthesis is accomplished by reacting D-glucose/D-xylose semicarbazone or thiosemicarbazone-derived 1, 3-oxazin-2-ones/thiones with aromatic amines under solvent free microwave irradiation conditions in a one-pot procedure. The present synthetic strategy involves aza-Michael addition followed by dehydrative ring transformation leading to higher yields of functionalized DHPMs in a short reaction time.



Scheme 1

References:

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CoMFA and CoMSIA 3D QSAR Studies on Phenothiazines, Traizole and Acridines Derivatives as Mycobacterium *tuberculosis* Inhibitor

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Using the Comparative Molecular Field Analysis (CoMFA) and the Comparative Molecular Similarity Indices Analysis (CoMSIA), the paper describes three-dimensional quantitative structure–activity relationship (3D-QSAR) models for the acute toxicity logMIC (MIC in $\mu mol\, l^{-1}$) of 92 Phenothiazines [1,2,3], triazoles [4] and acridines [5] derivatives as *Mycobacterium tuberculosis* (MTB) inhibitors. The CoMFA model produced statistically significant results, with the cross-validated and conventional correlation coefficients being 0.566 and 0.926, respectively. The best results were obtained by combining steric, electrostatic, donor, and H-bond acceptor fields in CoMSIA, in which case the respective cross-validated and conventional correlation coefficients were 0.645 and 0.872. The predictive abilities of CoMFA and CoMSIA were determined using a training set of 76 compounds and validated with a test set of 16 compounds. The results provided clear guidelines and reasonably good activity predictions for novel inhibitors design.

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Isolation and Amino Acid Sequencing of B-Amylase from *Sorghum bicolor* Leaves

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β-amylase allelic forms have different thermo stability and kinetic properties, which critically influence their malting quality. Beta-amylase has applications in the beer industry, in the production of maltose syrup, traditional use in the manufacture of infant food. Sorghum β-amylase is highly stable to heat. β-amylase was extracted from *Sorghum bicolor* (Var. Amarnath 2000) leaves and purified by the conventional method of enzyme purification. It was done by ammonium sulfate fractionation followed by gel filtration on Sephadex G-200 and ion exchange chromatography by DEAE Sephacel. The fractions were dialyzed overnight and lyophilized. β-amylase assay was done based on the colorimetric method using 3,5-dinitrosalicylic acid reagent [1]. Beta amylase activity was stable which was detected in the purified sample. Partially purified solutions could be stored for several weeks at 4 °C without significant loss of activity of beta amylase. The homogeneity of the purified product was done by PAGE. Glycoprotein nature of enzyme was studied by orcinol-H_2SO_4 acid method. The purified enzyme was digested with trypsin and the peptide fragments were sequenced by MALDI-LS/MS [2]. It has MW 55kDa, and a glycoprotein in nature. The protein closely resembles with maize β-amylase and most likely indicative of a common tertiary structure.

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Synthesis and ^{99m}Tc Labeling of Biotin Analog: Potential Candidate for Tumor Imaging

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Biotin is a water soluble B series vitamin, found in all living cells and serves as a coenzyme by binding covalently to carboxalating and decarboxalating enzymes. The interaction of biotin with chicken egg white avidin and its bacterial counterpart streptavidin are among the strongest noncovalent interaction known, with a dissociation constant of 10^{-5}M, which is 10^{+3}-10^{+6} fold higher than antigen-antibody interactions. This high affinity association is resistant to pH changes and chaotropic agents, thus providing stability in vivo. The specificity of biotin binding to streptavidin and avidin has had several medical and scientific applications, including monitoring of proteins at the cellular level, antigen and nuclei acid analysis and drug or toxin targeting as well as in vivo imaging of targeted cells

Considering all these properties and applications of biotin we have developed a targeted radiopharmaceutical for imaging purpose. A novel chelating agent conjugated with biotin has been synthesized and characterized on the basis of spectroscopic techniques (FT-IR, EI-MS, ^{1}H NMR). The chelate was synthesized by the reaction of nitro benzyl malonate and triethylene-tetra amine. The nitro group was converted to amine derivative by using stannous chloride as a reducing agent. Then the conjugation of chelate with biotin was performed at pH 8-9 by using triethylamine,as base. The efficiency of radiolebelling with ^{99m}Tc was more than 95% and radio complex was stable under physiological conditions for more than 24 hrs. The complex shows relatively good blood clearance with $T_{1/2}$(F) and $T_{1/2}$(S).The radiotracer was maximally accumulated in liver and kidney showing their route of excretion by renal as well as hepatic pathway. A significant uptake in tumor shows its potential for tumor imaging.

Ribosomal RNA Gene Based Diagnosis of Malarial Parasites

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Malaria is one of the leading infectious diseases in the world, with 300–500 million clinical cases and 1–3 million deaths each year. PCR is a very sensitive and specific technique and can be used for the detection, identification and quantitative measurement of low parasitaemia of *Plasmodium* species, thus making it an effective tool for diagnostic purposes and useful for epidemiological and drug studies. Detection of the parasites causing human malaria, i.e. *Plasmodium falciparum*, *Plasmodium vivax* and *Plasmodium malariae* is of clinical importance in order to decide on appropriate treatment. The Ribosomal RNA gene cluster is reported to be highly conserved among species. This poster describes the development of a 18S rRNA based Multiplex PCR, based on a format reported in literature (Das *et. al*, 1995) for the detection and identification of these *Plasmodium* species.

PCR based detection system has been devised for detecting all the three species of human malaria parasites *Plasmodium falciparum*, *Plasmodium vivax* and *Plasmodium malariae* based upon their 18S rRNA gene. Using conventionally extracted infected patient material, we have shown bands at ~1.4 kb for *P.falciparum*, ~880bp for *P.malariae* and ~ 500 bp for *P.vivax.* Preliminary evaluation of the system on material derived from simplified lysis procedures has given encouraging results. This system has been used to evaluate severe malaria cases and have been partially reported in the literature (Kochar *et. al*, 2005).

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Synthesis and *in vitro* Antibacterial Activity of Some Novel Thioacetamide Substituted Oxadiazole

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A new series of 5-(pyridinyl)-2-[{2-(aryl/pyrimidinylamino)-2-oxoethyl}-thio]-1,3,4-oxadiazole were synthesized and studied its in vitro antibacterial activity against some mutant bacteria. The biological screening against different gram positive and gram negative bacteria were reported as preliminary results showing a promising activity.

The comparative study of aryl thioacetamide and pyrimidinyl thioacetamide substituted oxadiazole was carried out which shows new direction of research. The positive results obtained from in vitro antibacterial screening, further directed to investigate the multiple biological activities. Among both the series the compounds containing pyrimidinyl thioacetamide are more active with compare to the aryl thioacetamides.

Preparation and Antimicrobial Activity of Schiff's Bases/ 4-Thiazolidinones/ 2-Azetidinones/ 2-Substituted Benzyl Amino Derivatives Having Pyrimidine Moiety

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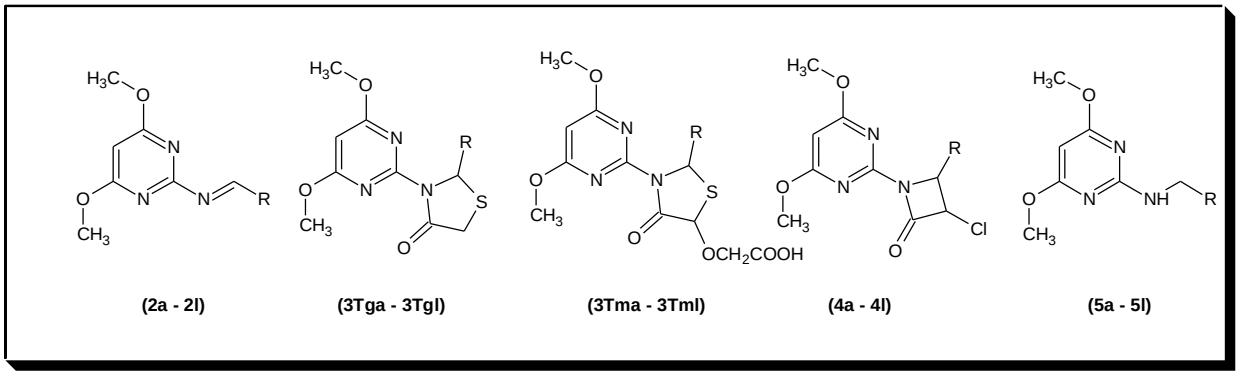
2-Substituted benzylidene amino 4,6-dimethoxy pyrimidines **(2a-2l)**; 2-aryl-3-(4',6'-dimethoxy pyrimidine)-5H-4-thiazolidinones **(3Tga-3Tgl)**; 2-aryl-3-(4',6'-dimethoxypyrimidine)-5-carboxymethyl-4-thiazolidinones **(3Tma-3Tml)**, 1-N-(4',6'-dimethoxypyrimidine)-4-aryl-3-chloro-2-azetidinones **(4a-4l)**; 2-substituted benzylamino-4,6-dimethoxy pyrimidines **(5a-5l)** have been synthesized. The products have been assayed for their antimicrobial activities. Some of the products showed moderate activity in comparison with known standard drugs viz. ampicillin, chloramphenicol, norfloxacin and greseofulvin.



The constitution of the products has been characterized by IR, ^{1}H-NMR, Mass spectral study and elemental analysis.

Bioinspired Coordination Chemistry on Complexes of Ni(II) and Co(II) with Amide Ligands Derived from Heterocyclic Amines

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Bioinspired coordination chemistry is one of the emerging areas of study at present. The importance and versatility of amide group containing in biological systems have promoted the selection of this class of ligands and their complexes for the study. Transitional metal complexes with potential biological activity are the focus of extensive investigations. The present work describes the synthesis, spectral, thermal and biological investigations of few amide group containing ligands with nickel (II) and cobalt (II) ions. The synthesized ligands are derived from heterocyclic amine and can serve as a mimic to biological systems. A method for the synthesis of complexes has been developed by the use of microwave irradiation, which is in agreement to Green chemistry approach, and results have been found better than conventional synthesis. In all the complexes it has been observed that ligating sites are amide oxygen and pyridyl nitrogen as revealed by the i.r. spectroscopy. Although we were unable to get single crystals for X-ray studies, electronic, vibrational and e.s.r. spectroscopic data showed the distorted octahedral and square planar geometry for the complexes. Antimicrobial activity of ligands and all the complexes have been carried out on two fungi and two bacteria. The effects of NiL and CoL on cell viability have also been tested using the amide assay and the results indicate that the NiL had certain effect on cancer cells.

Synthesis of Novel Arylaminopropan-2-Ol Derivatives: Potential β-Blockers

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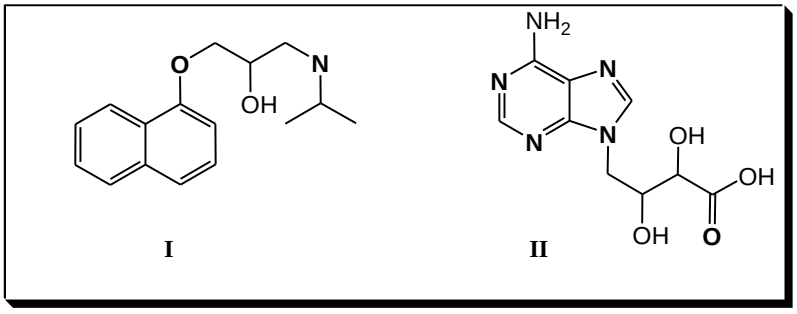
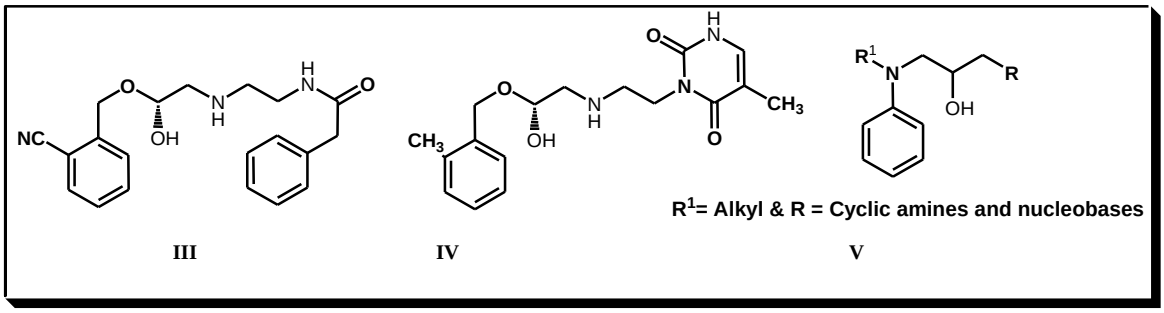
Studies have shown that various analogues of 3-(aryloxy)-1-(alkylamino)-2-propanol such as Propanolol (**I**) are excellent β-blockers [1]. Eritadienine (**II**), which was isolated from Japanese mushroom and other purine analogues were also found to have hypolipidemic activity [2]. The drugs like Epanolol (**III**) and Primidolol (**IV**) are the well known third generation β-blockers, which bind to the β_1-receptors using additional hydrogen bonding interactions.





Further it has been found that replacing the ether linkage on the side chain of the phenoxy-2-propanol by *N* retains its activity and shows tissue selectivity [3-6]. In the light of this we have synthesized a series of compounds (**V**) where alkylamino group replaces ethereal linkage as potential β-blockers.

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Synthesis and *in vitro* Anti-HIV Activity of Some Novel Triazine Based Heterocycles as Non Nucleoside Reverse Transcriptase Inhibitors (NNRTIS)

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Several derivatives of s-triazine[1] show antimicrobial, antibacterial and herbicidal activities. They are also used for the treatment of HIV infections [2]. Urea and thiourea derivatives[3,4] are also reported to possess antibacterial, antimicrobial, antifungal, anticancer and anticonvulsant activities. Encouraged by this observations we decided to synthesized novel coumarin based s-triazine derivatives[5] as Non nucleoside reverse transcriptase inhibitors (NNRTIs) and evaluated for their in vitro anti-HIV activity against the HIV-1 (IIIB) and HIV-2 (ROD) strains including RT mutant strains like K103N and Y181C as RES056. The synthesized compounds were characterized by FTIR, ^{1}HNMR spectral data together with elemental analysis.

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Advanced Oxidation Process: Decolorization and Percentage Reduction of COD of Bifunctional Reactive Dye

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Photocatalytic degradation of Bifunctional Reactive dye has been investigated using the concentrated sunlight illumination and a semiconductor. Batch experiments were conducted to study the effect of different variables on the photo degradation. The variables such as effect of concentrated solar energy, dosages of catalyst and time were used to identify the significant effect and interaction in the batch studies; it was found that the decolorization and COD reduction Potential of semiconductor was strongly affected by concentration of solar energy, amount of semiconductor and time. Optimum condition of the variables for the maximum decolorization and COD reduction are dye concentration 100mg/l, ZnO (2 mg/l) and time (6hrs). The maximum percentage of decolorization and COD reduction has been found 98 % and 91 % respectively.

Microwave Assisted Synthesis, Anti-tubercular Activity and 3D-QSAR Study of 4-Arylaminocoumarin Derivatives

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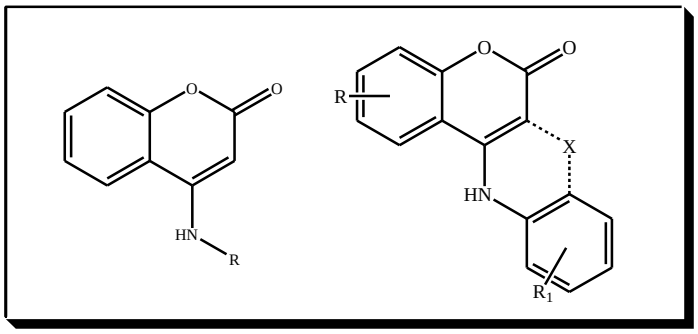
The synthesis, screening, and 3D-QSAR analysis of a set of substituted 4-Aryl/Heteroarylaminocoumarin derivatives were carried out. A small library of title compounds was synthesized by microwave assisted method. This method of synthesis has the advantage of reduction in the number of moles of amine required to synthesize the target compounds while maintaining good yields. All synthesized compounds were screened against *M. tuberculosis* $H_{37}Rv$ strain and the results obtained were analyzed by 3D-QSAR methods. In all, four different models were generated using atom-fit and field-fit alignment strategies. The CoMFA model **(Model 3)** based on field-fit alignment was the best with a correlation coefficient (r^2) of 0.952 and a cross-validated r^2 (q^2) of 0.365. The results are shown.



Where R, R_1 = Alkyl, Aryl, Heteroaryl, X = Hetero atom appended fused/unfused system

Virtual Screening for Anti Malaria Activity from Library of Synthetic Heterocyclic Compounds

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Malaria is a preventable infection that carries with it an enormous global burden. Malaria is present to varying degrees in 105 countries, the majority of which contain drug-resistant strains. Over 40% of the world's populations live in malaria-endemic areas. Plasmodia species are the parasites responsible for malaria. Only 4 of the over 100 species of plasmodia are infectious to humans. The majority of cases and almost all deaths are caused by *Plasmodium falciparum*. *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae* cause less severe disease. Over 90% of all malaria cases occur in Africa, and most are caused by *P. falciparum.* Compared to HIV and cancer less attention has been paid in theses filed with reference to computer aided drug discovery approach towards the development of novel anti malaria drug candidate. Currently Chloroquine, Quinine Atovaquone–proguanil and Primaquine are used as common chemotherapy. We conducted a virtual screening using a ligand library of synthetic heterocyclic entities (Imidazolines, Azetidinones, Acetamide derivatives etc.) The docking studies were carried out was against successful target (1-deoxy-D-xylulose-5-phosphate reductoisomerase, Dihydropteroate synthetase, Enoyl-ACP reductase etc.) and research target (Peptide deformylase, Acetyl-CoA carboxylase 1, Beta-ketoacyl-ACP synthase III, Dihydroorotate dehydrogenase, mitochondrial etc.).

Evaluation of Antioxidant Potential of Some Designed Polyphenols by Cyclic Voltametry

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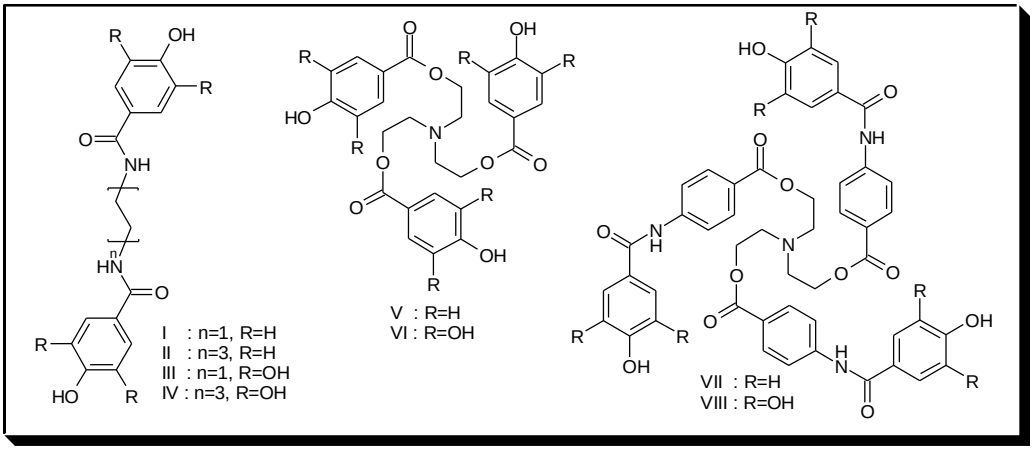
Eight polyphenolic compounds (I-VIII) were so designed that they may be categorized according to some regular structural features [1], and synthesized and their antioxidant potentials have been studied with an aim to establish structure-activity relationship. For this, linear and star type compounds were prepared incorporating different number of phenolic functions at the termini and on the periphery respectively. In case of linear compounds, the spacer lengths between the terminal phenolic units were varied. Star type compounds were prepared using the same core, but the lengths of the arms were varied. The antioxidant potentials of the compounds were studied by monitoring the change of the oxidation potential in the redox cycles of 1,4-diaminobenzene in presence of the compound (I-VIII) by Cyclic Voltametry [2]. 1,4-diaminobenzene has two oxidation waves in DMF due to formation of a radical cation and a diiminium dication respectively. The linear compounds (II – IV) delayed the oxidation of 1,4-diaminobenzene to the radical cation. In presence of compound (I), having 4-hydroxybenzoyl group at the termini and a shorter spacer has delayed the first oxidation of 1,4-diaminobenzene to the radical cation and further, it scavenged the radical cation, formed, resulting in disappearance of the second oxidation wave. In presence of the star type compound (V), having 4-hydroxy-benzoyl group on the periphery, oxidation waves of 1,4-diaminobenzene were not observed and in presence of the compound (VI), containing 3,4,5-trihydroxybenzoyl group on the periphery, these were just delayed as done by the linear compounds. The compounds VII and VIII also delayed the oxidations, but not significantly.



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Synthesis, Physico-Chemical Investigations *in vitro* Biological Studies of Co(Ii), Ni(Ii) and Cu(Ii) Complexes with 2-Amino-4-Phenyl-1,3-Thiazole Schiff Base

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A series of metal complexes of cobalt(II), nickel(II) and copper(II) have been synthesized with newly synthesized biologically active ligand. The ligand was synthesized by the condensation of 2-amino-4-phenyl-1,3-thiazole with 8-formyl-7-hydroxy- 4-methylcoumarin. The probable structure of the complexes has been proposed by elemental analyses and spectroscopic (i.r., Uv-Vis, e.s.r, FAB-mass and thermo analytical) data. Electro chemical study of the complexes is also reported. The elemental analyses of the complexes confine to the stoichiometry of the type $ML_2.2H_2O$ [M=Co(II), Ni(II) and Cu(II)]. All the complexes are more soluble in DMF and DMSO and are non-electrolytes. All these complexes have been screened for their antibacterial (*Escherichia. coli, S. aureus, S. pyogenes and P. aeruginosa*) and antifungal activities (*Aspergillus niger, Aspergillus flavus and cladosporium*) by MIC method. The brine shrimp bioassay was also carried out to study their invitro cytotoxic properties.

How to Live Young, Active, Dynamic and Healthy: The Answer is Antioxidants

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In our body continuous fight goes on against infection and diseases. A number of functions and activities like breathing and smoking etc. produce free radicals in our body which attack our healthy cells making them weak and more prone to diseases like cancer and that of heart. Free radicals cause damage to our cells, and it's believed that this cumulative damage is what causes aging and eventually death. It happens as a result of regular metabolism, but is accelerated by pollution, excessive exposure to sunlight, alcohol and smoking. Oxidation is a normal process that takes place in the body. Free radicals containing oxygen, known as reactive oxygen species (ROS), are the most biologically significant free radicals. They have the radicals superoxide and hydroxyl radical, plus derivatives of oxygen that do not contain unpaired electrons, such as hydrogen peroxide, singlet oxygen, and hypochlorous acid. Damaged cells may lead to health problems such as cancer, artery and heart diseases, cataracts, diabetes, and some deterioration that goes with aging. Antioxidants do a great job of protecting healthy cells of our body from the damage caused by free radicals.

The antioxidants Vitamin C, Vitamin E and beta carotene, and some minerals including selenium, can counteract the effects of free radicals. They reduce the damage free radicals may do to arteries that contribute to heart disease, or the damage to other cells that may increase the risk of cancer. Beta carotene is one of 50 carotenoids in foods that convert to vitamin A in the body. It is usually found in red and orange colored fruits and vegetables and in some dark green ones where the color is hidden by chlorophyll. Foods high in carotenoids include: Red, orange, deep-yellow and some dark-green leafy vegetables, carrots, sweet potatoes, broccoli, apricots, cantaloupe, mangoes, red and yellow peppers.This paper is an attempt to highlight the importance of Antioxidants for our health and also how their use can make us young, active, dynamic and healthy.

Synthesis of Novel 2'-Deoxy-2'-Amino-α-L-*Arabino*-Nucleosides

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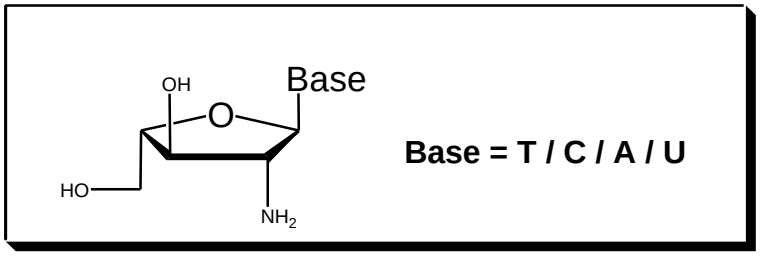
The immense potential of oligonucleotide analogues as therapeutic agents or diagnostic molecules has stimulated intensive research on nucleic acid mimics during the last few years [1]. In recent past, 2'-deoxy-2'-amino nucleosides have been used to generate nuclease resistant aptamers against basic fibroblast growth factor and human IFN-gamma [2]. In other cases, these modifications have been investigated with the aim of developing oligomers with improved antisense properties [3,4]. On the basis of our literature search, there are several reports where both the synthesis and activity data of 2'-Deoxy-2'-amino-□-L-*arabino*-nucleosides has been discussed. On the contrary, corresponding □-L-*arabino*nucleosides are almost unknown and need to be explored. Keeping these aspects in view, we are working towards the synthesis of novel 2'-deoxy-2'-amino-□-L-*arabino*-nucleosides. The details of the work will be discussed in the poster.



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[4] J. Wengel, *Acc. Chem. Res*. **1999**, *32*, 301.

Indole Derivatised Analogues as Novel Radiopharmaceuticals

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Schiff bases and their biologically active complexes have been often used as chelating ligands in the coordination chemistry of transition metals as radiopharmaceuticals for cancer targeting, agrochemicals, as model systems for biological macromolecules, as catalysts and as dioxygen carriers. These ligands are able to stabilise many different metal ions in various oxidation state and also promote chelation and provide extra stability to the metal centres in different biochemical recations.

Further hetrocyclic carbonyl compounds are of great interest since they exhibit numerous biological activities such as antitumor, antimicrobial and antibacterial activity etc. Imidazole and indole complexes are one of the most biologically important ligands. In this article, we report the synthesis and biological study of a novel Schiff base having indole moiety. It was derived from the condensation reaction of indol 3 carboxyladehede and histidine .

This indole derivative was synthesised in 2 steps having higher yield more then 85%.The novel compounds was labeled with ^{99m} Tc by direct labeling method using stannous chloride as reducing agent. at optimized conditions of pH, stannous ion concentration and incubation time to achieve the maximum labeling efficiency (>95%).It forms stable complex with ^{99m} Tc with high radiochemical purity(98%) and showed significant accumulation in tumor site. Blood kinetic study showed a quick wash out from the circulation and biological half life was found to be t½(F) ¼ 1 h 15 min; t½(S) ¼ 10 h 05 min. Receptor ligand assay on human tumor cell line U-87 MG and KB did not show specific receptors for the conjugate. The maximum uptake was after 1 hr of treatment which was non-specific binding. In vitro cytotoxicity was evaluated by MTT assay, which revealed enhanced dose dependent cytotoxicity on U-87 MG and KB cell line. Excellent quality radioimages of tumor bearing mice were recorded showing rapid clearance of background activity, visualization of tumor at 3 h and fast clearance rate from kidneys analogue which was further evidenced in biodistribution studies, shows that this compound is potential candidate for tumor imaging.

A Concise and Efficient Synthesis of Naturally Occurring 5-(3-indolyl)-oxazoles

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Compounds containing 5-(3-indolyl)oxazole scaffold are important heterocycles which are isolated from different organisms and are known to display wide range of biological activities [1]. Among 5-(3-indolyl)oxazoles, Pimprinine and Pimprinethine were isolated from *Streptoverficillium clivareticuli* and lipophilic extracts of *Streptomyces cinnamomeus*, respectively. The analogues WS-30581 A and WS-30581 B were isolated from *Streptoverticillium waksmanii* are shown to display potent inhibitory effects of platelet aggregation [1]. Recently, Labradorin 1 and Labradorin 2 were isolated from *Pseudomonas syringae pv. Coronafaciens* and reported to exhibit very good inhibitory activity against various human cancer cells [1]. Although, many procedures are reported for the synthesis of 5-(3-indolyl)oxazoles, however, straightforward and simple methods are quite limited [2]. Reported direct synthesis of 5-(3-indolyl)oxazoles involves rhodium catalyzed reaction of diazoacetylindole with nitriles, and aza-Wittig-type reactions of iminophosphorane derived from 3-azidoacetyl-1-methylindole with isocyanates and acid chlorides [2]. Herein we report a direct and high yielding protocol for the synthesis of 5-(3-indolyl)oxazoles from 3-acetylindole using easily accessible reagent [hydroxy(2,4-dinitrobenzenesulfonyloxy)iodo]benzene. Details about this synthesis will be presented in the conference.

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In vitro Formation of Chlorogenic Acid

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Chlorogenic acid, a pharmacologically important compound, is a phenolic compound occurs in certain commonly used medicinal herbs. We looked for the compound in cultured cells of *Varthemia persica*. We have evaluated the conditions for establishment of callus cultures of *V. persica* and for the biotechnological production of chlorogenic acid. Callus was initiated by culturing seedling of *V. persica* on MS basal medium supplemented with different concentrations of kinetin, naphthalene acetic acid and 2, 4 –diphenoxy acetic acid. Also, the influence of light, and phytohormones on the production of chlorogenic acid was examined. Kinetin stimulated the production of chlorogenic acid. Replacement of 2,4-D with NAA did not alter the chlorogenic production. The content of chlorogenic acid decreases during five consecutive subculture cycles. Reduction in productivity with subculturing has been attributed to genetic changes or epigenetic changes. The ability to induce the accumulation of chlorogenic acid in the *V. persica* cell line tissue offers an opportunity to produce a phenolic compound with therapeutic value.

Synthesis And Antimicrobial Screening Of Ethyl-1-N (2,4-Dinitro Phenyl) Substituted 1,4-Dihydroquinoline-4-On-3 Carboxylates

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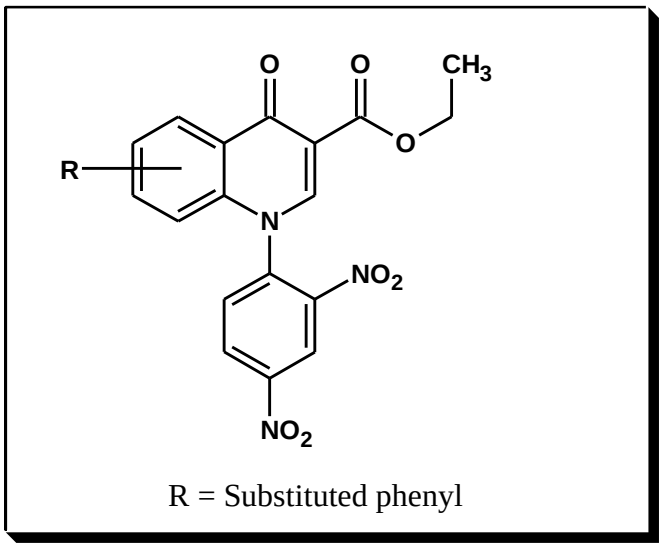
In view to various biodynamic properties of 4-quinolones, the synthesis of Ethyl-1-N-(2,4-dinitro-phenyl)-substituted-1,4-dihydro-quinoline-4-one-3-carboxylates have been undertaken by the cyclocondensation of different different ethyl-substituted-1,4-dihydroquinole-4-one-3-carboxylates with 1-chloro-2,4-dinitrobenzene in the basic condition.



R = Substituted phenyl

The constitutions of the products have been delineated by elemental analyses, IR, PMR and Mass spectral data.

The products were assayed for their *in vitro* biological assay like antibacterial activity towards *S. pyogens* MTCC-442 and *S. aureus* MTCC-96 (Gram positive) and *E. coli* MTCC-443 and *B. subtillis* MTCC-441 (Gram negative) bacterial strain and antifungal activity towards *Aspergillus niger* MTCC-282 and *Candida albicans* MTCC-227 at different concentrations (µg/ml) : 0 (control), 5, 25, 50, 100, 250, for their MIC (Minimum Inhibitory Concentration) values. The biological activities of the synthesized compounds were compared with standard drugs.

In vitro Bio-Production of Natural Pesticide Azadirachtin through Callus Cultures of *Azadirachta Indica* A. Juss

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The use of *in vitro* technique for the production bioactive secondary metabolites is an alternative and sustainable approach, among various approaches callus culture is good for known as well as for new biological active metabolites. Azadirachtin, a triterpenoide have received considerable attention of scientific community and environmentalist due to its potential insecticidal properties.

Callus culture of *Azadirachta indica* were established utilizing leaves, cotyledons, anthers and ovaries on MS (Murashig and Skoog's) medium supplemented with plant growth regulators viz; bezyladenine (BA), Kinetin (Kn), napthalene acetic acid (NAA), indole acetic acid (IAA), and 2,4-dichlorophenoxy acetic acid (2,4-D) singly as well as in combination with there different concentration to obtained optimum growth of callus, after growth evalvation the tissues were harvested after 2,4, and 6 week separately for leaves, cotyledon, anther and ovaries being taken as explants. The tissues were dried, weighed and extracted in different solvent and analyzed for azadirachtin content.The callus obtained from Leaves, cotyledons, anthers and ovaries were evaluated separately for azadirachtin concentration, the maximum amount of azadirachtin (870 µ/g dry weights) was obtained from 6 week old leaf segment derived callus which was obtained on MS medium supplemented with NAA (5 mg/l) and BA (5mg/l).

The present work describes *in vitro* method for azadirachtin production and examined Effectiveness of various plant growth regulators, organic ($C_{12}H_{22}O_{11}$) and inorganic nutrients KNO_3 & $(NH_4)_2\ SO_4$ in promoting stock callus through different explants.

Synthesis and Antifungal Activity of some Novel pyrazol-1'-ylpyrazolo [1, 5-*a*] pyrimidines

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N-containing heterocycles like pyrazolopyrimidines are a class of nonbenzodiazepine drugs. The recent discovery of Zaleplon as an ideal hypnotic drug has stimulated further interest in the pyrazolo[1,5-a]pyrimidine chemistry. Pyrazolo[1,5-a]pyrimidines are widely used in the field of pharmaceuticals as antimetabolites, HMG-CoA reductase inhibitors, COX-2-selective inhibitors, 3', 5'-cyclic AMP phosphodiesterase inhibitors. Encouraged by these results, we wanted to explore the antifungal activities of some new pyrazol-1'-ylpyrazolo[1,5-a]pyrimidines as this nucleus exhibits diverse pharmacological activities such as antitrypansomal, antianxiety, antischistosomal, antiepileptic, anxiolytics, antidepressant and oncolytics. We hereby report a convenient route to synthesise pyrazol-1'-ylpyrazolo[1,5-a]pyrimidines and their antifungal activity. The condensation of 3-amino-5-hydrazinopyrazole dihydrochloride with pentane 2,4-dione affords pyrazol-1'-ylpyrazolo[1,5-a]pyrimidines. However, with unsymmetrical diketones i.e. substituted benzoylacetones, the reaction may give rise to four regioisomeric pyrazol-1'-ylpyrazolo[1,5-a]pyrimidines- (3'-methyl-5'-aryl pyrazol-1'-yl-5-methyl-7-aryl-), (3'-methyl-5'-aryl pyrazol-1'-yl-5-aryl-7-methyl-), (3'-aryl-5'-methyl pyrazol-1'-yl-5-methyl-7-aryl-) and (3'-aryl-5'-methyl pyrazol-1'-yl-5-aryl-7- methyl-), as formation of regioisomers can not be avoided. But the TLC and ^{1}H NMR examination of crude reaction mixture revealed that reaction with aryl 1,3-diketones led to the formation of single isomer of pyrazol-1'-ylpyrazolo[1,5-a]pyrimidines alongwith 3(5)methyl-5(3)arylpyrazoles as a byproduct obtained by C-N bond cleavage in various solvents employed like EtOH-H_2O and H_2O. It was worthy to note that C-N bond cleavage could be suppressed when water was employed as the solvent and pyrazol-1'-ylpyrazolo[1,5-a]pyrimidines were obtained in excellent yield. Thus, this route provides an effective, economic and environmentally friendly method to synthesize these fused pyrazoles. Rigorous analysis of NMR (^{1}H and ^{13}C) unambiguously support structure for the right isomer. The 3'-methyl-5'-aryl pyrazol-1'-yl-5-methyl-7-aryl pyrazolo[1,5-a]pyrimidine is shown to be the regioisomer formed. Some of the compounds were tested in vitro for their antifungal activity against *Aspergillus terrus*, *Alternaria alternata*, *Fusarium oxysporum,* and *Helminthosporium sp*. and have shown promosing activity against these pathogens.

Studies on the Synthesis of Functionalised Bicyclo[2.2.2]Octenones and its Transformation to Diquinane and Homoisotwistane Frameworks

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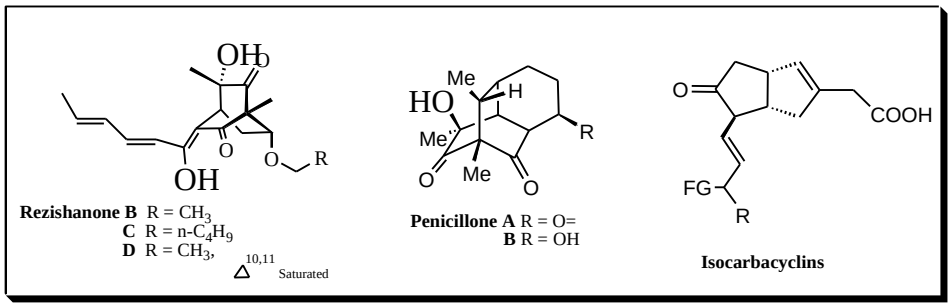
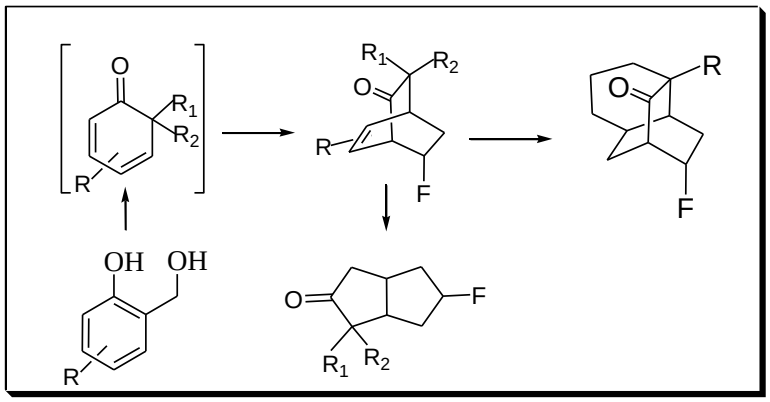
There has been an upsurge of interest in the synthesis and chemistry of functionalized bicyclo[2.2.2]octanes. This is presumably due to its versatile role as a building block in organic synthesis since these systems undergo various types of regio- and stereoselective transformations by virtue of its rigid framework and the interactions among functional groups. Moreover, the presence of bridged bicyclo[2.2.2]octane framework in several recently isolated natural products such as rezishanones (sorbicillins) and penicillones that exhibit interesting biological activities has further enhanced the interest in such system.



We have developed a unique methodologies for the synthesis of highly functionalized bicyclo[2.2.2]octenones by cycloaddition of cyclohexa-2,4-dienones with electron rich, electron neutral as well as electron deficient dienophiles. After having facile preparation of bicyclo[2.2.2]octenones, we tried to explore the use of this in creating the basic framewoek of different natural products by using the reactivity of bicyclo[2.2.2]octenone in ground and excited state. Thus, we utilized the functionalized bicyclo[2.2.2]octenones for the construction of homoisotwistane and prostacyclin frameworks.



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In vitro Antioxidant Activity Profile of Natural and Semisynthetic Furano-Flavonoids

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Flavonoids, the ubiquitous phytochemicals occurring in higher plants have been found to have strong antioxidant effect substantiating their key role in the amelioration of disorders involving oxidative stress such as diabetes mellitus, dyslipidemia and atherosclerosis. Under the aegis of our ongoing program on drug discovery on antioxidant agents, we have isolated three furano-flavonoids **1**-**3** and a rare flavonol glycoside **4** for the first time from the aerial parts of *Indigofera tinctoria* and evaluated their antioxidant properties. The results depict that furanoflavonoids viz, **1** and **2** substantially inhibited the concentration of the superoxide ion by 22.7% and 15.3% respectively at the conc. of 200 µg in the enzymatic system whilst the respective percentage inhibition in the non-enzymatic system was of a higher order at 33.0% and 27.6% at the conc. of 400 µg. Furthermore, derivatives of the leads also exhibited significant inhibition, the most active being derivative displaying 34.82% inhibition in the enzymatic system at 500 µg. The most promising compound was **4**, lowering the oxygen conc. by 46.8% and 54.6% in a dose dependent manner at 250 µg and 500 µg respectively.

New Pyridoquinolones and their Microbial Studies

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An amide derivatives of pyridoquinolones were synthesized by using N^1-substituted phenyl sulfanilamides, phenyl thioureas and phenyl amines at C-3 position of 1-hydroxyethyl-6-chloro-4-oxo-pyrido[2,3-h]quinoline-3-carboxylic acid **XIII**. And we get substituted 1-hydroxyethyl-6-chloro-4-oxo-pyrido[2,3-h]-3-{N^4-[N^1-(substituted-phenyl)sulfanilamido]-carbonyl} quinoline $\mathbf{XV_{1\text{-}12}}$, 1-hydroxyethyl-6-chloro-4-oxo-pyrido[2,3-h]-3-[N-(substituted phenylthioureido)carbonyl]quinoline $\mathbf{XV_{13\text{-}24}}$ & 1-hydroxyethyl-6-chloro-4-oxo-pyrido[2,3-h]-3-[N-(substituted phenylamino) carbonyl]quinoline $\mathbf{XV_{25\text{-}36}}$. Synthesized compounds were characterized by elemental analysis and spectral data, their antibacterial and antifungal activity at 100 μg/ml & 200 μg/ml concentrations using cup-plate method have been tested. We found some of the compounds exhibit appreciable activity.

A Novel System for Decarboxylative Iodination

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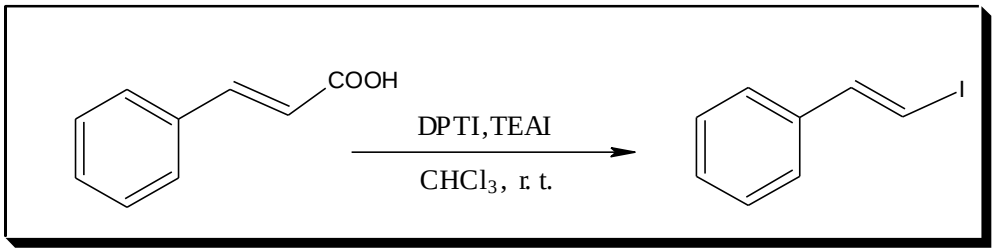
Decarboxylative iodination is a useful reaction in organic chemistry for the synthesis of halogenated organic substances. Hunsdiecker reaction and its modifications represent the reported literature methods for halodecarboxylation. We present a novel method for decarboxylative iodination of α,β-unsaturated carboxylic acids using diphosphorus tetraiodide (DPTI) in combination with tetraethylammonium iodide (TEAI) at room temperature. The method is simple, mild and high yields of the corresponding α,β-unsaturated iodides, for both aliphatic as well as aromatic substrates, were obtained.



Scheme 1

Iodo-decarboxylation of cinnamic acid using DPTI and TEAI.

A Novel System for Synthesis of Nitriles from Carboxylic Acids

Vikas N. Telvekar, **Hemchandra K. Chaudhari**, Rajesh A. Rane, Harish S. Kundaikar, Kavit N. Patel
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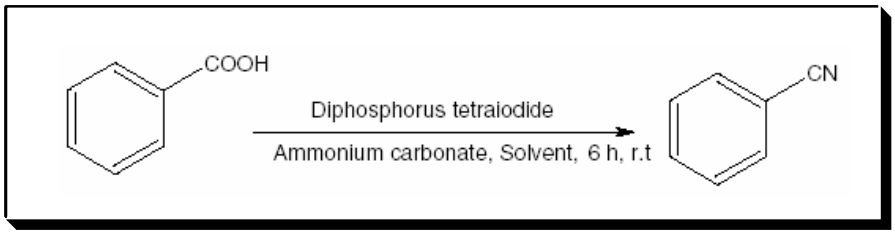
A variety of methods are available for conversion of carboxylic acids to nitriles. These conversions consist of two or more steps, which require isolation of intermediates and has some limitations like use of more complex reagents. We used Diphosphorus tetraiodide in combination with ammonium carbonate at room temperature for direct conversion of carboxylic acids to corresponding nitriles with high yield. The reaction was carried out in presence of various anhydrous solvents. It was observed that the reaction did not take place in the presence of acetonitrile. while in chloroform and dichloromethane, the reaction rate was slow. When anhydrous carbon disulfide was used as solvent, the reaction rate was fast and yield was high. This method suitable for the conversion of aromatic, heterocyclic aromatic and aliphatic carboxylic acids to their respective nitriles. The method is mild and gave good to excellent yield of nitriles with both aliphatic and aromatic substrates.



Scheme 1

Conversion of benzoic acid into benzonitrile using diphosphorus tetraiodide and ammonium carbonate in various solvents.

Synthesis of Acridine Derivatives and Evaluation them for Anticancer Activity

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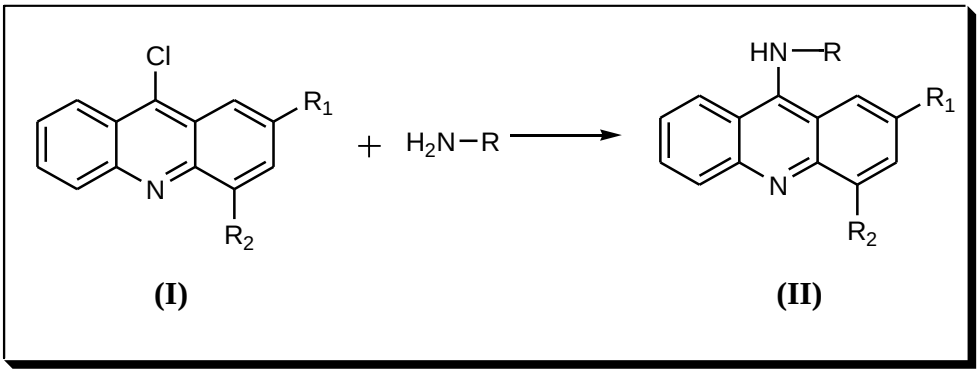
A number of acridine derivatives (II) have been synthesized by the condensation of 9-chloro-2,4-substituted acridines with various amines. These compounds have been fully characterized by IR, ^{1}HNMR, MS and elemental analysis. These well characterized acridine derivatives have been screened for anticancer activity against a panel of seven cancer cell lines i.e. colon (502713), lung (A-549), breast (MCF-7), colon (HCT-15), colon (COLO-205), liver (HEP-2) and neuroblastoma (IMR-32). These compounds exhibited interesting anticancer activity against various cancer cell lines.



(I) **(II)**

Where: R, R_1 and R_2 are various substituents.

Synthesis and Antiulcer Activity of Novel Pyrimidylthiomethyl- and Sulfinylmethyl Benzimidazoles as Potential Reversible Proton Pump Inhibitors

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Pyridylmethylsulfinyl benzimidazoles (PMSB's), like omeprazole and its congeners referred as proton pump inhibitors are the most widely employed class of drugs for the treatment of acid peptic ulcers and hyperacidity. However, due to their irreversible inhibitory nature of the H^+/K^+ATPase, they have various side effects. An attempt has been made to replace the basic pyridine ring of the PSMB's with less basic bioisosteric pyrimidine ring to produce reversible inhibition of the proton pump. Series of novel pyrimidylthiomethyl benzimidazoles (**II*a-c***) and pyrimidylsulfinylmethyl benzimidazoles (**III*a-c***) have been prepared and evaluated for the anticancer activity, by the pylorus ligation of rats (Shay method). Compounds **II*a*** and **III*a*** when evaluated significantly decreased the gastric acid secretion, free acidity, as well as, gastric ulcers in the pylorus ligated rats and the effects are dose dependent and comparable to omeprazole. Of the two compounds the sulfinyl derivative **III*a***, is more effective than the thio analogue, **II*a*.**

Synthesis of α-Aryl- α -(4',6'-Dimethoxy-2'-Aminopyrimidine)-Ethane Nitrile/Thioethanamide/Ethanamide/Ethanoic Acid Derivatives as Potential Antimicrobial Agents

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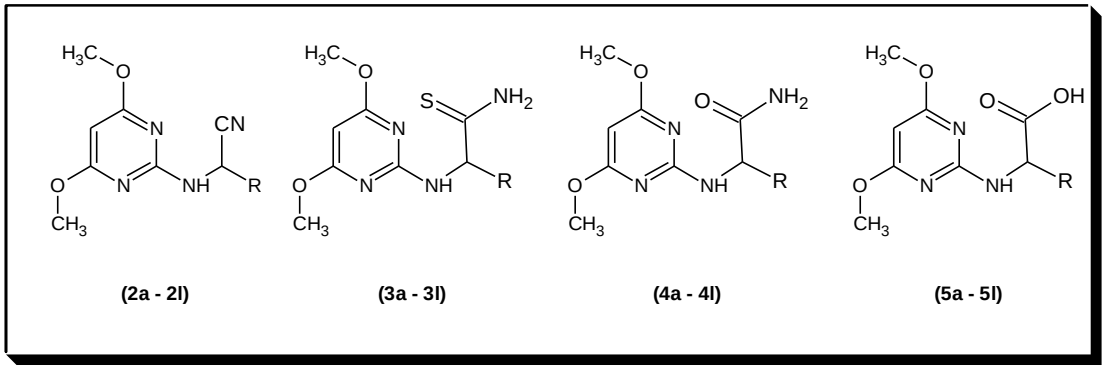
[b]Shree M. and N. Virani Science College, Rajkot-360 005, Gujarat, India

α-aryl-α-(4',6'-dimethoxy-2'-aminopyrimidine)ethanenitrile **(2a-2l)**; α-aryl-α-(4',6'-dimethoxy-2'-aminopyrimidine)thioethanamide **(3a-3l)**; α-aryl-α-(4',6'-dimethoxy-2'-aminopyrimidine)ethanamide **(4a-4l)**; α-aryl-α-(4',6'-dimethoxy-2'-aminopyrimidine)ethanoic acid **(5a-5l)** have been synthesized. The products have been assayed for their antimicrobial activity. Some of the products showed moderate activity in comparison to standard drugs viz. ampicillin, chloramphenicol, norfloxacin and greseofulvin.



The constitution of the products has been delineated by IR, ^{1}H-NMR, Mass spectral study and elemental analysis.

Synthesis and Pharmacological Evaluation of Some New Cyclohexanones and Indazoles

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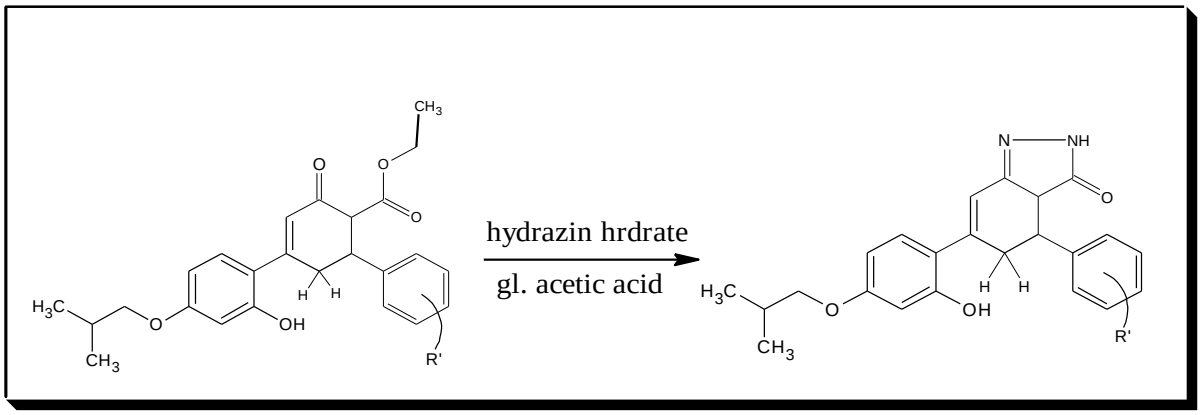
The chemistry of heterocyclic compounds has attained greater interest because of its useful application in medicine, agriculture and industrial chemistry. Now a days more and more attention has given to the synthesis of heterocyclic compounds bearing a nitrogen and oxygen containing ring system, like indazole, mainly because of the interest concerning their various spectrum of pharmacological activities.

Here, 4-(substituted phenyl)-6-(2-hydroxy-4-isobutoxyphenyl)-4, 5-dihydro-2H-indazol-3(3aH)-one are synthesized from ethyl-6-(substituted phenyl)-4-(2-hydroxy-4-isobutoxyphenyl)-2-oxocyclohex-3-enecarboxylate, on reaction with hydrazine hydrate in presence of glacial acetic acid respectively. The compounds were evaluated for their antimicrobial activity. The compounds were established on t he basis of elemental analysis, IR, NMR and MASS spectral data.



Scheme 1

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A Study of The Interaction of Tegaserod Maleate with Calf Thymus DNA by Spectroscopic Methods

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The present paper describes the investigations on the mechanism of interaction of tegaserod maleate (TGM) with calf thymus DNA (ct DNA) by spectrofluorimetric and UV-vis absorption methods. The interaction of TGM with ct DNA resulted in hypochromic and bathochromic shifts. Analysis of fluorescence data revealed the presence of static quenching mechanism. Binding constant of TGM-ct DNA was calculated based on fluorescence and absorption measurements and these values were found to be in the range of 10^4 M^{-1}. Competitive experiments using ethidium bromide and quenching studies using potassium iodide were carried out to predict the nature of binding between TGM and ct DNA. These results indicated that the interaction pattern between TGM and DNA to be intercalative. Effects of pH on fluorescence of TGM and TGM-DNA systems were also investigated. The utility of the proposed study for the determination of trace amounts of DNA gave satisfactory results

Microwave-Assisted Synthesis of N- arylquinoline Derivatives Catalyzed by DMAP and their Biological Activities

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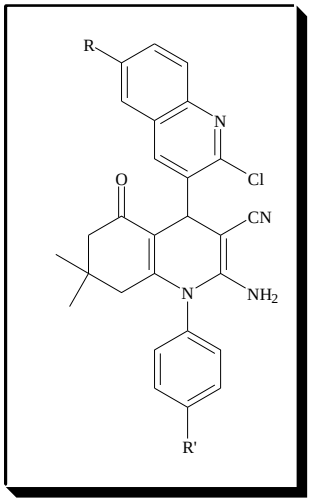
A series of 2-amino-4-heteroaryl-1-aryl-7,7-dimethyl-5-oxo-1,4,6,7,8-pentahydrquinoline -3-carbonitrile derivatives 3(a-t) have been synthesized by reaction of 2-(2-chloro quinolyl-6-(un)substituted-3-ylmethylene)malononitrile(1a-d) and 3-arylamino-5,5-dimethylcyclohex-2-enone(2a-e) under microwave irradiation catalyzed by 4-(N,N-dimethylamino) pyridine(DMAP). This rapid method produces pure product in high yield. All synthesized compounds have been characterized by elemental analysis, IR, NMR and screened for their antifungal and antibacterial activity.



(3a-t)

Where R= CH_3,Cl,H,OCH_3
R'= CH_3,Cl,H,$NHCOCH_3$,OCH_3

Synthesis and Resolution of Chiral Potential Multifunctional Therapeutic Agent

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Chirality is a fundamental property of biological systems and reflects the underlying asymmetry of matter and therefore it is considered as an important aspect in the therapeutic efficacy and safety of drugs. Chiral considerations are now integral parts of drug research and development and of regulatory processes. More than 50% of the 500 top selling drugs in the world today are single enantiomers. Recently, it has been strongly argued that a therapeutically inactive isomer in a racemate should be regarded as an undesirable impurity with respect to therapeutic efficacy and safety, thus the racematic drug can be considered as only 50% "pure". The concomitant development of stereoselective synthetic methodologies and separation technologies has permitted to build up a considerable expertise and appropriate tools to respond to the specific needs related to this particular aspect of life sciences.

The resolution of racemates into optical antipodes is a well-known process and this technology has found application in industry for obtaining optically active synthetic drugs. drug therapy. Keeping this in mind synthesis and resolution of novel selective estrogen receptor modulator- substituted 2,3-diarylbenzopyran has been carried out.

Synthesis of Antibacterial & Antifungal Quiazoline Scaffold using Microwave Technique and their Comparison with Conventional Technique

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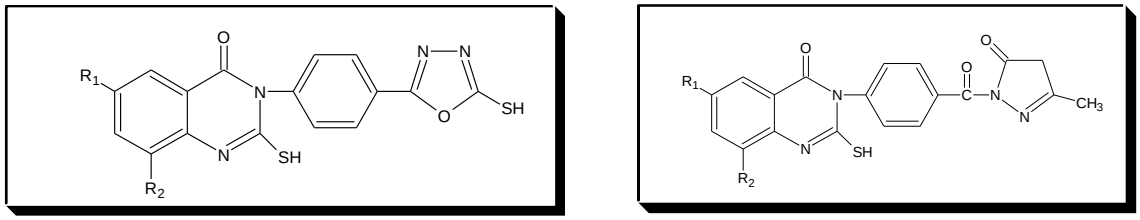
The quinazoline ring skeleton is widely found in alkaloids and many biologically active compounds. Quinazolone a nitrogenous heterocycle, proved to posses a multitude of biological potency including anticancer, antiproliferative agents, antibacterial, anti-inflammatory, anticonvulsant, CNS depressant and anti-HIV agents. 1,3,5-thiadiazoles system having three hetero atoms at symmetrical positions are known to exhibit antitubercular, herbicidal, receptor antagonists activities. Microwave irradiation (MWI) in organic synthesis presently is useful widely.

Here we have synthesized a series of 6, 8-subsituted-2-mercapto-3-[4 -(5-mercapto-1, 3, 4-oxadiazol-2-yl) phenyl]quinazolin-4(3H)-one and 6, 8-subsituted- 2-mercapto- 3-{ 4-[(3-methyl- 5-oxo- 4, 5-dihydro- 1H-pyrazol-1-yl) carbonyl]phenyl}quinazolin-4(3H)-one. Comparison study between Microwave and Conventional technique for the synthesized series has been knowledgeable. The instrument will be use for the Microwave reactions is QPro-M Microwave Synthesis System manufactured by Questron Technologies Corporation, Ontario Î4Z 2E9, Canada. All the synthesized compounds have been screened for antibacterial and antifungal activity. The structure of synthesized compounds will be confirmed by elemental analysis and spectral data.



R_1 = H, Br, NO_2 R_2= H, Br

Scheme 1

A Convenient, Rapid and Eco-friendly Synthesis of Benzimidazole Heterocyclic Moiety containing Ether Linkage As Potential Pharmacological Agents

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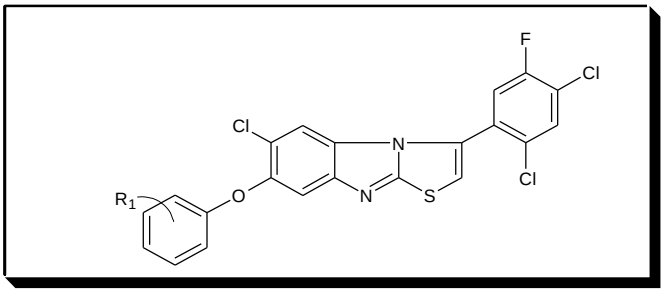
In the pharmaceutical field, there is a need for new and novel chemical inhibitors of biological functions. Our efforts are focused on the introduction of chemical diversity in the molecular frame work in order to synthesizing pharmacologically interesting heterocyclic compounds bearing the benzimidazole moiety by using environmentally benign procedure under microwave irradiation (MWI) in presents of catalytically amount of poly phosphoric acid (P_2O_5 + H_3PO_4) which are endowed with various types of pharmacological properties [1] such as antituberculosis [2] and antimicrobial [3]. All the newly synthesized compounds were elucidated by elemental analysis and spectral data and tested for their antimicrobial and antituberculosis activity using standard drugs.



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Molecular Iodine-Catalyzed One-Pot Synthesis of Some New Hantzsch 1,4-Dihydropyridines at Ambient Temperature

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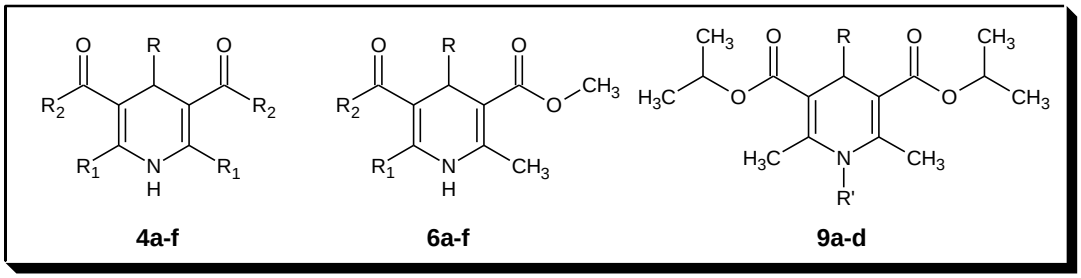
Hantzsch 1,4-dihydropyridiens (1,4-DHPs) and their derivatives has gained great importance in the field of organic and medicinal chemistry, they display fascinating array of pharmacological properties [1-2]. The dihydropyridine skeleton is common in many drugs such as nifedipine, nicardipine, amlodipine and others, which are effective as cardiovascular agents and also use for the treatment of hypertension. [3]. 1,4-DHPs have been explored for their calcium channel modulation [4] and the heterocyclic rings are found in a variety of bioactive compounds such as vasodilator, bronchodilator, antiatherosclerotic, antitumor, antidiabetic, geroprotective and heptaprotective agents [5]. Moreover they posses neuroprotective, platet anti-aggregation activity [6]. The tremendous drug activity of these compounds has attracted many chemists to synthesize these molecules.



Where R & R' = Aryl
R_1 & R_2 = Alkyl

An efficient and simple one-pot synthesis of some new symmetrical, unsymmetrical and N-substituted Hantzsch 1,4-dihydropyridiens using molecular iodine as catalyst form an aldehyde, 1,3-dicarbonyl compound and ammonium acetate / aromatic amine in ethanol is described. This new method has the advantage of good-excellent yields (80-95%) and short reaction time (2.5-5 h) at ambient temperature.

References:

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Palladium Mediated Desymmetrization of Meso Bicyclic Hydrazines: Stereoselective Synthesis of Functionalized Cyclopentenes

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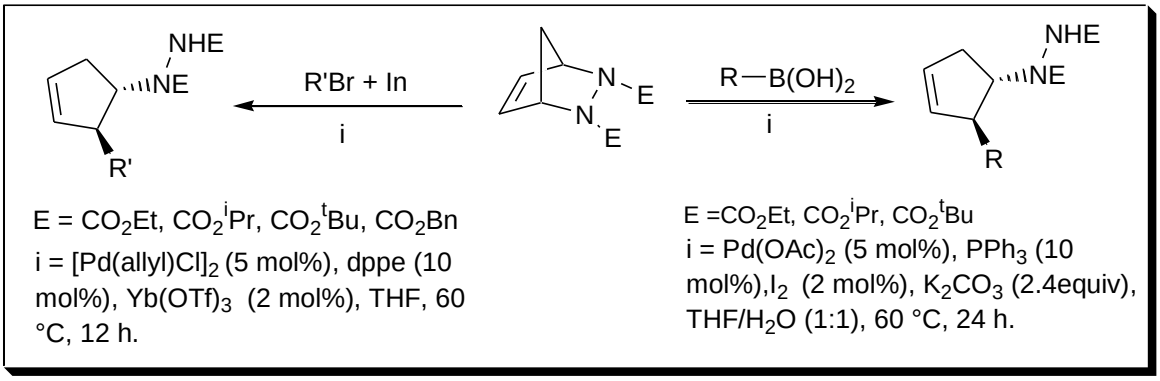
The stereoselective synthesis of cyclopentane derivatives continue to hold tremendous amount of synthetic potential as intermediates in the construction of a variety of biologically active molecules which act as glycosidase inhibitors, anti-HIV and anti-tumor agents [1]. 1,2-Disubstituted cyclopentanes are well known for their activity as small potent potentiators of AMPA receptors and COX-2 inhibitors. Nucleoside type antibodies such as nikkomycins and polyoxins [2], glycosidase inhibitors like mannostatins and polyhydroxycyclopentitol containing natural products are some of the biologically active disubstituted cyclopentenes [3].

Desymmetrization of meso compounds provides an efficient route to asymmetric synthesis of high value in limited number of steps. Modifications of the classical Suzuki reaction have always elicited great interest, especially when it is used for the cross-coupling with alkenes [4]. As part of our sustained interest in the chemistry of meso bicyclic olefins [5], we undertook an investigation of the palladium catalyzed reactions of organoboronic acids with these substrates (Scheme 1). The reaction afforded *trans*-3, 4 disubstituted cyclopentene in good to excellent yields [6]. The desymmetrization of meso bicyclic alkenes with oragnoindium reagents, derived from various alkyl or aryl bromides and indium metal, afforded *trans* disubstituted cyclopentene [7]. and the results are presented in scheme 1.



Scheme 1

References:

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Synthesis and Biological Activity of Some New Benzofuran Derivatives

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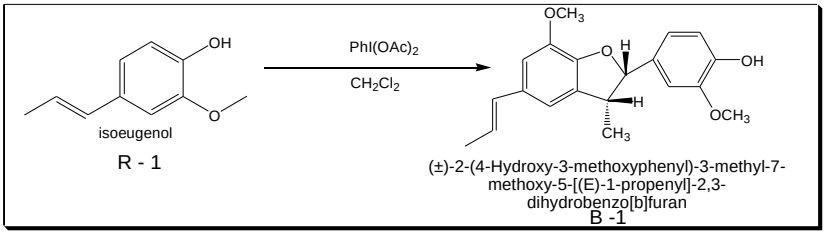
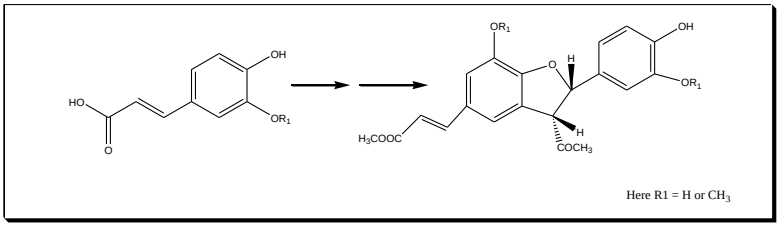
A series of synthetic furan lignans, especially dihydrobenzofuran lignans, obtained by biomimetic oxidative dimerization of caffeic and ferulic acid methyl esters followed by derivatisation reactions was tested for its Antibacterial [4,5,6] and Antioxidant [7,8] activity.Similarly, dehydroisoeugenol, a synthetic furan lignan was prepared by dimerisation of isoeugenol[1] using iodobenzene diacetate in dichloromethane at room temperature for 60 hours. These furan lignans were further diversified to their corresponding ether and ester derivatives for potential "Antibacterial" candidates.The basis of the research was the synthesis of dehydrodiisoeugenol and its derivatives. The dehydrodiisoeugenol was prepared using the following synthetic route:



Scheme 1

A number of ether and ester derivatives of the above compounds were prepared under different conditions. Ethers were prepared using alkyl halides in K_2CO_3 and the esters were synthesized using either acid chlorides, or directly from the carboxylic acids using DCC (dicyclohexylcarbodimide) and DMAP (dimethylaminopyridine). Similar dimerization of the caffeic acid and ferulic acid methyl esters were carried out in the presence of Ag_2O. The caffeic acid and ferulic acid derivatives were prepared using the following general scheme [2, 3].



Scheme 2

These compounds have shown promising "Anti-Angiogenic" activity. [2] Attempts were made to synthesize novel compounds by fusing these compounds with other compounds showing independent activity to synthesize more potent derivatives.

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Synthesis of Some New 1-(Substituted)-3-Methyl-4-(Hydrazone)-2-Pyrazolin-5-One as Antimicrobial Agents

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In view of the potential biological activities of hydrazono-2-pyrazolin-5-one [1-4] some new 1-(substituted) -3-methyle-4- (hydrazono)-2-pyrazoline-5-one are synthesized. The synthesis involves the treatment of ethylacetoacetate with different diazonium salts in the presence of sodium acetate. The product obtained is later on treated with thiosemicarbazide, isonicotinic acid hydrazide, N- (5-chloro-6-fluoro-1, 3-benzothiazole-2-yl) hydrazinecarbothioamide and N-4H-1, 2,4-triazol-4-yl hydrazinecarbothioamide to furnish 1-thiocarbamoyl-3-methyl-4- (hydrazono)-2-pyrazolin-5-one, 1-isonicotinyl-3-methyl-4-(hydrazono)-2-plyrazolin-5-one, 1-(5-Chloro-6-Fluro-1, 3-benzothiazole-2-yl) thiocarbamoyl-3-methyl-4- (hydrazono)-2-pyrazolin-5-one and 1-[(1,2,4-triazole-4-yl) carbothioamide]-3-methyl-4-(hydrazono)-2-pyrazolin-5-one respectively. These compounds were tested for their antimicrobial activities using cup plate technique and showed significant antibacterial activity gainst S. aureous (gram +ve), E. coli (gram –ve) bacteria and antifungal activity against A.niger fungi. DMF was run as a control and test was performed at 200, 100, 50, 25 μg/ml concentration. Ofloxacin and ketoconazole was used as a standard drug.

References:

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Glipizide Matrix Patches

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The purpose of the study was to investigate the effects of copolymer, plasticizer and chemical enhancer on the release/permeation profiles of glipizide from the polymer matrix patches. The experimental data would help in developing transdermal systems with the drug. The matrix patches containing glipizide were prepared using ethyl cellulose (EC) as the main polymer, polyvinyl pyrrolidone (PVP) as the copolymer, dibutyl phthalate (DBP) as the plasticizer and l-menthol, oleic acid and n-Octanol as the chemical enhancers. The release and permeation data from the matrix patch containing 300 mg EC, 150 mg PVP, 30% DBP and 15 mg drug is satisfactory and tensile strength of the patch is over 6 MPa. The experiments were carried out in the modified Keshary – Chien diffusion cell at 37ºC ± 0.5 for 8 hours. It is interesting to note that the percent release of the drug decreases with the addition of even 1% of any chemical enhancer listed above. The matrix patches having 200 mg PVP and either 1% l-menthol or 1% oleic acid gives satisfactory release and permeation data. The matrix patches were also prepared with ATBC, DBS, ATEC and TEC as the plasticizer. The quality and the release profiles of the patches were not satisfactory.

Here two combinations are given only.

Patch Code	EC: PVP: Glipizide+30%DBP	% release
G6	300:150:15	63
G9	300:200:15	48

References:

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Synthesis and Biological Evaluation of Porphyrin-flavin Conjugates in Photodynamic Therapy

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Photodynamic therapy (PDT) is a noninvasive therapeutic technique for the treatment of a number of tumoral afflictions and other benign diseases. PDT relies upon the selective accumulation of photosensitiser into cancerous tissues followed by irradiation of the diseased area. Among the various classes of proposed PDT drugs porphyrin derivatives remain so far the only one approved by the FDA for human treatment. Following our interest in the development of cationic porphyrin conjugates with potential use in medicine, we have coupled the flavin moiety with porphyrin using the click chemistry. In this way, we have designed new porphyrin-flavin conjugates with different linker between the porphyrin and falvin moieties. The synthesized compounds have been characterized by different spectroscopic studies such as UV-visible, ^{1}H NMR and mass-spectra. Details of synthetic procedure and biological properties will be presented in the conference.

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Synthesis of Some Novel Benzoxazine Derivatives as Potential COX-2 Inhibitors

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Anti-inflammatory agents are an important group of compounds in clinical use [1]. Anti - inflammatory activity is now-a-days synonymous with COX-2 inhibitory properties [2]. Benzoxazinones have been found to possess a number of useful biological activities - anti-inflammatory activity being one of them. In continuation of our earlier work [3] on Benzoxazinones, it was considered worthwhile to synthesise new Benzoxazinones with potential anti-inflammatory activities.

Thus, simple or N - substituted benzoxazinones were reacted with chloroacetyl chloride under Friedel Crafts conditions to obtain 6-substitutedbenzoxazinones which on reaction with bifunctional derivatives, such as aminopyrazole thiols or benzimidazole thiols, gave novel benzoxazinone derivatives. The products were characterized by their spectral data and tested for their anti-inflammatory properties. Results of our studies in this direction will be presented.

References:

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Reaction Engineering of Multiphase Catalytic Pharmaceuticals Processes

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Chemical processes used to manufacture pharmaceuticals, often involve the production of high value-added products with an annual basis of a few kilograms to several thousand metric tons. Conventional processes used in industry for the manufacture of pharmaceuticals are largely based on stoichiometric organic synthesis, but these lead to a serious waste disposal problem [1]. The focus in earlier days was more on quality of the final products, even though the overall yield to the desired product in many situations was very poor. This was acceptable due to the large difference between the selling price and manufacturing cost of these products. For this reason, issues related to reactor design and environmental needs were considered to be on a low priority [2]. However, in recent years, more stringent environmental regulations and increasing competition has resulted in the development of new processes where catalysis and reactor design have gained increasing attention [1].

A review of the recent developments in emerging multiphase catalytic pharmaceutical processes for the manufacture of various key chemicals, and an overview of reaction engineering principles needed for reactor design and interpretation of performance of reactor will be presented. It gives an overview of recent applications in pharmaceuticals where heterogeneous and homogeneous catalyzed multiphase chemistries have been identified that are more efficient and represent safer operation with decreased environmental impact when compared to existing processes. The classification of the various types of reactions that are typically encountered, along with distinguishing features of these reactions and commonly used multiphase reactor types have been discussed. The summary of key reaction engineering issues that occur in multiphase catalytic processes in pharmaceutical industry, along with some thoughts on future needs and challenges

References:

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Synthesis and Biological Evaluation of Isoxazoles Derivatives

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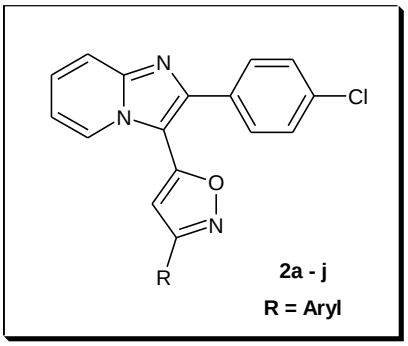
Large number of biologically active compounds possess imidazo[1,2-a] pyridine moiety. Isoxazoles are reported for many therapeutic applications which are anticonvulsant, anticancer, muscle relaxant, antibacterial and hypoglycemic etc. In the study of developing new targets, a skeleton structure based on isoxazole is determined.

The strategy employed for the synthesis involves the cyclocondensation of (2*E*)-3-[2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]-1-aryl-prop-2-en-1-ones **(1a-j)** with hydroxylamine hydrochloride and sodium acetate in glacial acetic acid gives 2-(4-chlorophenyl)-3-[3-aryl-isoxazol-5-yl]imidazo[1,2-*a*]pyridines **(2a-j)**.



All the synthesized compounds have been characterized by Elemental analyses, IR, ^{1}H-NMR and Mass spectral studies and purity of the compounds have been checked by thin layer chromatography. Screening of these new heterocycles for their various biological activities is in progress.

One-Pot Synthesis of Aldehyde from 1, 2-diols

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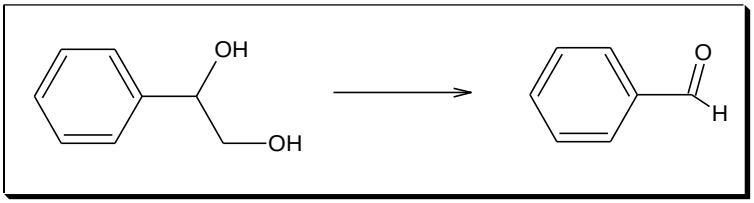
A simple and mild system for one-pot synthesis of aldehydes from 1,2-diols using lead tetra acetate as an oxidizing agent. Lead tetraacetate is widely used in organic chemistry. However, it is moisture sensitive, hazardous to handle and costly. So it was prepared in situ by combination of Lead diacetate and tert-butyl hypochlorite at room temperature and, used for cleavage of 1,2-diols to get the corresponding aldehydes. Further it was seen that excess of tert-butyl hypochlorite form corresponding acid chloride.



Scheme 1
Reagents and conditions:
a) 2.0 mmol tert-butyl hypochlorite;
b) 2.2 mmol tert-butyl hypochlorite.

Aqueous Mediated Reactions: A Green Protocol

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The pursuit of Green Chemistry is a growing culture among the community of chemists across the globe. In response to the social need for developing green chemistry, we too have made our contribution in this domain. We have developed green synthesis for various biologically active compounds that may serve as future medicines using water as reaction media. Water can undoubtedly be considered the cleanest solvent available. The use of this non-traditional solvent provides a new approach emphasizing pollution prevention through the design and use of cleaner processes can help the chemical enterprise to achieve a sustainable future. Under the framework of Green Chemistry, we have designed the synthesis of pharmaceutically important different scaffolds by coupling microwave technique with water including many multicomponent reactions like Biginelli reaction [1] and Hantzsch reaction [2]. In this regard, we will discuss several synthetic examples of bioactive heterocycles where we have proven water as highly benefically and green solvent.

Thus avoiding the organic solvents during the organic synthesis, this technique leads to a clean, efficient and economical technology (green chemistry); safety is largely increased, work up is considerably simplified, cost is reduced with enhanced selectivities. Details of this work will be discussed during the conference.

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Design and Synthesis of Inhibitors for Methionine S-Adenosyltransferase (MAT) of Mycobacterium Tuberculosis.

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Mycobactrium tuberculosis (Mtb) is a successful pathogen that overcomes the numerous challenges presented by the immune system of the host. In the last 40 years very few anti-TB drugs have been developed, while the drug resistance problem is increasing; thus there is a strong need to develop new anti-TB drugs active against both the acute & chronic growth phases of the mycobacterium. Methionine S-adenosyltransferase (MAT) is an enzyme involved in the synthesis of S-adenosylmethionine (SAM), which is essential for mycolipid biosynthesis. As an anti-TB drug target, Mtb-MAT has been well validated. The homology model of Mtb-MAT has been constructed using the X-ray structure of E. coli MAT (PDB code: 1MXA) & rat MAT (PDB code: 1QM4) as templates, by comparative protein modeling principles. The docking studies helped in finding out the orientation and conformation of the known and designed ligands.

The set of known molecules comprising of amino acid analogues, purines derivatives such as uric acid, xanthine and theophyline were taken for the docking study. It was found that the cavity of the Mtb-MAT had large number of interacting points with ligands that helped in designing the structurally diverse class of inhibitors. The de novo drug design used to identify new fragments for designing the MAT novel inhibitors. From the study, we have found fluoren amine, 2,7-dimethyl-3-ethylamine indole, tetrahydoquinoline derivatives, tetrahydronaphthilinone derivatives and some benzthiozole derivatives as top-scoring hits. The fragment 2,7-dimethy-3-ethylamine indole was taken as a lead molecule and on further designing it revealed five best fit structurally diverse novel derivatives, which were then subsequently taken up for synthesis. The synthesis and testing for the inhibitory activities are underway.

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Synthesis, Spectral, Antibacterial and Computational Investigations of Schiff Base Pyrazolone Compounds

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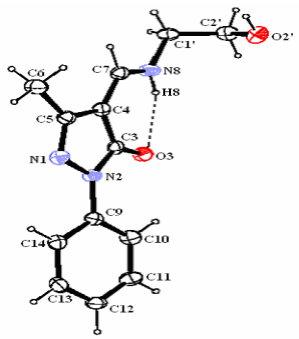
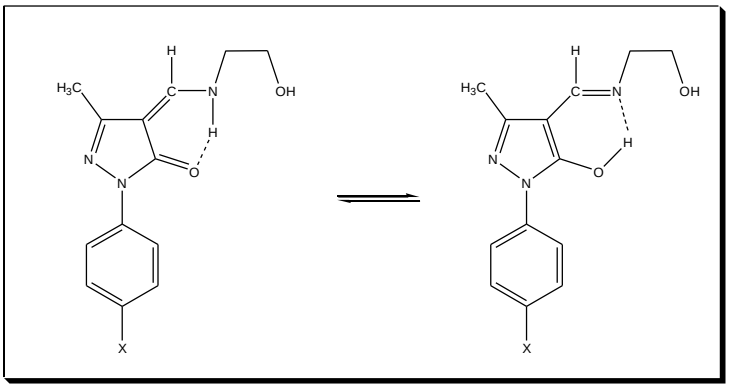
Pyrazolone are key structure in numerous compound of therapeutic importance [1]. Compound containing this ring system are known to display diverse pharmacological activities such as antibacterial [2], antifugal [2], anti-inflammatory [3], analgesic [3], and antipyretic [3]. Recently many articles reported the pyrazolone base compounds as anticancer [4], anti-tumor [5] agents. Due to variety of applications of this class of compound, the studies on these derivatives were the subject of many researchers including ours [6-7]. We herein report the synthesis of pyrazolone derivative, 5-hydroxy-3-methyl-1-phenyl-1H-pyrazole-4-carbaldehyde (I); 5-hydroxy-3-methyl-1-p-tolyl-1H-pyrazole-4-carbaldehyde (II); 4-(4-formyl-5-hydroxy-3-methyl-pyrazol-1-yl)-benzenesulfonicacid (III) and its corresponding schiff base 4-[(2-hydroxy-ethylamino)-methylene]-5-methyl-2- phenyl-2,4-dihydro-pyrazol-3-one(HL^1); 4-[(2-hydroxy-ethylamino)-methylene]-5-methyl-2-p-tolyl-2,4-dihydro-pyrazol-3-one(HL^2); 4-{4-[(2-hydroxy-ethylamino)-methyl]-3-methyl-5-oxo-4,5-dihydro-pyrazol-1-yl} benzene sulfonic acid (HL^3). These compounds were characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR, electronic spectra and mass spectrometry. The X-ray single crystal determination of one of the representative compound was carried out which suggests existence of amine-one tautomeric form in the solid state. Antibacterial screening is performed for all these compounds and with reasonable confidence we conclude that the activity is increasing with addition of schiff base (azomethine) group. Also it is significantly vary with substitution at phenyl ring of pyrazolone.

The electronic structure of the same representative compound was optimized using 6-311G basis set at HF level ab *initio* studies to predict the coordinating atoms of the compound.



X-ray structure of HL^1



X = H, CH_3, SO_3H

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Side Chain Modified 8-aminoquinolines as Potential Antimalarial Agents

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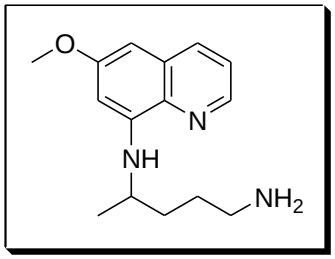
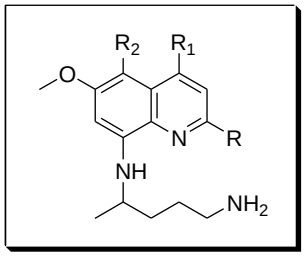
Malaria is one of the most serious parasitic infections in the third world countries. Primaquine (PQ, **1**) an 8-aminoquinoline, is a clinical drug of choice for radical cure of relapsing *P. vivax* and *P. ovale* malaria. But PQ has some serious side effects, thus it is far from being an ideal antimalarial drug.



1



2

The accumulation of 8-aminoquinolines in the parasite food vacuole is a part of their weak base properties and it can be increased by introducing basic groups either in the ring or in the side chain of 8-aminoquinolines. So a series of side chain modified analogs of PQ and other 8-aminoquinolines (**2**; R, R_1, R_2 = alkyl or alkoxy groups) has been synthesized by attaching 1, 2, or 3 alkylamine linkers to the side chain of parent 8-aminoquinolines. Some compounds of this series have shown activities better than PQ against chloroquine (CQ) sensitive D6 and CQ resistant W2 strain. Such modification may lead to analogs which retain tissue-schizontocidal activity of PQ with improved blood-schizontocidal activity.

In this presentation, synthetic procedure followed to synthesize above mentioned side chain modified analogs of 8-aminoquinolines and their biological activity will be discussed.

The Molecular Recognition of Dipeptide by Oligoglycyl Head Group of Amphiphile: A Quantum Chemical Study

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In the present work, we presented an analysis of the unusual recognition specificity exhibited by marked difference in the binding behavior of dipeptide with amphiphilic head group when subtle relative change of N-terminal and C-terminal of the dipeptide are made. Recently, in a series of detailed experiments, binding of aqueous dipeptides, GlyX and $X^{/}$Gly (X = Leu, Phe, Pro, Ala; $X^{/}$ = Leu, Phe) with dialkyl oligoglycyl amphiphiles is studied. It is observed that GlyX are specifically bound to $2C_{18}BGly_2NH_2$ while $X^{/}$Gly is insignificantly bound. We first studied the conformational energy variation of GlyPhe, PheGly and model of $2C_{18}BGly_2NH_2$ amphiphile using semi-empirical and *ab-initio* methods in vacuum. Using the individual energy optimized monomer structure of amphiphile and peptide, we studied the binding energy of optimized GlyPhe: amphiphile pair and PheGly: amphiphile pair structures at 1:1 and 1:2 ratio at the same level of theory using a population of structures. Binding of GlyPhe is favorable over the binding of PheGly at various levels of theory (semi-empirical and *ab-initio*). It is noted that the hydrogen bonding pattern in the GlyPhe binding is more effective than that in the PheGly binding. In the population of low energy structures, PheGly: amphiphile structures have more exposed area around the hydrophobic Phe group than the GlyPhe: amphiphile structures. Relatively more PheGly: amphiphile structures have intermolecular orientation unsuitable to contribute to the population of head group structures relevant in aqueous interface. Summarizing, significantly better binding capacity of GlyPhe over the PheGly with amphiphile, is due to the difference in hydrogen bonding interaction pattern, hydrophobic effect and possible orientations of the amphiphile and peptide at interface, relevant to the condensed phase monolayer structure. All the three factors cooperatively lead to favorable recognition of GlyPhe over PheGly as observed in experiment. A calculation of the ratio of the amphiphile-peptide bound complex to the initial concentration of the amphiphile indicates that the diffusional process at the peptide interfaces could be significantly influenced by hydrogen bonding.

Exploitation of Triose Phosphate Isomerase as a Drug Target in *Leishmania donovani*

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In Kinetoplastida, the seven glycolytic enzymes converting glucose to 3-phosphoglycerate are localized in glycosomes whereas in other organisms glycolytic enzymes are cytosolic. These enzymes have some different properties that may serve as a good drug target for development of new anti-trypansomatid drugs. Inhibition of glycolytic pathway reduce the synthesis of ATP would lead growth arrest completely to parasites.

In this study Primers were designed to amplify the **Triose Phosphate Isomerase** gene of *L. donovani***,** which interconverts dihydroxyacetone phosphate to glyceraldehyde-3 phosphate from the available sequence of *L. mexicana*. The 756 bp DNA fragment amplified in the genomic DNA of *L. donovani was* cloned in the pGEMT easy cloning vector using restriction sites at 5 ' and 3 ' of the primers. Positive clones were confirmed by restriction digestion analysis. The complete sequence of *Ld*TIM ORF (756 bp) was confirmed by nucleotide sequencing of recombinant pGEMT-TIM clone. The nucleotide sequence of *Ld*TIM has been deposited in GenBank under Accession No. DQ 649411.

It has been observed that, the percentage of GC content in ORF is 62.03%. *Ld*TIM shows 49.2 %, 46.3%, 66.6%, 88.10% identity with *Human*, *Mouse*, *T. cruzi*, and *L. mexicana* respectively. Signature sequences are from 165-175. The residues constituting the subunit interface are highly conserved among the enzyme of *L. donovani*, *L. mexicana* and *T. brucei*, but are mostly different from those in the enzyme of other organisms. In *L. donovani* the glutamate was found at position 66 as *L. mexicana* , instead of glutamine in all other available sequences. The glutamine is thought to be important for the stability of the dimeric enzyme. In *L. donovani* one extra amino acid was found at C- terminal of the protein which could be exploited. It has also cysteine residue at position 15 which has been a target of various studies with a view towards developing selective covalent inhibitors importantly human has methionine at this position.

It may be concluded that the Triose Phosphate Isomerase gene of *L. donovani* may be used for inhibition of ATP synthesis as well as development of new drugs. Protein purification and biochemical characterization is underway.

Conversion of Alcohols to Carbonyls and Monohydroxy Phenols with UHP in Ionic Liquid: Use of Acidic Amberlite Resin (IRA-120) as Catalyst

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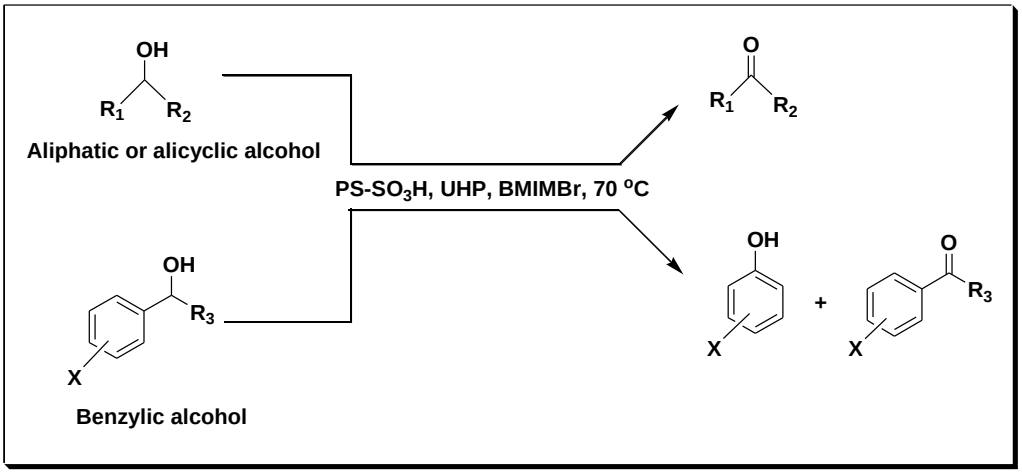
Oxidative transformation of alcohols to carbonyl and other industrially important molecules such as phenols is one such attractive area due to the wide ranging utility of these products as precursors and intermediates for many drugs, resins, vitamins, fragrances, plasticizers, pharmaceuticals, disinfectant, bis-phenol A and other uses. Apart from the conventional methods [1] there have been several reports for preparation of such oxidative products using oxygen or hydrogen peroxide as the oxidants under the influence of different metal catalysts [2- 4].



Scheme 1

We observed that aromatic alcohols, on oxidation with urea-hydrogen peroxide in presence of acidic Amberlite IR-120 resin in ionic liquid at 70 ^{o}C produced phenols and carbonyl compounds in 30-60 minutes. Under similar condition aliphatic and alicyclic alcohols yielded carbonyl compounds only.

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Toxoplasma Gondii Ferredoxin-NADP$^+$ Reductase (TgFNR): Role of Ionic Interactions in Stabilization of Native Conformation and Structural Cooperativity

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The apicoplast and the proteins present therein are parasite-specific targets for chemotherapy of apicomplexan parasites. Ferredoxin-NADP$^+$ reductase (FNR) is an important enzyme present in the apicoplast of *Toxoplasma gondii* that operates as a general electron switch at the bifurcation step of many different electron transfer pathways. In spite of its importance as drug target not much structural information on the enzyme is available. Using fluorescence and CD spectroscopy in combination with enzyme activity measurement and size exclusion chromatography we studied the pH dependent changes in structural and functional properties and inter-domain interactions in recombinant TgFNR to understand the interactions responsible for stabilization of native conformation and modulation of functional activity of the enzyme. Under physiological conditions, the recombinant TgFNR is stabilized in an open conformation. The open conformation of the enzyme was found to be essential for its optimum functioning, as induction of compactness/rigidity by modulation of pH, leads to decrease in the functional activity. In native conformation, strong interactions exist between the NADP$^+$- and FAD-binding domains thus making the enzyme a structurally cooperative molecule. Under acidic conditions (pH about 4), the inter-domain interactions present in native TgFNR were lost and the enzyme became structurally non-cooperative. The pH induced structural alterations in the NADP$^+$ binding domain, more precisely compaction of the conformation leading to its stabilization against thermal denaturation. The studies demonstrate the significance of electrostatic interactions both in stabilization of native conformation and maintenance of structural cooperativity in TgFNR.

Pharmacophore Hypothesis for Atypical Antipsychotics

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A three-dimensional pharmacophore hypothesis was developed for atypical antipsychotics in order to map common structural features of highly active compounds by using **HipHop** in **CATALYST** program. The pharmacophore hypotheses were generated using twelve standard drugs as training set and validated using five pre-clinical candidates as test set. The most predictive hypothesis (Hypo1) comprised five features *viz.* two hydrophobic regions, two hydrogen bond acceptors and one aromatic ring. In the absence of information like crystal structure of 5-HT_{2A} receptor and binding mode of antipsychotics with 5-HT_{2A} receptor, this hypothesis will serve as a potentially valuable tool in the design of novel atypical antipsychotics acting primarily at 5-HT_{2A} and D_2 receptors.

Design and Synthesis of Inhibitors against Malaria *Plasmodium falciparum* Dihydroorotate Dehydrogenase (*Pf*dhodh)

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Malaria is one of the major health problems of many tropical and subtropical countries and causes more than two million deaths per year. Due to drug resistance by the malarial strain there is a pressing need to synthesize newer molecules which act on different targets. DHODH, located in the outer membrane of the mitochondria is a crucial enzyme in *de novo* pyrimidine biosynthesis pathway. It catalyses the fourth step in the pathway which reduces dihydroorotate to orotate using flavin nucleotide as the cofactor. *Pf*DHODH can be exploited as a novel drug target for development of new antimalarial agents. Several derivatives of benzanilide, naphthamide, and urea have been reported to inhibit *pf*DHODH. Using molecular modeling methods we have designed *in silico* more than 80 virtual derivatives of the above mentioned compounds and docked and scored them in the active site of *pf*DHODH using the program GOLD (GOLD 3.0.1 CCDC, UK). Based on the docking scores we have focused attention on synthesis of some of compounds using microwave technique. Prior to biological evaluation we carried out prediction of activity of the new molecules using the 3D-QSAR technique Comparative molecular field analysis (CoMFA) (Sybyl 7.1)**.** The CoMFA show that an electrostatic contour around the most active benzanilide. Electronegative atom on the aryl amine ring of benzanilid (red contour) will improve activity. The aryl carboxy ring is seen to be surrounded by (blue contours) depicting requirement of an electron withdrawing group. The steric contour suggests that bulky substitutions on ortho and meta positions of aryl carboxy ring and minimal para substitution on aryl amine ring will improve the activity. The aryl carboxy could also be converted to other ring system like naphthalene. All synthesized compounds were confirmed by NMR and IR spectroscopy. Based on the antimalerial activity these molecules can be pursued as important leads for further development.

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Synthesis of imidazole derivatives of benzenepropane as possible dual function spermicides

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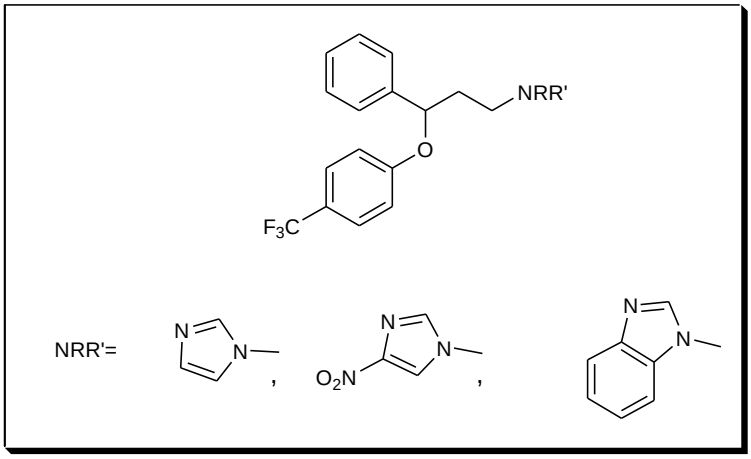
Most heterosexual women want to reduce the risk of acquiring a STD [1] as well as to control their fertility, has made developing user-controlled, topical vaginal microbicides, an urgent global need [2,3]. Several imidazole derivatives of benzenepropane were prepared and evaluated for the spermicidal activity along with anti-fungal, anti-trichomonas, and anti-bacterial activity. The compounds were prepared according to scheme 1. β-Chloropropiophenone (**1**) was reacted with appropriate 3-substituted imidazoles in presence of triethylamine in DMAC/ toluene to provide 3-substituted imidazolyl-1-phenyl-1-propeophenone. These propanones were reduced to corresponding hydroxy compounds with sodium borohydride in methanol, which were condensed with 4-chlorobenzotrifluoride in DMAC in presence of sodium hydride to give 3-substituted-1-phenyl-1-(4-trifluoromethylphenoxy)-propane. The compounds have shown varying degree of biological activities. Fluoxetine, fluconazole, metronidazole and nonoxynol (N-9) have been taken as standard [4]. The SAR will be discussed.



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Design of Thiophosphoryl Dendrimers: Computational and Synthetic studies

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Dendrimers are synthetic, highly branched, mono-disperse macromolecules of nanometer dimensions. The unique properties of dendrimers are high degree of branching, multivalency, globular architecture and well-defined molecular weight, made them promising new scaffolds for drug delivery. Dendritic hosts provide shelter to drug guests in three ways by 1) Covalent or non-covalent linkage, 2) Indirect attachment of drugs with usage of spacer and 3) Encapsulation. Computational studies are superior tools to predict the surface chemistry of the dendrimers and their compatability with the therapeutic agents. The design of self assembling phenomenon in dendrimeric drug delivery with molecular modeling techniques is a novel approach in the field of formulation technology. From quantum mechanics we found binding strength between thiophosphoryl dendrimers (core) and different class of drugs which have complementary Molecular Electrostatic Potential Surface (MESP) to the dendrimer surface. This Complementarity between surfaces of dendrimer and of drug leads to formation of three hydrogen bonds during interaction which is the major stabilizing force to hold the drug molecules to the dendrimers. Based on that idea we have designed and going to synthesize these self assembled complexes.

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Synthesis and Anti-Tubercular Activity of (*Z*)-2-(Nitroimidazolylmethylene)-2(3*H*)-Benzofuranone Derivatives

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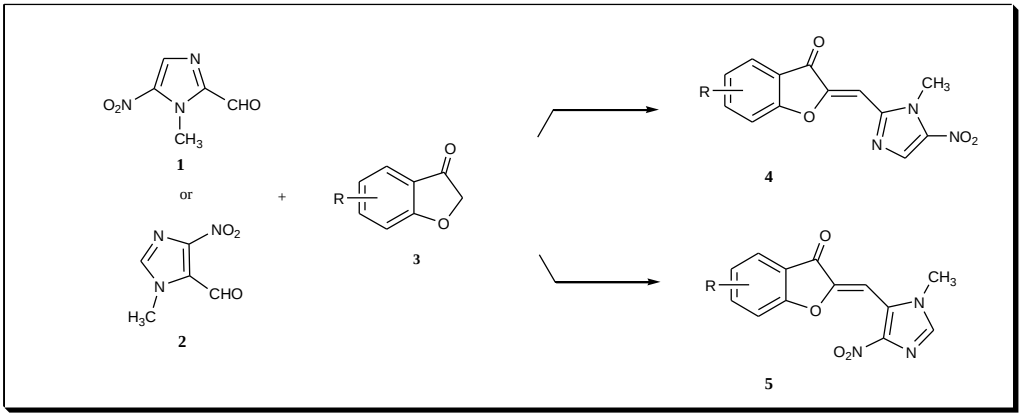
The recent emergence of outbreaks of multidrug resistant tuberculosis (MDR-TB) poses a serious threat to the treatment of the disease. Tuberculosis (TB) has undoubtedly increased in prevalence in most countries due to human immunodeficiency virus (HIV) epidemic. In response to these alarming statistics and trends, WHO declared TB to be a global public health emergency. Therefore, there is a necessity of searching for and synthesizing new active compounds with less side effects.

The use of nitroheterocyclic drugs (such as 5-nitroimidazoles) as antibacterial, antiprotozoal, and anti-cancer agents is well-established [1]. Furthermore, a series of (*Z*)-2-benzylidene-6,7-di- hydroxy-3(2*H*)-benzofuranones have shown antibacterial activity by inhibiting the chorismate synthase, a key enzyme in the shikimic acid pathway which is essential for the synthesis of aromatic amino acids in bacteria [2].

The title compounds were prepared according to the scheme shown below. 3(2*H*)-Benzofuranones **3** are key intermediates for the production of the desired compounds. Condensation of latter **3** with corresponding carbaldehyde **1** in acetic acid, in the presence of catalytic amount of sulfuric acid afforded compound **4**, while title compound **5** was prepared by a different method in acetic anhydride in the presence of anhydrous sodium acetate [3].
All the synthesized compounds were screened against *M. tuberculosis* $M_{37}Rv$ and shown excellent activity in comparison with rifampicine as the reference drug.



Scheme 1

References:

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Synthesis of Side Chain Modified 4-aminoquinolines as Antimalarial Agents

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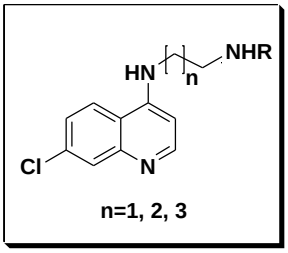
Despite over 100 years of drug development efforts, malaria remains one of the most devastating infectious diseases in the world. The current epidemic is fueled by the development of drug-resistant strains of *P.falciparum*, the parasite responsible for the most deadly cases of malaria. Research over the past two decades has shown that despite worldwide resistance to chloroquine and emerging resistance to mefloquine, there is still significant potential to discover new quinoline antimalarials with activity against even the most drug-resistant strains of *P. falciparum.*

Therefore in search of novel and potent antimalarial compounds we have synthesized large number of compounds by making modifications to the basic side chain of 4-aminoquinoline using various heterocyclic amines.



Some of the above synthesized compounds have shown promising antimalarial activity against *P. falciparum* with MIC values in the range of 0.125 - 0.03μg/ml

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N-Substituted 2, 4-Thiazolidinediones: Synthesis, Antidiabetic Activity and QSAR Study

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Bharati Vidyapeeth University, Pune-411 038, India.
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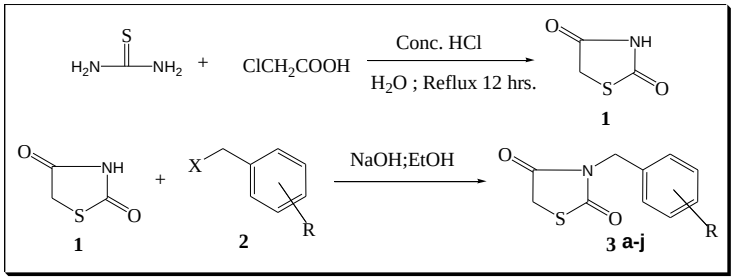
Peroxisome proliferator activated receptor-gamma (PPARγ) is transducer proteins because it plays an important role in type-2 diabetes mellitus. It has been reported that 2,4-thiazolidinediones activate PPARγ receptor. With this knowledge, a series of N-substituted 2,4-thiazolidinediones derivatives were synthesized and screened for antidiabetic activity using alloxan induced diabetes mice model and oral glucose tolerance test.



Scheme 1

Ten different N-substituted 2, 4-thiazolidinediones were synthesized using thiourea, chloroacetic acid and different substituted benzyl halides as starting material. The structures of finally synthesized compounds were confirmed by FT-IR and ^{1}H-NMR. 3-Benzyl-2,4-thiazolidinedione and 3-(4-methoxy-benzyl)-2,4-thiazolidinedione showed hypoglycemic activity comparable to Pioglitazone. Other compounds showed moderate activity. These compounds were also evaluated for glucose tolerance using Oral glucose tolerance test (OGTT). This study indicates that a free hydrogen at N in this series is not necessary for exhibiting activity. QSAR analysis of these N-substituted 2, 4-thiazolidinediones was also performed using multiple linear regression (MLR) analysis. The validity of the regression was confirmed by correlation coefficient, standard deviation and F-test value. From the QSAR equation it was found that thermodynamic and electronic parameters show good correlation with biological activity.

References:

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Design of 2-Furoic Acid Hydrazide Derivatives as Sodium Channel Blockers Useful in the Treatment of Neuropathic Pain

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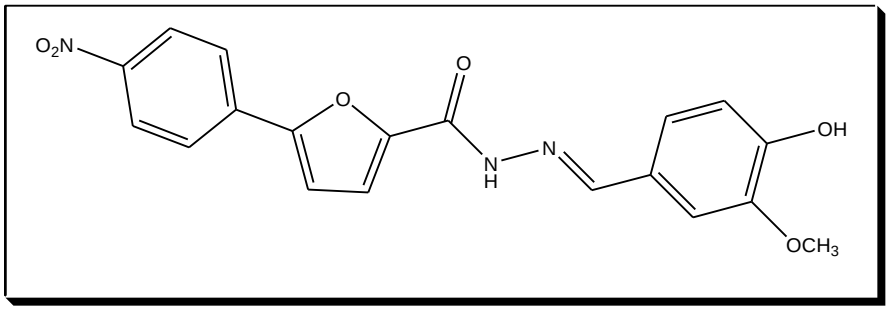
Neuropathic pain can be described as pain associated with damage or permanent alteration of the peripheral or central nervous system. At present, there are very few effective and well tolerated therapies for neuropathic pain. The most effective agents are use-dependent inhibitors of sodium channels namely phenytoin and carbamazepine [1]. The mechanisms of neuropathic pain in relation to the voltage-gated sodium channels have been reported in the literature [2].

The titled compounds were synthesized in BITS Medicinal chemistry laboratory according to earlier reported procedures. All of the synthesized compounds were evaluated for their antiallodynic and antihyperalgesic activities in the Chronic Constriction Injury (CCI) [3] and selective segmental L5 Spinal Nerve Ligation (SNL) [4] models of neuropathic pain. All experiments were approved by the Institutional Animal Ethics Committee. Four nociceptive assays aimed at determining the severity of behavioral neuropathic responses namely allodynia and hyperalgesia were performed, which involved measurements of spontaneous pain, dynamic allodynia, cold allodynia and mechanical hyperalgesia.

Statistical significance was determined for drug effects by one-way ANOVA, and bonferroni's post hoc test was used for individual comparisons with control values. Significance was assigned to a P value of less than 0.05.

Compounds were administered intraperitoneally at 100 mg/kg dose level on day 9 post-surgery. The control group rats received the vehicle (PEG 400). The pre-dose screening values were used as the animal's baseline scores. Compounds **4** and **11** significantly ($p<0.05$) reversed allodynic and hyperalgesic responses when compared to the control up to 2.5 h post-treatment in both the models of neuropathic pain.



Compound 4

References:

[1] Yogeeswari P, Vaigunda Ragavendran J and Sriram D, *Exp. Opin. Drug Discov.* **2007**, 2, 169.
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Rapid and Short Synthesis of Cryptosanguinolentine

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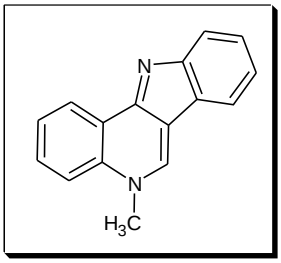
Natural products isolated from different sources serve as the lead compounds for the discovery of new drugs. *Cryptosanguinolentine* [1], an indoloquinoline alkaloid, possesses an angular indolo [3,2-c] quinoline ring system, isolated from *Cryptolepis sanguinolenta*, a shrub indigenous to tropical West Africa, which has been used in folk medicine as an antimalarial agent [2,3]. In view of interesting biological properties of indoloquinoline alkaloids, we report a facile, rapid and high yielding protocol for the synthesis of cryptosanguinolentine involving reaction of 1-methyl-2, 3-dihydro-quinolin-4(1*H*)-one and phenylhydrazine in presence of *p*-TSA at moderate temperatures. Further, in order to study quantitative structure-activity relationship, a diverse library of cryptosanguinolentine analogues was also prepared. Detail of this study will be discussed in the presentation.



Cryptosanguinolentine

References:

[1] Jean-louis Pousset, Marie-Therese Martin, Akino Jossang and Bernard Bodo, *Phytochemistry* **1995**, *39*, 735.
[2] (a) Peczyriskc-Czoch, W. Pognan, F. Kaczmarck, L. Boratyriski. J, *J. Med. Chem*. **1994**, *37*, 3503. (b) Seth Y. Ablordeppey, *Bioorg. Med. Chem.*, **2007**, *15*, 686. (c) Seth Y. Ablordeppey, *Bioorg. Med. Chem.* **2002**, *10*, 1337.
[3] (a) Molina, A. Vaquero, J. J. GarciaNavio, J. L. AlvarezBuilla, J. Pascula Terasa, B. Gago, F. Rodrigo, M.M. Ballesteros, M. *J. Org. Chem.* **1996**, *61*, 5587.

Synthesis and Biological Evaluation of Some New Pyrazoline

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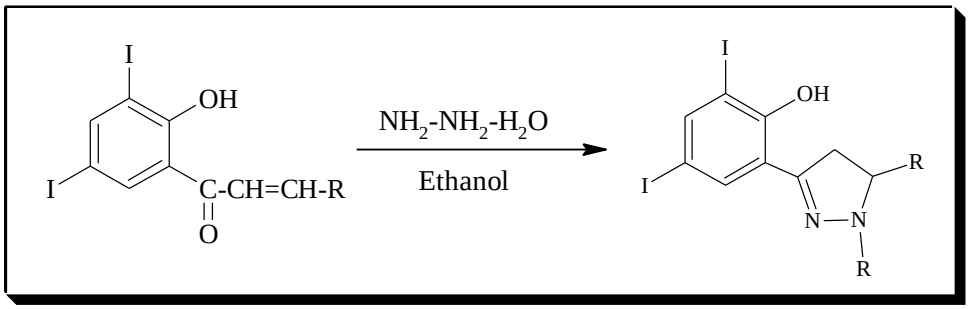
Heterocyclic compounds have captured our attention for many reasons chief among them are their biological activities. Here we have synthesized heterocyclic compounds, which were found to possessing multifarious antimicrobial activity, substituted pyrazoline have drown considerable attention due to their wide rang of pharmacological activities. In view of this we now report the synthesis of some new heterocycles viz.2- pyrazoline and their derivatives.
The main compound 2- pyrazoline have been prepared by reaction of substituted chalcones with hydrazine hydrate in ethanol yielding the desired pyrazoline which on treatment with acetic acid, benzoyl chloride gives substituted acetyl pyrazoline and benzolyl pyrazoline respectively. The structural assignment of the compounds was based on elemental analysis and UV, IR, NMR, MASS spectral data. All the synthesized compounds have been screened for their antimicrobial activity.



References:

[1] A.Levai, *J. Heterocyc.l Chem.*, **2002,** *39*, 1.
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Synthesis of N-{2-[4-(substituted)piperazin-1-yl]-2-oxoethyl}acetamides as Novel D_2 Antagonists

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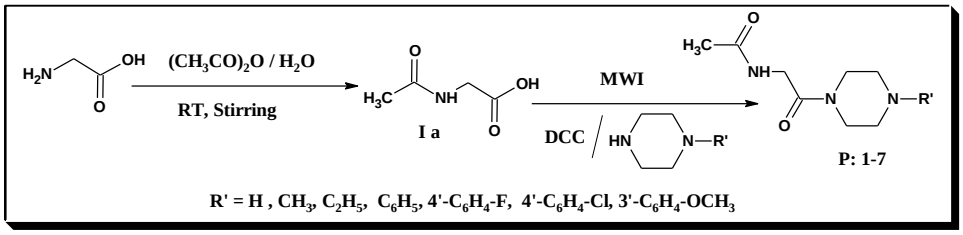
Chemistry Group, Birla Institute of Technology & Science, Pilani,
Rajasthan – 333 031, India.

Dopamine is a very important neurotransmitter responsible for modulation of psychomotor activity. Excessive dopaminergic activity in the mesocorticolimbic pathway has been implicated as the principal pathway involved in the etiology of psychoses. Most of the antipsychotic drugs block D_2 receptors. Non selective blockade of Dopamine receptors in the tuberoinfundibular pathway and the nigrostriatal pathway is responsible for the 'extrapyramidal' side effects of most of the antipsychotic drugs. The present study includes synthesis and screening of N-{2-[4-(substituted)piperazin-1-yl]-2-oxoethyl}acetamides as novel D_2 receptor blockers.

All the synthesized compounds are characterized by various spectroscopic techniques such as ^{1}H NMR, mass, elemental analysis and IR. Among the compounds synthesized P1 was found to be the most potent, exhibiting 90 % D_2 antagonism in the climbing mouse assay model.



Scheme1

Green Chemistry: Solid State One-Pot Synthesis of Benzopyrans and Quinolines Derivatives

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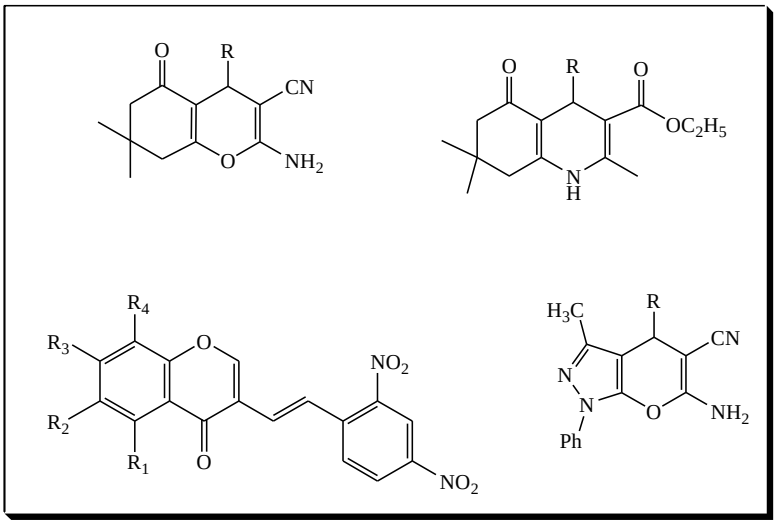
In modern organic chemical research, Wender defined the "Ideal Synthesis" as one in which the target components are produced in one step, in quantitative yield from readily available and inexpensive starting materials by resource-effective and environmentally acceptable process. The one-pot multicomponent condensations represent a best technique to perform a near ideal synthesis because they possess one of the aforementioned qualities, namely the possibilities of building-up complex molecules with maximum simplicity and brevity.

With increasing environmental concerns, more and more chemists are devoting in the area of "Green Chemistry". Avoiding organic solvents during the reactions in organic synthesis leads to a clean, efficient, and economical technology (green chemistry); safety is largely increased, work-up is considerably simplified, cost is reduced, increased amounts of reactants can be used in the same equipment, and the reactivities and sometimes selectivities are enhanced without dilution. Due to all these advantages there is an increasing interest in the use of environmentally benign reagents and procedures.



In the present work we have described novel routes for the synthesis of Benzopyran and Quinoline derivatives using green chemistry approaches such as multicomponent one-pot synthesis, solid state reactions coupled with application of grinding technique, microwave irradiation.

Synthesis of Substituted Quinolinyl Pyrimidines as New Class of Antimalarial Agents

Moni Sharma[a], Kumkum Srivastava[b], S. K. Puri[b] and Prem M. S. Chauhan[a *]
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Central Drug Research Institute, Lucknow 226001, India
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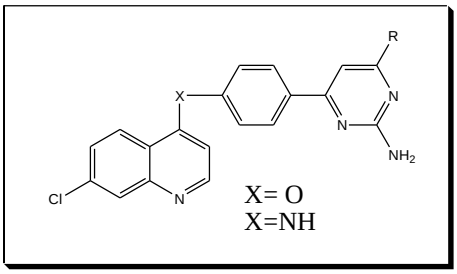
A Series of quinolinyl pyrimidines were synthesised and evaluated for their *in vitro* antimalarial activity against *Plasmodium falciparum*. Out of synthesised compounds, some compounds have shown MIC in range of 1-2µg/ML. These compounds are in vitro more active than Antimalarial drug pyrimethamine. The synthesised compounds can be new lead in antimalarial chemotherapy.The synthesis and biological activity will be discuss during conference.



Monitoring Protein Induced "Necklace" Formation with Surfactant Molecules and Characterization of Interactions Involved Using Twisted Intramolecular Charge Transfer (TICT) Fluorescence of Trans-2-[4-(Dimethylamino)Styryl] Benzothiazole

M. Sowmiya, Subit K. Saha*, Pradipta Purkayastha*
Birla Institute of Technolgy & Science Pilani -333 031, Rajasthan, India

Steady-state and time resolved fluorescence and fluorescence anisotropy of a potential probe molecule, trans-2-[4-(dimethylamino)styryl]benzothiazole (DMASBT) showing twisted intramolecular charge transfer (TICT) fluorescence have been used to monitor the interactions between bovine serum albumin and sodium dodecyl sulfate. Different types of interactions involved have been monitored nicely using the above mentioned fluorescence characteristics of DMASBT. The binding constant and the number of binding sites per protein molecule have been calculated using a new method. The nature of binding has been determined. The micropolarity at the binding sites of the probe molecule has also been calculated.

Novel, Facile & Eco-Friendly Green Chemical Synthesis of Some Important Drug Intermediates & API's

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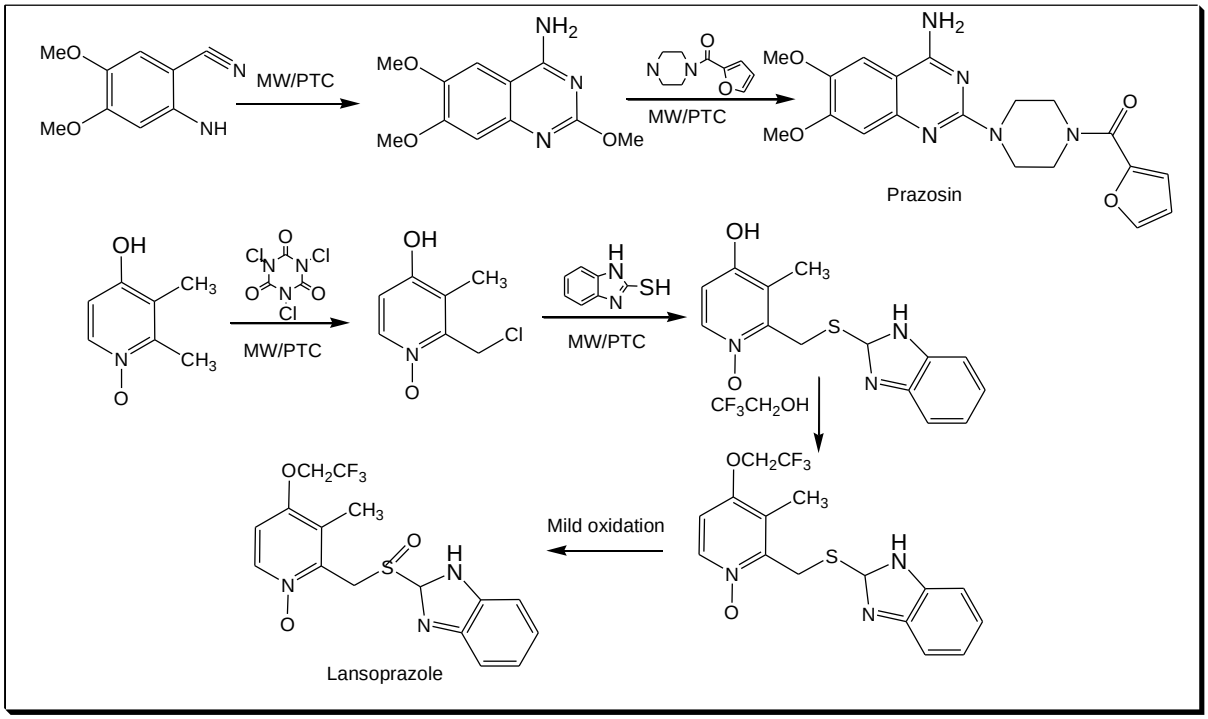
The concept of Phase Transfer Catalysis is known since 1965. Since then it has been systematically developed & applied successfully to the Drug & Pharma industry besides the other industries. Relatively simple, inexpensive & ecofriendly conditions & the resultant products in high yields & purity have made this field very attractive and popular. Another useful technique is Microwave Assisted Organic Synthesis (MAOS), is the becoming popular and finding applications in industrial chemistry. Both these techniques are useful tool of Green Chemistry. Side chain chlorination, *N*-alkylation, *N*-acylation, condensation, nucleophilic displacements *etc* are important reactions in the synthesis of various API's as well as their intermediates. Herein, we are presenting successful use of these Green Chemical Techniques for the facile, ecofriendly, high yielding & faster synthesis of intermediates of API's like Lansoprazole, Thioridazine, Prazosin & Cinnarizine, as shown below. A few examples are as follows.



A Smart Drug-loaded Bioplate using *Lotus corniculatus* Biomaterial for Transmucosal Drug Delivery

N. V. Satheesh Madhav, **M. S. Uma Shankar*** and Arvind Yadav
Novel drug delivery research laboratory, Pharmacy College Azamgarh
Itaura P.O. Chandeshwar, Azamgarh, U.P., India
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The current aim of our research work is to formulate and evaluate bioplates loaded with gentamicin using a novel mucoadhesive biomaterial from *Lotus corniculatus* seeds for transmucosal delivery. The bioplates were formulated by using *Lotus corniculatus* biomaterial with other co-processing agent and gentamicin. The different formulations were formulated by varying the concentration of biomaterial. The formulated biomaterial were subjected for various evaluation methods like thickness, surface pH, swelling index, weight variation, content uniformity, drug-exicipient interaction study, mucoadhesive test and *in vitro* drug release study using novel M-S static diffusion apparatus. Our experiment results revealed that the formulations exhibited uniform thickness, optimal swellability and promising mucoadhesivity. The drug release from the bioplate showed in a controlled manner for a period of 10 hrs by zero order patterns. Finally, conclusion was drawn that the biomaterial can serve as a potential promising retardant for delivering drugs in a controlled manner.

Yttrium Tiflate Catalyzed Synthesis of Benzofuran and Benzo[b]thiophene Derivatives in Ionic liquids

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Benzofurans and bezo[b]thiophenes derivatives are important class of heterocyc;ic compounds that are widely distributed in nature. They are common motif in many biologically active natural and synthetic products [1]. Substituted benzofuran and ben[b]thiophenes exibit antifungal, anticancer, antiviral, immunomodulatory effects and antioxidant activity [2]. They also find application in various other fields of chemistry and agriculture such as brightening agents, polymer adhesive etc.

There are some reports for the synthesis of benzofurans and benzo[b]thiophene derivatives under acid catalyzed conditions [3]. However some disadvantages are associated with these methods such as use of hazardous & corrosive reagents, use of volatile organic solvents etc. Thus there is a need of a simple and environmentally friendly method to generate these biologically and chemically important compounds. We have developed a route for the syntheses of 3-arylbenzofuran and 3-arylbenzothiophene derivatives by cyclodehydration of α-aryloxyketones and α-arythioketone catalyzed by yttrium triflate in ionic liquids. This procedure provides a facile, efficient and environmentally friendly synthesis of 3-arylbenzofuran and 3-arylbenzothiophene derivaties. Details of of this synthetic procedure will be presented.

References:

[1] McCallion, G D, *Curr. Org. Chem.* **1999**, *3*, 67.
[2] Buu-Hoi, N. P. P; Bisagni, E; Royer, R and Router C. *J. Chem Soc.* **1957**, 625
[3] Chen, Z; Wang, X.; Lu, W.; Yu, J.; *Synlett*, **1991**, 121 (and refernces therein)

Sperm Immobilizing Activity of Seven Newly Synthesized Dihydropyridine Analogues

M. Vosooghi*, H. R. Sadeghipour Roodsari, M. Amini$_b$, Z. Naghibi Harat, P. Daneshgar and A. Shafiee.
Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Sperm motility plays an important role in normal fertilization process of mammalian. Role of external factors on the regulation of sperm motility has been studied extensively. Acrosomal reaction of human spermatozoa is highly associated with T-type Ca^{2+} channels and that is mainly mediated by calcium influx through α-1H-T-type Ca^{2+} channels. Nifedipine, a calcium channel blocker (CCB) inhibits progersterone-induced acrosomal reaction and complete loss of sperm motility. In the present work, the activity of seven newly synthesized dihydropyridine analogues on the motility of sperm were determined and compared to nifedipine as standard drug. Elongation of alkyl ester groups in compounds **6a-g** caused a gradual increase in sperm motility reduced value. Consequently, the size of alkyl is important in the activity of test compounds. Compound 6a, dimethyl 1,4-dihydro-2,6-dimethyl-4-[2-(2-chlorophenyl)thiazol-4-yl]-3,5-pyridine dicarboxylate was the most active compound.

Preparation and Biological Evaluation of 4- Substituted Phenyl -2-(M-Phenoxyphenyl) -1-H-1,5-Benzodiazepines

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Rajkot-360 005 (Gujarat) India
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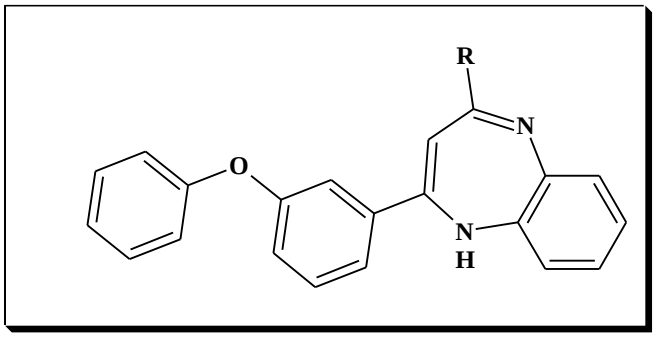
m-Phenoxy benzaldehyde is associated with wide spectrum of biological activities like antimicrobial, anti-inflammatory, anthelmentic, analgesic, antidepresent, anti HIV, antitubercular, anticancer, CNS depresent and fungicidal properties. Some benzodiazepines can be used as therapeutic agents for the treatment of depresant, antitumor etc.. Synthesis of 4-substituted phenyl-2-(m-phenoxyphenyl)-1H-1,5-benzodiazepines (I_{a-j}) have been undertaken by the the cyclo condensation of 1-substituted phenyl-3-(m-phenoxy phenyl)-2-propene-1-ones with o-phenylene diamine in the presence of acidic medium.



(I) R=Substituted phenyl

The constitution of the products (I_{a-j}) have been supported by using elemental analyses, IR, ^{1}H NMR and mass spectral data.The products (I_{a-j}) were assayed for their *in vitro* biological assay like antimicrobial activity towards gram positive and gram-negative bacterial strain and antifungal activity at different concentrations for their MIC values.
The biological activities of the synthesized compounds were compared with standard drugs like *Ampicillin, Cefalexin, Erythromycin, Clotrimazole, Amoxycillin, and Griseofulvin.*

Pharmacogenomics

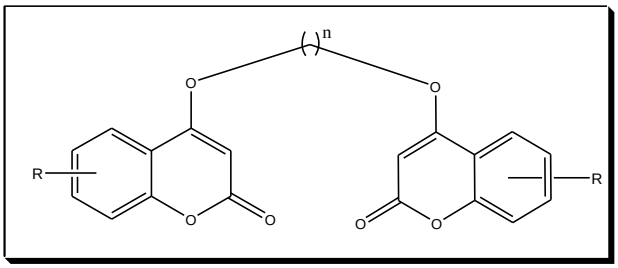
M. Ramya[a] and Y. Harini [a, b]
[a]Department. of Biotechnology, K.L.C.E, Guntur Dist, India.
[b]Department of Biotechnology, K.L.C.E, Guntur Dist, India.
e-mail: malireddyramya@gmail.com, harini_bt211@yahoo.co.in

Pharmacogenetics is the study of the impact of heritable traits on pharmacology and toxicology. Pharmacogenomics examines how your genetic makeup affects your response to drugs. Researches in the field are working on applying human genome knowledge to pharmaceuticals by identifying genes that account for varying drug reactions in different people. Eventually; they hope to be able to customize drug therapies for specific patient populations or even individuals. A drug does not have the same effect on every individual. Genetics decide the rate and extent of drug absorption, distribution, metabolism and excretion. About 2 to 3 percent of hospitalizations are due to adverse drug reactions. We can highlight this concept as "therapy with the right drug at right dose in the right patient". Pharmacogenemics combines traditional pharmaceutical sciences such as biochemistry with an understanding of common DNA variations in the human genome. An extension of pharmacogenetics is the discovery that genetic polymorphisms have the potential to affect a drug's action. The interplay of genotype and drug efficacy has been defined as pharmacogenomics. There are many applications and benefits of pharmacogenomics. The main applications of pharmacogenomics are in cancer, Alzheimer's disease; Parkinson's disease is mainly focused. We are now going to present how this pharmacogenomics is helpful in designing a drug for the above mentioned diseases.

Synthesis and Biological Activity of Various Bis-(4-Coumarinoxy) Methane Using Substituted 4-Hydroxy Coumarins

Akshay M. Pansuriya[a], **Mahesh M. Savant[a]**, Chirag V. Bhuva[a], Sudhir K. Joshi[b], Yogesh T. Naliapara[a], Anamik K. Shah[a]
[a]Department of Chemistry, Saurashtra University, Rajkot- 360 005, India
[b]Kotak Science College, Rajkot- 360 005, India

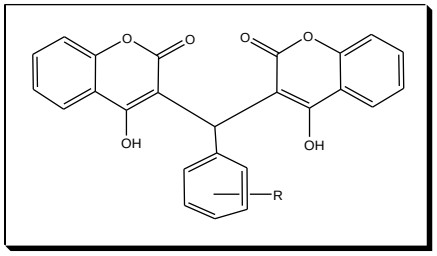
Naturally occurring coumarins are reported for wide range of biological activity. Earlier many dimeric, tetrameric coumarins were synthesized and reported their anti- HIV, anti coagulant activity. Here we synthesized various dimeric 4-hydroxy coumarins having methylene as central linker.



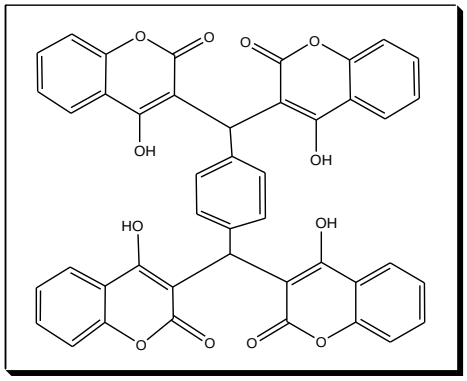
1a-m n= 1, 2

Many dimeric coumarins with or without linker have been reported for biological activities especially

1. Dimeric coumarins



2. Tetrameric coumarins



Determination of Stability on Basis of Anthocyanins Content in Kokum Juice

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The purpose of stability testing was to provide evidence on how the quality of medicinal product varies with the time under influence of a variety of environmental factors such as temperature and humidity. Hence, kokum juice was subjected to accelerated stability studies and evaluated by anthocyanins content. Anthocyanins are present in the fruit of Garcinia indica and other species of garcinia, are responsible for colour of kokum juice. The anthocyanins in juice was studied during three month period in accelerated conditions i. e., at 40 ºC ± 2 º C / 75 % RH ± 5 %RH. The total acidity, brix and pH of the formulation were also monitor as the parameter of stability testing. The study was carried out as per the ICH guidelines [1].

The method used for total anthocyanins determination involves the UV spectroscopy. Measurement of the absorbance done at 510 nm on sample diluted with pH 1.0 and 4.5 buffers. The pigment content was calculated in absolute quantities with the aid of extinction coefficients taken from literature [2]. Kokum juices kept in stability chamber at 40 ºC/75 % RH. 30 ml of juice were withdrawn from four samples of capacity 200 ml each on 0, 1 and 3 Month intervals. The degradation of anthocyanins in kokum juice samples was observed which is in the limits of acceptance criteria according ICH guidelines.

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Design and Synthesis of Side Chain Modified 4-Aminoquinolines as Antimalarial Agent

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Malaria is a protozoal disease responsible for about 2 million deaths each year. The large percentage of casualty occurs in tropical regions especially south Asia and Africa. For last several decades Chloroquine (CQ) is maintaining its reputation as first line drug in the treatment of malaria .Chloroquine acts at the erythrocytic stage of the parasite life cycle by interfering with the polymerization of heme which is toxic to the parasite .But the emergence of CQ resistant strains of *plasmodium falciparum* alarmed the requirement of profound research for new entities or analogs of existing molecules to answer the problem of resistance. The resistance toward 4-aminoquinoline is not target specific but compound specific as other closely related compound was found active against resistant strains of plasmodium.

In the quest of superior CQ analogs which could be active against resistant strains, few new molecules were designed and synthesized From the available literature two points attracted our attention. (i) 7-chloro-4-aminoquinoline nucleus is most suitable for antimalarial activity, particularly, inhibition of hematin formation and accumulation of the drug at the target site (ii) The role of carbon chain length in the amino alkyl side chain has also been investigated, and the results suggest carbon atoms in the side chain of CQ has significant impact on activity.

Considering these two facts we have designed few molecules which are closely related to the Chloroquine. The modifications in the side chain of CQ have been done according to bioisosteric concepts. Details of synthetic procedure and biological activities of these compounds will be discussed in detail.

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Involvement of p53, p21 and BCl_2 Family Members in CC Induced Apoptosis in MCF-7 and MDA MB-231 Human Breast Cancer Cells

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Centchroman (CC) is a candidate antibreast cancer agent undergoing Phase III Multicentric Clinical Trials in Stage III/IV Breast Cancer [1,2]. We have already demonstrated that CC displays antineoplasticity in the MCF-7 (ER+ve) Human Breast Cancer Cells (HBCCs) [3]. Apoptosis is the major player implicated in its cytotoxicity in MCF-7 and MDA MB-231 (ER-ve) HBCCs [4]. In the present study, we have explored the molecular basis of its antineoplasticity in these cell types using benchmark Antiestrogen (AE) Tamoxifen (TAM) as a positive control.

Cycloheximide (CHX, protein synthesis inhibitor) and Actinomycin-D (ActD, RNA synthesis inhibitor) significantly attenuates CC induced apoptosis thus confirming the involvement of RNA and Protein synthesis pathways therein. Flow Studies demonstrate that the treatment of CC with pan-Caspase inhibitor Z-VAD-fmk, down-regulates apoptosis thus signifying the role of caspases in invoking cell-death. CC induces the expression of Cdk (Cyclin-dependent kinase) inhibitor, p21 in both the cell types. However, unlike MDA MB-231, phospho-p53 (Ser 15) and Bax (proapoptotic protein) expression was found to be elevated in CC exposed MCF-7 specifically. This, therefore, confirms that CC induced Cell-cycle arrest involves p53 independent-p21 expression in MDA MB-231 cells. Moreover, BCl_2 (antiapoptotic protein) level was decreased in both the cell types by CC treatment. It is hypothesized that the balance between pro- and antiapoptotic elements regulates the cybernetics of apoptosis.

Our data thus indicates that CC induced apoptosis through critical regulation of RNA and Protein synthesis supplemented adequately by Caspases, p53 and BCl_2 family members.

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[3] Srivastava, S., Sharma, R., Balapure, A.K. *Indian J. Pharm.* **2004**, *36*, 238.
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Improved and Rapid Synthesis of New Coumarinyl Chalcone Derivatives and their Antiviral Activity

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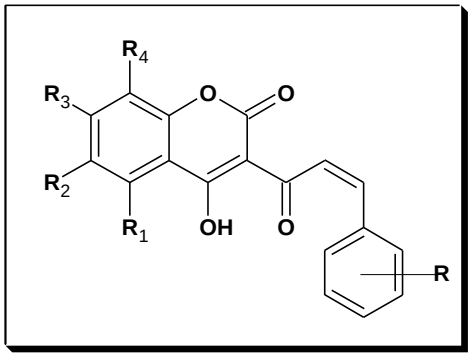
Two closely related coumarins, 4-hydroxy-8-isopropyl-5-methylcoumarin and 4-hydroxy-6-chloro-7-methyl coumarin were prepared by single step synthesis which was further acetylated at C-3 and further converted to the respective Chalcones. The preparation of Chalcones is carried out by a modified method which drastically reduce the reaction time considerably from 48 hrs to 3 to 4 hrs. Two series of eighteen new compounds, which were evaluated for possible antiviral activity.



R_1, R_2, R_3 and R_4 = Different Substituents
R = Various EWG or EDGs

Ab Initio and DFT Investigations on CH-π Interactions between Saccharides and Aromatic Amino Acids in Transport of Maltose through Maltoporin

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CH-π interactions are weak, non-conventional hydrogen bonds largely governed by dispersive and charge transfer interactions. The presence of an aromatic residue apposing the carbohydrate moiety, as observed in the crystal structures of several carbohydrate-binding proteins, is an example of CH-π interactions. The dependence of the energetics on the geometry of CH-π interactions is beginning to be understood [1-2]. Previous studies from our laboratory indicated that the strength of these interactions can vary between 1 and 7 kcal/mol [3]. Hence, our interest is to characterize the CH-π interactions using quantum chemical calculations by considering the binding of α-D-glucose to maltoporin as the model system. This transport protein has six aromatic residues - Y6A, Y41A, W74B, F229A, W358A and W420A (the suffix is the subunit identifier) - forming a helix-shaped "greasy" slide all along the pore. Mutation of even one of these residues leads to a substantial decrease in the stability constant of binding. We have performed gas phase ab initio calculations at MP2/6-31G** level of theory and also DFT calculations. The results from these will be presented.

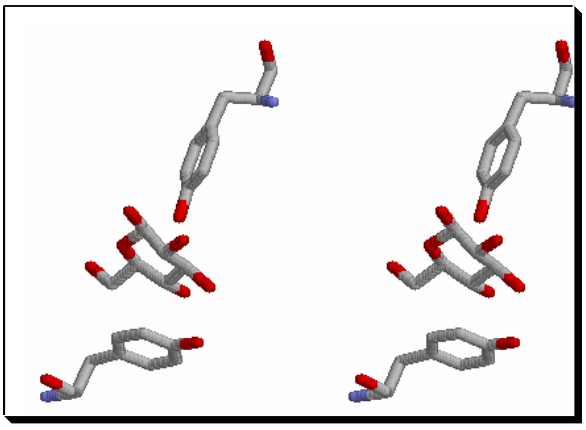

Figure: Stereoview of S3 binding site in 1MPM (PDB ID) maltoporin. α-D-glucose stacked between aromatic residues Y6A (bottom) and Y118A (top). These residues constrict the porin channel and provide specificity.

References:

[1] Fernandez-Alonso M.C., Canada F. J., Jimenez-Barbero J. and Cuevas G. *J. Am. Chem. Soc.* ***2005,*** *127,* 7379.
[2] M. S. Sujatha., Y.U. Sasidhar, and P.V. Balaji, *Protein Science,* ***2004****, 13,* 2502.
[3] M. S. Sujatha., Y.U. Sasidhar, and P.V. Balaji, *Biochemistry,* ***2005,*** *44,* 8554.

Synthesis and Antimicrobial Evaluation of Indazole Derivatives bearing Furan Nucleus

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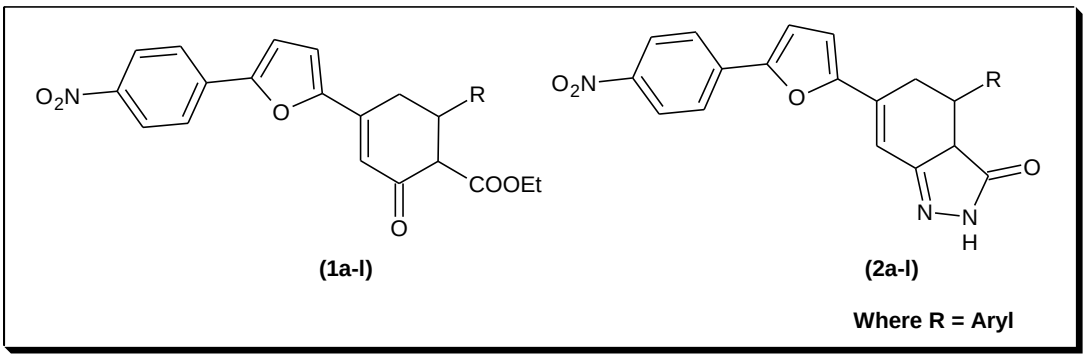
Indazoles are the well known heterocycles which are present in variety of natural product and medicinal agents. Indazole ring system is associated with diverse biological activities such as antimicrobial, anticancer, antiinflammatory, fungicidal, herbicidal, insecticidal etc. In view of these it was thought of interest to develop a molecule which is biologically more potent and less toxic. With this findings we have synthesised some new indazole derivatives which summarized as under.



The synthesis of the title compounds are achieved by the multistep reaction, followed by the synthesis of α,β-unsaturated ketones from the base catalysed condensation of substituted acetophenones and 5-(4-nitrophenyl)furan-2-carbaldehyde. These on reaction with ethyl aceto acetate in presence of K_2CO_3 in acetone yielded cyclohexenones **(1a-l)**. Compounds **(1a-l)** on condensation with hydrazine hydrate in presence of acetic acid in ethanol gives indazoles **(2a-l)**.

All the synthesized compounds have been characterized by IR, ^{1}H-NMR and Mass spectral studies and purity of the compounds have been checked by thin layer chromatography. All synthesized compounds have been assayed for their antimicrobial activities against different bacterial strains and antifungal activity against *A. niger*.

Synthesis of Glycosyl Amino Acid and Peptide Building Blocks by Ferrier Reaction via Glycal Route

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In recent years Glycopeptides gained importance both in terms of their synthesis as well as their potential as safe and effective drug of future. Despite the daunting challenges associated with the preparation of glycopeptides in the laboratory, the chemical synthesis could yet prove to be the most viable way to provide 'precision tools' for glycoibiology. The glycosylation of peptides in biological systems induces many important structural and functional changes. To study these effects, convenient, rapid access to large numbers of glycosylated peptides is desirable. The chemical synthesis of glycosides or oligosaccharides generally involves reaction of a donor and acceptor in presence of Lewis acids. However, the use of Lewis acid is often a limiting factor for the rapid synthesis of glycopeptides due to non compatibility of the substrates and other reaction conditions of the protected amino acids and growing peptide chain. The synthesis of glycopeptides hitherto limited to the use of glycol-amino acid building blocks. Therefore, an attractive approach for the synthesis of glycopeptides could be developed where the glycosylation reaction is performed under mild acidic conditions or ideally under neutral conditions. Among various available methods, efficient and selective construction of glycosidic linkages can be achieved by the Ferrier reaction. Due to the synthetic versatility of the 2, 3-unsaturated glycoside, this method has proven useful for a wide range of applications including the synthesis de-oxy saccharides. The exceptional synthetic value of the Ferrier process, however, has not been translated significantly to carbohydrate chemistry. Recently a direct *O*-Glycosylation was reported in excellent yields under mild conditions viz. Zinc(II) diethyl and palladium acetate[1] and molecular iodine alone as catalyst where the glycosylation is Ferrier reaction is carried out under neutral conditions as compared to, normally used, highly acidic Lewis acid catalysts.[2]

Prompted by these reports we have successfully attempted the synthesis of glycosylation of appropriately protected amino acid and dipeptide. The glycosylation are carried out on Boc-Ser-OMe and Z-Phe-Ser-OMe as shown in figure-1 under different experimental conditions and stoichiometry to make glycosylated monomer (**1**) and glycopeptide (**2**) respectively in excellent yield. During this study we have developed a new procedure for O-linked glycopeptides and glycoamino acid under extremely mild reaction condition. The details of the synthetic procedures, experimental conditions, data and yields etc. will be presented.

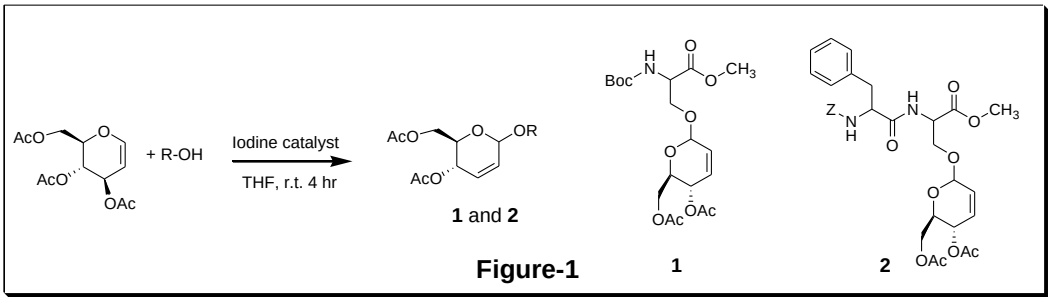

Figure-1

References:

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An Expert Diagnostic System for the Detection and Classification of Lesions in Mammograms

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The mammography is the most effective procedure for an early diagnosis of the breast cancer. In this paper, an algorithm for detecting massive lesions in mammography images will be presented. The database consists of digital images acquired in from the MIAS public database which consists of images of different class such as fatty, glandular and dense containing both normal as well as cancerous images. A reduction of the surface under investigation is achieved, without loss of meaningful information, through segmentation of the whole image, by means of a ROI Hunter algorithm. The ROI hunter algorithm not only segregates the massive lesion but also predicts the further spread of the cancer .In the classification step feature extraction by pectoral muscle suppression is achieved using a connected component labeling approach which has delivered an accuracy of over 80% in the images. Further it was tried to classify them on the basis of their geometric features and form a knowledge base to be used for the development of the neural network which would improve the efficiency and computational cost.

Virtual Screening for Protein Kinase Inhibitor for Anti Cancer Application

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The protein kinase superfamily represents both an enormous opportunity and a unique challenge for drug discovery. Protein kinases play central roles in the cellular economy and it is well known that a large number of diseases involve aberrant protein kinase activity. Protein kinases represent a major class of drug targets for the pharmaceutical industry, and the identification of kinase inhibitors with novel and diverse chemotypes is therefore a high priority. We have conducted a virtual screening using a ligand library of synthetic heterocyclic entities (Imidazolines, Azetidinones, Acetamide derivatives etc.). Docking studies were carried out for successful target (Platelet-derived growth factor receptor, Receptor protein-tyrosine kinase erbB-2 and Urokinase-type plasminogen activator) and research target (Cell division protein kinase 6, Mitogen-activated protein kinase, Proto-oncogene tyrosine-protein kinase SRC, RAF proto-oncogene serine/threonine-protein kinase, Serine/threonine protein kinase 12, Serine/threonine-protein kinase PLK1, Thymidine kinase, Tyrosine-protein kinase etc.).

Synthesis and Study of Controlled Release of Aceclofenac by Using New Type of Acrylic Polymer

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New acrylic type polymeric systems having degradable ester bonds linked to aceclofenac were synthesized and evaluated as materials for drug delivery. Methacryloyloxy(2-hydroxy)propyl-4-isobutyl-_-methylphenyl acetate (MOPE), a new methacrylic derivative of aceclofenac in which the drug is separated from the methacrylic backbone by an oxy(2-hydroxy)propylene spacer arm and hydrolytically labile ester bond, was synthesized from reaction of glycidyl methacrylate with aceclofenac. The resulting drug containing monomer was copolymerized with methacrylamide, 2-hydroxyethyl methacrylate, N-vinyl-2-pyrrolidone or n-butyl methacrylate by free radical polymerization method in N,N-di-methylformamide (DMF) solution, utilizing azobisisobutyronitrile as initiator at the temperature range 65–70 0C. The obtained polymers were characterized by FT-IR, 1H NMR and 13C NMR spectroscopy. Gel permeation chromatography (GPC) was used for determination of average molecular weights of drug–polymer conjugates and showed that the polydispersity indices of the polymers are in the range of 1.9–2.3. Drug release studies were performed by hydrolysis in buffered solutions (pH 1.23 and 7.4) at 37 0C. Detection of hydrolysis by UV spectroscopy at selected interval showed that the drug can be released by selective hydrolysis of the ester bond at the side of drug moiety. The release profiles indicated that the hydrolytic behavior of polymeric prodrugs is strongly based on the hydrophilicity of polymer and the pH of the hydrolysis solution. The hydrophilic polymers containing aceclofenac were hydrolyzed in buffer solutions rather than the hydrophobic polymers.

Synthesis and Pharmacological Evaluation of Heterocyclic Indole Derivatives

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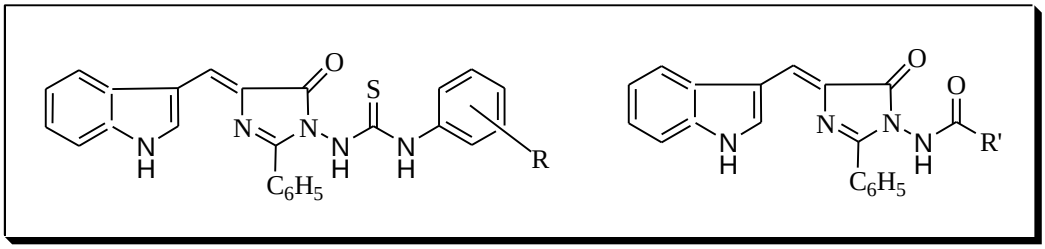
Imidazole and indole residues are probably the most well known heterocycles, which are common and important feature of a variety of natural products and medicinal agents. Compounds carrying indole residue e.g. indomethacin, tenidap are NSAIDs and have shown to exert its anti-inflammatory effects. Indole the potent basic pharmacodyanamic nucleus has been reported to possess a wide variety of biological properties viz, anti-inflammatory, anticonvulsant and antimicrobial. Furthermore, imidazole nucleus forms the main structure of some well-known components of human organisms i.e. the amino acid histidine, vit-B_{12}, histamine and biotin. It is also present in the structure of many natural or synthetic drug molecules i.e. cimetidine, azomycin and metronidazole. Besides these, imidazole/imidazoline nucleus containing compounds exhibited a wide spectrum of biological activities such as anti-inflammatory, analgesic and anticonvulsant. Encouraged by these observations and in continuation of our research work on the synthesis of heterocyclic compounds, we report herein, the synthesis of a hybrid molecule containing both the indole and imidazole residues. The structure of the newly synthesized compounds was supported by IR, ^{1}H NMR and Mass spectral data. These compounds were investigated for their, anti-inflammatory, analgesic, ulcerogenic activities and lipid peroxidation. These results clearly indicated that few of the hybrid molecules having both indole and imidazole residues showed significant anti-inflammatory and analgesic activities. Among these 4-(1*H*-Indol-3-yl-methylidene)-2-phenyl-1-[2-(6-methoxy-2-naphthyl)-propanamido]-5-oxo-imidazoline showing maximum anti-inflammatory and analgesic activity with minimum ulcerogenicity and lipid peroxidation has emerged as a lead compound.



A Simple, Efficient and Environmentally Benign Synthesis of Thiosemicarbazides Using Microwave Irradiation

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[b]Department of Bioengineering, University of Pittsburgh, 260 Kappa Drive, RIDC Park, Pittsburgh, PA 15234 (USA),
e-mail: shaan_organic@yahoo.co.in, sharmanawal@gmail.com

In times where emphases are put on speed, diversity, and efficiency in the drug discovery process, microwave-mediate strategies offer significant advantages over conventional linear-type syntheses. It is well known fact and most of pollution control boards/ agencies have given much attention toward alarming situation of tons of waste generation as a result of commercial production of variety of active pharmaceutical ingredients (API's) as well as their key intermediates. Growing concerns to minimize or eliminate toxic waste generation by pharmaceutical and biotech industries, have attracted attention of many research teams all over the globe and many groups have already begin to explore alternative environmentally safe synthetic technologies for making life saving pharmaceutical products.

We have attempted to synthesize biologically important thiosemicarbazides using microwave irradiations. This novel method provide better yields, much lower reaction time, cleaner products without generation of solvents waste or other via products reaction. Many thiosemicarbazides have shown characteristic anticonvulsant, antifungal, plant growth promoting, antibacterial, and anti-tubercular biological properties. The synthetic procedure involves simply mixing the reactants and subjecting them for microwave irradiation for 2-8 minutes and isolating the products. However, in few cases it require purification of product, still it offer more economical and environmentally benign technology to synthesize these molecules. The purity was determined using TLC and melting points and structural elucidations were carried out by ^{1}H-NMR, IR and Mass spectral studies. Details of experiments and spectral data will be presented during conference.

Synthesis and Antitubercular Activities of Some New Imidazolyl-2,6-Dimethyl-3,5-Bis-N-Substituted Phenylcarbamoyl-1,4-Dihydropyridines

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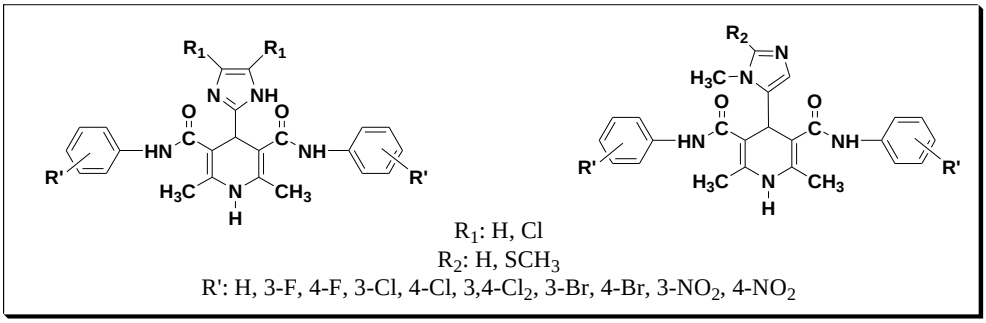
The recent emergence of outbreaks of multidrug resistant tuberculosis (MDR-TB) pose a serious threat to the treatment of the disease. Tuberculosis (TB) has undoubtedly increased in prevalence in most countries due to human immunodeficiency virus (HIV) epidemic. In response to these alarming statistics and trends, WHO declared TB to be a global public health emergency. Therefore, there is a necessity of searching for and synthesizing new active compounds with less side-effects.

The antitubercular activities of pyridine analogues of NAD were reported in 1956. It was recently observed that the lipophilic precursors of pyrazinoic acid and nicotinic acid were more active may be due to better penetration of the compounds into the cell wall of *M. tuberculosis* [1-3]. In view of this, it was of our interest to synthesize some new imidazolyl-1,4-dihydropyridine-3,5-dicarbamoyl derivatives with lipophilic groups. These compounds may act as precursors and after penetration into the cell wall may lead to the 3,5-carboxylate anions by enzymatic hydrolysis.

The title compounds were prepared by condensation of different acetoacetanilides with substituted imidazolecarboxaldehydes in methanol with excess amount of ammonia and were screened against *M. tuberculosis* $M_{37}Rv$. Among them, some derivatives showed moderate activities in comparison to rifampicin as a reference drug.



R_1: H, Cl
R_2: H, SCH_3
R': H, 3-F, 4-F, 3-Cl, 4-Cl, 3,4-Cl_2, 3-Br, 4-Br, 3-NO_2, 4-NO_2

Scheme 1

References:

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Design and Synthesis of Y- Shaped PPARγ Agonists

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PPARγ agonists are used as oral hypoglycemic for the treatment of Type-II diabetes mellitus. But, many of them have been reported to have hepatic or cardiac toxicity which calls for the design of new safer and potent PPARγ agonists. The crystal structure of PPARγ shows that the ligand binding domain (LBD) is μ or Y- shaped. Agonist like Rosiglitazone takes a "U shaped" conformation within the receptor. It is possible that Rosiglitazone docks in the LBD in both tail-up or tail-down conformation leaving one arm unoccupied of Y-shaped LBD. Docking experiment helped us knowing that Y-shaped ligands, which can occupy both tail-up and tail-down conformation simultaneously scores better than reference drug Rosiglitazone. Further experimentation proved that both the arms of cavity are not similar. Y-shaped ligands with relatively greater hydrophilicity in upper arm (compared to lower arm, as per docking pose) than molecules which have similar hydrophilicity on both the arms are scoring even better. Based on this idea we designed and synthesized potential PPARγ ligands.

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Microwave Promoted Synthesis of Pyridone Derivatives Employing Urea and Lewis Acid under Solventless Condition

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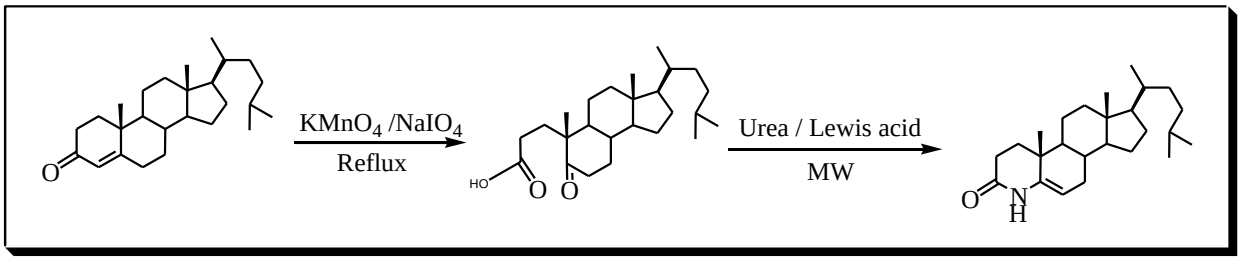
The pyridone constitutes an important class of 4-aza heterocycles of both natural and synthetic origin. Moreover, several pyridone derivatives are well known to exhibit antitumor activity, inhibitor of aromatase, treatment of prostate cancer respectively. During recent years, a large number of modified steroids containing nitrogen in the steroidal skeleton have been synthesized, which are viewed in literature. Studies on its biological activity showed that a vast number of such compounds are employed in regular clinical practice [1]. The A-ring annelated 4-aza heterosteroid such as Finasteride are well known drugs against benign prostatic hyperplasia (BPH) which affects adult males [2]. In addition, Finasteride is also used in the treatment of hair loss [3] and in the prevention of prostate cancer. The literature report for the synthesis of 4-aza heterosteroids generally included the cyclization reaction of keto acids employing CH_3NH_2 under autoclave at 180^o C for 8 hrs [2]. Herein, we report a convenient synthesis of pyridone derivatives from steroidal conjugated carbonyl compounds using new reaction strategies. This involves two reaction steps – (a) cleavage of conjugated carbonyl compounds using reagent system $KMnO_4$ / $NaIO_4$, (b) cyclization reaction employing urea and lewis acid under microwave irradiation for 3 min to afford the product 4-aza heterocycles in good yield.



Scheme1

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Homology Modeling and Docking Studies on Human Histamine H_1-receptors

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Histamine, a biogenic amine formed by decarboxylation of the amino acid L-histidine and is found in large quantities in most tissues, mainly in the granules of mast cells. It controls a multitude of physiological functions by activating specific receptors on target cells and acts as one of the major inflammatory mediators as well as a neurotransmitter in the central nervous system. Histamine exerts its effects by binding to four different histamine receptors (H_1-H_4), which all belong to the large family of G protein-coupled receptors (GPCR), which are transmembrane proteins on a cell's surface that can interact with both the environment outside and inside the cell. The GPCRs are integral membrane proteins that possess seven membrane-spanning domains or transmembrane helices. The ligands bind to the portion of the GPCR on the outside of the cell, activating the GPCR by allowing it to bind with a G protein and setting off a series of events within the cell. Much drug development today is focused on finding chemicals that affect the ability of the ligands to bind with the GPCR, thereby either inhibiting or accelerating the cellular process. The GPCRs play a crucial role in many diverse disease processes. In mammalian smooth muscle, endothelial, and brain tissue, histamine activation of H1 receptors predominately triggers Gq/11 protein activation with subsequent stimulation of phospholipase (PLC) and formation of inositol phosphates (IP) and diacylglycerol. In the first half of last century, research in the histamine field completely focused on the role of histamine in allergy, resulting in the development of several potent "anti-histamines". Research and development of H_1 ligands largely has focused on antagonists that are used for their anti-allergy effects in the periphery. Recent understanding of the clinical importance of H_1 receptors in brain, however, suggests the pharmacotherapeutic potential of H_1 agonists in neurodegenerative and neuropsychiatric disorders.

The H_1 receptor is involved in many of the symptoms of allergic reactions and the "antihistamines" or histamine H_1 antagonists are widely used to relieve allergic symptoms. Despite the therapeutic importance of the H_1 receptor for many years the molecular features of the H_1 receptor protein were not known. We describe homology modeling of the H_1 receptor based on the X-ray structure of bovine rhodopsin. The protein model has been generated by applying homology modeling and docking studies.

Synthesis and Antimicrobial Activity of Substituted Cyclic Enediynes

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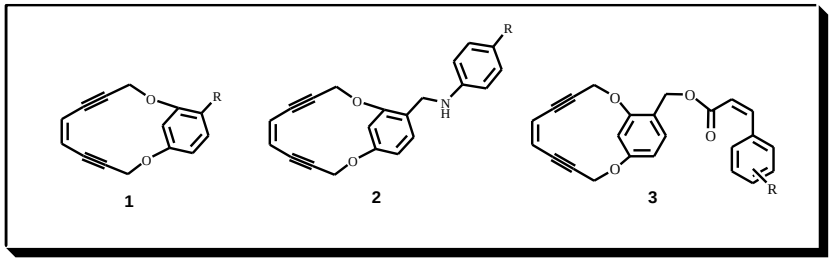
The novel chemical framework and potent antitumor activity of the enediyne natural products such as calicheamicin, dynemicin, esperamicin, and neocarzinostatin has fostered interest in the development of simple enediynes with low thermal cyclization temperature [1-4]. It is well established that thermally labial enediynes exhibit anticancer activity, while there are few scattered examples in the literature about the biological importance of thermally stable enediynes [5]. As part of our ongoing efforts towards the synthesis of biologically active compounds [6-11], herein we report synthesis thermal reactivity and antimicrobial activity evaluation of various cyclic enediynes (**1**), cyclic enediynes amine conjugates (**2**), and ester (**3**).



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Utilization of Wasteland Halophytes to Prepare Few Formulations and their Impact on Taste and Flavor

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Halophytes are known as salt tolerance plants. In India, number of halophytes is found which grow up on wasteland and are used only as animal fodder. The present work is the continuation of our earlier work where we have developed a novel method for the production of sazi from wasteland halophytes; here we report the novel method of utilization of sazi for the preparation of papad (an Indian snack). Sazi, a salty material, which have been prepared from three different halophytes i.e. *Haloxylon salicornicum*, *Salsola baryosma* and *Suaeda fruticosa*. In the present work, few formulations of this material have been prepared and their effect has been investigated on the taste and flavor of papad. It has been observed that 0.5 to 1.5% sazi provides best results in terms of taste and flavor while higher concentrations provide bitterness. Further better results are obtained in the presence of binder and stabilizer. Antimicrobial activities of this material and all formulations have been investigated on few bacteria and fungi such as *Escherchia coli*, *Staphylococcus*, *Aspergillus flavus* and *Aspergillus niger*. Antacid activity of these formulations has also been reported.

A Combination of $AlCl_3$, Ionic Liquid and MW: An Efficient Method for Dehydration and 1,3-Dipolar Cycloaddition

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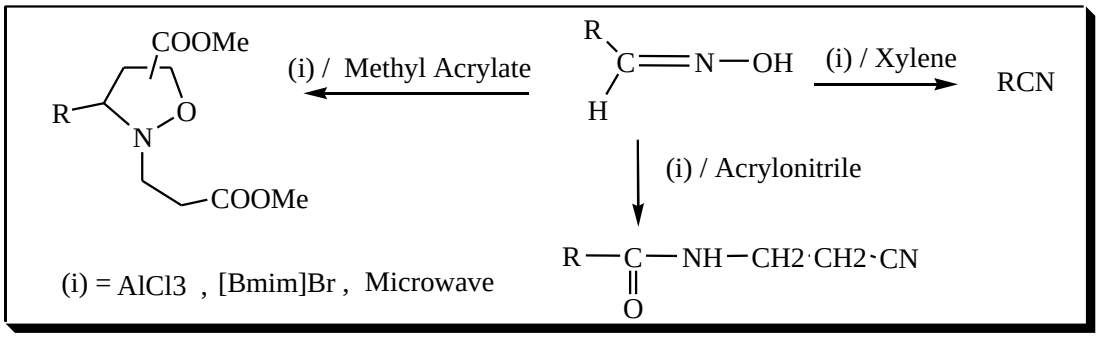
Recently room temperature ionic liquids have been used very effectively for various reactions due to their solvating ability, simple work-up procedure and recyclability. Ionic liquids are highly polar, but noncoordinating and they catalyze the reactions giving better selectivity. Advantages like rapid reactions, high yields and selectivity in microwave-assisted reactions are well known in recent years. We have been using this methodology for some other reactions [1]. In our earlier work [2], indole-2-carboxamide was obtained when Vilsmeier Haack reagent was treated with indole-2-aldoxime followed by treatment with boiling NaOH. However treatment with only water furnished corresponding nitrile. In view of our interest in microwave assisted reactions and the importance of ionic liquids as solvents, it was decided to use them in combination, for dehydration reaction of aldoximes and the results are described herein. Ionic liquids being polar and ionic in character, couple to microwave irradiation efficiently and consequently may be ideal microwave absorbing entities for organic reactions. There are reports of preparation of ionic liquids using microwave irradiations, and many ionic liquids are effectively used for various organic transformations [3].



Use of a combination of ionic liquid in presence of aluminium chloride and microwave irradiation was shown to be a very efficient and high yielding method for the dehydration of aldoximes and also for 1,3-dipolar cycloadditions. Surprisingly, the presence of acrylonitrile rendered an unusual formation of substituted amide.

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Loss of Interaction with K3.28 (192) in 3rd Transmembrane Loop of CB1 Receptor May Not be Sufficient to Evoke Neutral Antagonism

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The interaction of CB1 antagonist with K3.28 (192) in 3rd transmembrane loop of CB1 receptor has been reported to be essential for evoking an inverse agonistic response for biaryl pyrazole compounds. Inverse agonism stabilizes the receptor in its inactive state. In case of Rimonabant, the best studied biaryl pyrazole antagonist of CB1 receptor, the carboxamide oxygen of the C-3 substituent is directly involved in the hydrogen bonding with K3.28 (192) of the receptor helping it to stay in its inactive state thus empowering the inverse agonistic prowess. Efforts are being made to synthesize neutral antagonist for CB1R. One such example is 5-(4-Chlorophenyl1)-1-(2,4-dichlorophenyl)-4-methyl-3-[(E)-piperidinoiminomethyl]-1H-pyrazole (*J. Med. Chem.* **2006**, *49*, 5969-5987) developed by Patricia Reggio et al., where the interaction of carboxamide oxygen with lysine192 of the receptor has been compromised leading to a putative neutral antagonist compound. We synthesized 4-Chloro-*N*-{[4-(4-chlorophenyl)-5-phenyl-oxazol-2-yl]-methylamino-methylene}-benzene sulfonamide, a compound that was unable to interact with K3.28 (192) of the CB1 receptor *(Bioorg. Med Chem. Lett.* **2008**, *18*, 963-968). Both the compounds were found to be less potent as compared to Rimonabant when tested in vitro by cAMP assay in CHOK1-CB1R cell system. Further, when checked for their neutral antagonism in cAMP as well as p44/42 MAP kinase assay, the compounds turned out to be weak inverse agonist rather than neutral antagonist at concentrations higher than 1µM. We conclude that lack of K3.28 (192) interaction with CB1-R antagonist may not be sufficient for the compound to show neutral antagonistic activity.

Isocyanates as Potential Inducers of DNA Damage, Apoptosis, Oxidative Stress and Inflammation

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Isocyanates are a group of low molecular weight aromatic and aliphatic compounds containing the isocyanate group (-NCO). Isocyanates are important raw materials used in pesticide industry and for manufacture of polyurethane products. Although isocyanates are widely used for the production of of flexible and rigid foams, fibres, insecticides, coatings such as paints and varnishes, and elastomers but patho-physiological implications resulting from occupational and large scale accidental exposures are hitherto unknown. Preliminary evidence available in the literature suggests that isocyanates and their derivatives may have deleterious health effects causing immune alterations. However, molecular mechanisms underlying such an effect have never been addressed.

Using a combinatorial experimental strategy we have investigated the molecular mechanisms of the effect of isocyanates on DNA damage cell signaling function, apoptosis and ability of isocyanates to induce oxidative stress in lymphocytes cultures isolated from healthy human volunteers. A total number of fifty samples from either genders across various age groups were used for the study.

Flow cytometric assay for ROS marker, CMH_2DCFDA showed significant elevation following an hour of treatment and a trend of increase continued till 24 hrs of study period. Levels of two anti-oxidant defense system enzymes, Glutathione Reductase (GR) and Super Oxide Dismutase (SOD) assessed by ELISA recorded significant decrease. Phosphorylation of ATM, ATR, γ-H2AX and p-p53 studied using epi-fluorescence microscopy, western blot and flow cytometry showed significant higher activity after 6-12 hrs of treatment. Multiplex cytometric bead array (CBA) analysis for inflammatory mediators, interleukin-8 (IL-8), interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor (TNF) and interleukin-12p70 (IL-12p70) measured in culture supernatant showed distinct elevation of all indices following treatment of 24 hrs.

The results of our study provide unique evidence to the hitherto unknown molecular mechanisms of toxico-genomic consequences of isocyanate exposure.

Isolation and Physicochemical Screening of Biomaterial from *Cordia dichotoma*

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Cordia dichotoma is composed of highly mucilaginous pulp. The phytoconstituents of the pulp possesses mucilaginous, flavonoids and terpenoids. The current concept of our research work is to isolate the mucilage portion of the fruit pulp of *Cordia dichotoma* and to perform physicochemical screening of the biomaterial like solubility, color change point, chemical test, IR, NMR, and Mass spectra,. Our results revealed that the biomaterial showed good solubility in water, color changing point at 160^0C. The IR, NMR. Mass spectral data and the mucoadhesivity of the polymer by Shear stress method revealed that the biomaterial is polymeric in nature with high molecular weight polymer with a promising mucoadhesivity. IR spectral study clearly reveals that the biomaterial possesses hydroxyl and carbonyl group which are prime essential for mucoadhesivity. From this study, it clearly reveals that the biomaterial can be used as mucoadhesive agent for formulating various mucoadhesive drug delivery systems. *Invitro* mucoadhesive study showed that the biomaterial possesses good mucoadhesive property. Finally, conclusion was drawn that *Cordia dichotoma* biomaterial can possess a novel mucoadhesive property and it can serve as a bioprocessant for formulating transmucosal drug delivery systems.

Synthesis of Flavone Derivatives as Potential Biological Agents

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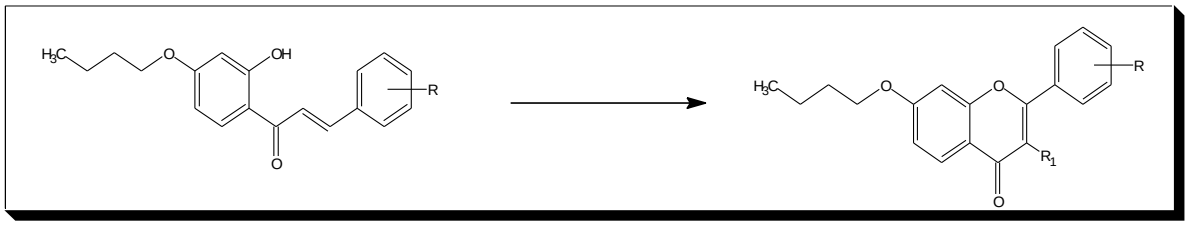
Flavones constitute a large segment of natural products. Synthesis of flvones and their derivatives have attracted considerable attention due to their significant biological effects investigated along with their corresponding chalcones against some bacterial as well as fungal strains.

Title compound 7-butoxy substituted flavones and 3-hydroxy-7-butoxy- substituted flavone have been synthesized from 2'-hydroxy-4'-butoxy substituted phenyl chalcone. The synthesized compounds have been characterized using IR, ^{1}H-NMR, ^{13}C-NMR and MASS spectral data along with elemental analysis.



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Studies on the Effect of Titatante Coupling Agent on the Mechanical Properties of Magnesium hydroxide Filled Ethylene Vinyl-Acetate Copolymer (EVA)

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Effect of treatment of coupling agent (a multiplex monoalkoxy titanate) on mechanical properties of composites made from Ethylene Vinyl-Acetate Copolymer and Magnesium hydroxide is reported here. The coupling agent in the form of solution (1.5%) was used for treatment of the filler. The treatment resulted in enhancement of mechanical properties of composites when compared with composites containing untreated magnesium hydroxide. The properties under consideration were tensile strength, modulus at percentage elongation at break, elastic modulus, hardness, etc. Although good reinforcement was observed due to treatment of 1.5% coupling agent, observed was very much remarkable compared to untreated once. Comparison of properties of composites filled with treated and untreated magnesium hydroxide established that treatment of magnesium hydroxide imparts better reinforcing properties. The properties under consideration were tensile strength, percentage elongation at break, elastic modulus, hardness, etc. Tensile strength was improved by 20% while percentage elongation at break was improved by 800% at (0.14) volume fraction.

Screening of Effective Taxane with Improved Anticancer Activity

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Multi drug resistance (MDR) is one of the characteristics of neoplastic (tumor) cells to resist a wide-variety of structurally and functionally distinct drugs and chemotherapeutic agents. MDR is mediated mainly by the ATP Binding Cassette transporter protein P-glycoprotein (P-gp). It is one of the mechanisms that tumor cells use to escape from chemotherapeutic agents. Multi drug resistance associated protein (MRP) and Breast cancer resistance protein (BCRP) are other proteins that act on the same mechanism to efflux drug out of the cell. These are very serious problems that may lead to recurrence of disease.

We had created TaxKB – Taxane Knowledge base, a database that contains physiochemical and drug related properties of taxanes. It contains a total of 11,000 entries in all. Physicochemical properties of 256 taxanes with 42 parameters, 2 dimensional and 3 dimensional structures and drug related properties in TaxKB are derived using on line tool and databases like PubChem and chemical, drug and ligand libraries.

Using the taxanes database (TaxKB), research is now being focused towards studying their anticancer activities. In order to rate and rank the antineoplastic activity of 256 taxane compounds, it need to be docked with modeled P-gp, MRP and BCRP because these structures are not available in PDB. With the docking property few more parameters like Number of Rotatable Bonds, Molecular polar surface area (PSA), Molecular volume etc will be calculated for taxane compounds.

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Synthesis and Antibacterial Activity of Substituted 1,2,3,4-tetrahydropyrazino[1,2-*a*]indoles Against Clinically Isolated Resistant Strains with Diminished Cytotoxicity in Human Cells

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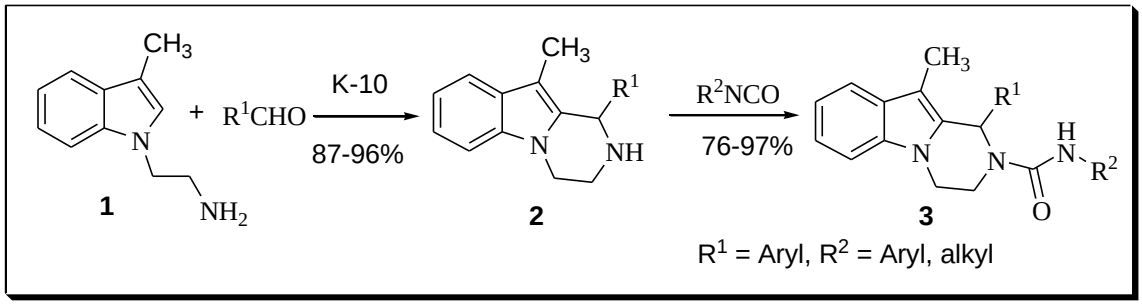
In recent years Pyrazino[1,2-*a*]indoles has attracted much attention, due to its medicinal importance. [1-3] A series of substituted 1,2,3,4-tetrahydropyrazino[1,2-*a*]indoles **2** have been synthesized using clay (K-10) under microwave irradiation, and its amides derivatives **3** were obtained by reacting compounds **2** with corresponding aryl or alkyl isocyanates. All the synthesized substituted 1,2,3,4-tetrahydropyrazino[1,2-*a*]indoles **2** and **3** were tested against clinically isolated resistant strains of *Pseudomonas, Proteus, E.coli* and standard strains *pseudomonas aeruginosa* (MTCC 1688), *Shigella flexneri* (MTCC 1457), *E.coli* (BL21) *Klebsiella planticola* (MTCC 2272)**.** All synthesized compounds showed mild to moderate activity. However, some derivatives were found to have potent activity against pathogenic resistant bacteria and standard bacteria used in the study with low cytotoxicity against a HEK cell lines.



Scheme 1

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Dissecting the Activity Profile of pyrido[2,3-d]pyrimidin-7-ones as CDK4 Inhibitors: a QSAR Study

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In the absence of an experimentally determined 3D structure of CDK4, QSARs have been explored to rationalize binding affinity in terms of physicochemical and structural parameters. The dataset consisted of 129 derivatives of pyrido[2,3-d]pyrimidin-7-ones compiled from three publications reported in the literature with biological testing performed using the same assay [1-3]. This was divided into a training set and test set of 108 and 21 compounds respectively. All the descriptors selected for the study have a physiochemical interpretation, which can guide a medicinal chemist to design prospective inhibitors, thus making these QSARs practically useful. Two QSAR models, a linear model using stepwise multiple linear regression (SMLR) and a non-linear model, with aid of splines, using Genetic Function Approximation (GFA) have been generated. Relevant parameters (r^2=0.607(SMLR) & 0.675(GFA)) and LOO cross-validation (q^2 = 0.527 & 0.624 respectively) as well as an external test set validation (r^2_{pred} = 0.627 & 0.700 respectively) judged the statistical significance and predictive ability of the models. The results gathered from these studies resulted in a better understanding of the specific nature of protein-ligand interactions that are crucial for CDK4 inhibition.

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Synthesis of Novel 2,4,6-trisubstituted Triazine Derivatives as Antitubercular agents

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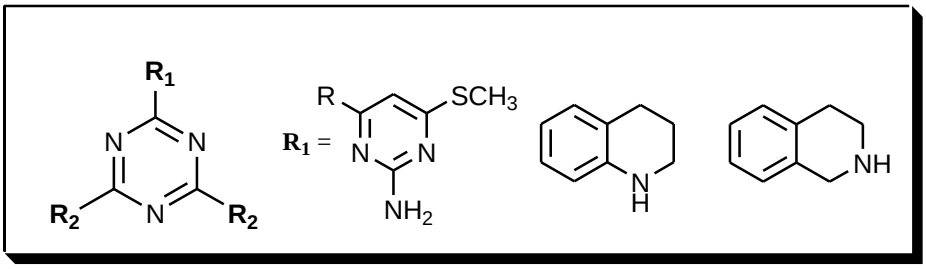
Tuberculosis (TB) is the greatest single infectious disease in the world. The mortality and spread of this disease has further been aggravated because of synergy of this disease with HIV. A number of anti-TB drugs are ineffective against this disease because of development of resistance strains. Internationally efforts are being made to develop new anti-tubercular agents.

As part of our ongoing research devoted to the synthesis of diverse heterocycles as anti-infective agents, We have synthesized some nontoxic 2,4,6-trisubstituted triazine derivatives which have shown effective antitubercular activity against *Mycobacterium tuberculosis* $H_{37}Ra$, in the range of 1.52-12.5 μg/mL.



Synthesis and Anticancer Activity of 2', 3'-Dideoxy Carbocyclic N^4-Hydroxycytidine

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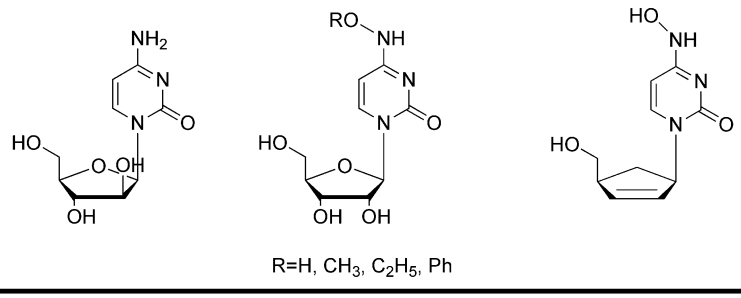
Enzymatic inhibition of biological methylation pathways essential for viral and cancer replication has shown promise in the design of new chemotherapeutics. Disruption of critical enzymes such as *S*-adenosyl-L-homocystine hydrolase (SAHase) [1], adenosine deaminase (ADA) [2] and DNA methyltransferases (MeTase) [3] has been shown to affect viral and tumor cell replication. In that regard, carbocyclic nucleoside derivatives, as a class, have shown potent inhibitory activity in both areas. Carbocyclic nucleosides are structurally modified such that they mimic the natural nucleosides enough to be recognized, but ultimately have the ability to disrupt subsequent biological processes [4].

N-hydroxy analogues of cytidine have historically been known for their antiviral and anticancer activities. For example, 2,2'-cyclo-l-β-D-arabinofuranosylcytosine (c-araC) shown in Figure 1 has been shown to be effective in the treatment of mouse leukemia L12101-3 and other tumors [5]. Several attempts have been made to develop analogues or derivatives of hydroxycytidines with increased potency. In that regard, interesting biological activity against several viruses such as SARS, influenza A and B, hepatitis and others have recently been reported [6]. Several substituted hydroxycytidines (Figure 1) have also shown potent activity against HSV and VZV [7]. As an extension of those promising leads, we have synthesized a series of carbocyclic analogues of N-hydroxycytidine that have exhibited promising activity against several cancer cell lines including breast and colon cancers. Their syntheses and biological studies are reported herein.

Figure 1



References:

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New Protolimonoids and Limonoids: Transformation of Naturally occurring 6α-acetoxyazadirone to New Limonoids

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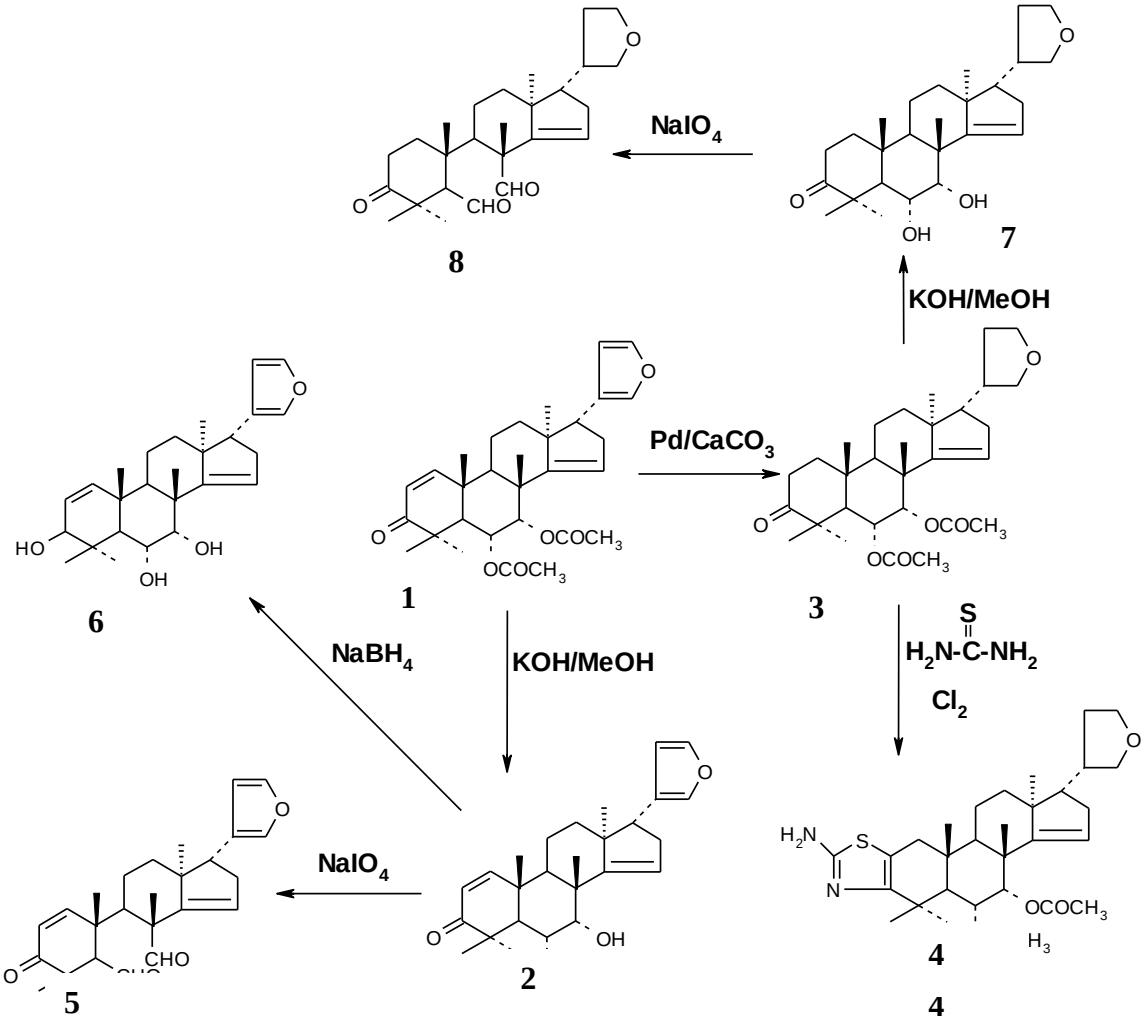
Paniculatin (**1**) (6α-acetoxyazadirone), a naturally occurring meliacin has been isolated from the fruits of *chisocheton paniculatus* Hiern. Chemical transformations on paniculatin were performed to give biologically important 2-aminothiazolo [4,5-d] [1,2,20,21,22,23-hexahydro] paniculatin (**4**), Dialdehyde compound of **2** (**5**), 3-hydroxy paniculatin (**6**), Dialdehyde compound of **7** (**8**). The structures of the new compounds have been elucidated on the basis of elemental analysis and spectral data.



Conjugate Addition of Pyrroles to α,β-unsaturated Ketones using Copper Bromide as a Catalyst

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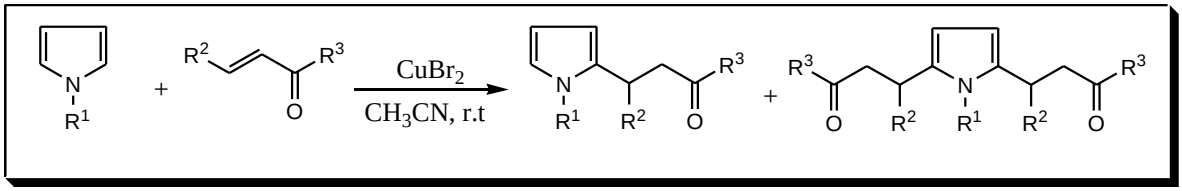
Pyrrole and alkylated pyrroles are present as important structural components, and can serve as precursors for the synthesis of, various biologically active compounds. Amongst the various methods available, useful procedure for *C*-alkylating pyrroles involves the Friedel-Crafts- type conjugate addition of pyrrole to a, ß–unsaturated aldehydes or ketones. Acid-catalyzed reactions of pyrrole are limited and require careful control of the acidity to prevent side reactions such as polymerization. As catalysts, indium chloride, bismuth nitrate, and yttrium triflate or metal triflates have all been used for this reaction. Recently, a microwave-assisted method was used for alkylation of pyrroles. There is only one report of the use of copper bromide as a catalyst for Friedel- Crafts- type conjugate addition of indoles. All the earlier reports mention the synthesis of monoalkylated pyrroles except for one where indium chloride was used as a catalyst. In the present study, a very efficient method using copper bromide as a catalyst has been developed to achieve the dialkylation of pyrroles within 10 minutes in good yields. N-methyl pyrrole with enones furnished mixture of diastereomers of dialkylated pyrroles, which were successfully separated and characterized.



1. R^1= H, **2** R^1= Me, **3** R^1= COPh, **4** R^2= R^3 = Ph, **5** R^2= Ph, R^3= CH_3, **6** R^2= 4-ClC_6H_4, R^3= 3-$MeOC_6H_4$, **7** R^2= 4-ClC_6H_4, R^3 = Ph, **8** R^2=2-$MeOC_6H_4$, R^3 = Ph.

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Effect of Various Extracts of *Capparis decidua* (50% ethanolic) on Pancreatic Islets of Streptozotocin Diabetic Rats

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The ethanolic extracts of bark and fruit extracts of *Capparis decidua* decreased the blood sugar level in streptozotocin diabetic albino rats. Level of significance for decrease in blood sugar after feeding alcoholic extract of *Capparis decidua* for 30days duration was highly significant. The extract feeding showed improvement in the histopathology of islets. Another important finding is that the total cholesterol decreased significantly as compared to untreated diabetic models.

Treatment groups	Initial 0 day	7th Day	15th Day	30th Day	% Deviation
Intact Control (Group 1)	90.43 ±4.36	86.19 ±7.73	89.76 ±5.01	90.06 ±13.51	0.40
Diabetic Control (Group 2)	457.41^{c} ±23.32	362.26^{c} ±25.62	425.54^{c} ±22.66	399.1^{c} ±30.48	12.7
Diabetic + *C. decidua* bark extract treatment (Group 3)	$426.25^{c,h}$ ±41.36	$135^{d,g}$ ±12.32	$129.5^{d,g}$ ±11.83	$114.50^{d,g}$ ±9.76	73.14
Diabetic + *C. decidua* fruit extract treatment (Group 5)	$316.50^{c,g}$ ±17.32	$86.50^{d,g}$ ±5.36	$82^{d,g}$ ±7.01	$71^{d,g}$ ±5.98	77.68

TABLE 1: Change In Serum Glucose Levels Of 30 Days Treatments Of Various Extracts Of *Capparis Decidua* In Albino Rats (Values Are Mean ± Se From 10 Animals In Each Group)

Group 2, 3, and 4 were compared with Group1

$P \leq 0.05$	= a
$P \leq 0.01$	= b
$P \leq 0.001$	= c
Non-significant	= d

Group 3 and 4 were compared with Group2

$P \leq 0.05$	= e
$P \leq 0.01$	= f
$P \leq 0.001$	= g
Non-significant	= h

Design and Synthesis of Peptidomimetics as DPP-IV Inhibitors

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Central Drug Research Institute, Lucknow, India

Diabetes mellitus is a major and growing public health problem throughout the world. About 90-95% cases of diabetes are related to diabetes II. This metabolic disorder afflicts 6% of the adult population in Western society and its worldwide frequency is expected to continue to grow by 6% per annum, potentially reaching a total of 200-300 million cases in 2010. [1] The disease is marked by the inability to manufacture or properly use insulin, and impairs the body's ability to convert sugars, starch etc. into energy. The long-term effects of elevated blood sugar (hyperglycemia) include damage to the eyes, heart, feet, kidneys, nerves, and blood vessels. [2] This clearly highlights the urgent need of novel therapeutic agents for the treatment of diabetes. Currently there is much focus on the glucagons-like peptide-1 (GLP-1) peptide hormone as the basis for a potential new treatment paradigm for type 2 diabetes. GLP-1 stimulates insulin secretion and biosynthesis and inhibits glucagon release. GLP-1 is rapidly degraded *in vivo* through the action of dipeptidyl peptidase IV (DPP-IV), to give its inactive form. [3] Inhibitors of GLP-1 degrading enzyme DPP-IV have been shown to be effective for the treatment of type 2 diabetes in animal models and in human subjects.[4] The most promising inhibitors of DPP-IV comprises aminoacyl pyrrolidides and thiazolidides fig.1(X = O, Y = CH_2, S). Based on the available information, we have designed and synthesized some of the peptidomimetics as DPP IV inhibitor. The details of the study will be presented.

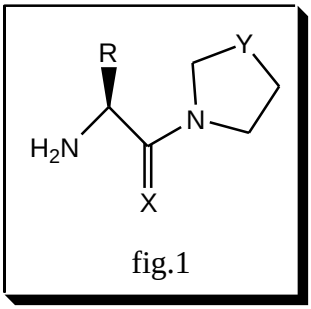

fig.1

References:

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Quantum Chemical Studies on the Conformational and Polymorphic Preferences of Hypoglycemic Sulfonylureas

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Sulfonylurea (SU) moiety has been exploited for wide range of therapeutic activities but mainly used as oral hypoglycemic agents. Conformational analysis of hypoglycemic sulfonylureas (SU) by semi-empirical, molecular mechanics and molecular dynamics methods has already been reported. Recently, 2nd generation SU (glimepiride, glipizide) have been reported to be equally active as PPARγ agonist as Thiazolidinedione (TZD) drugs like pioglitazone. So, we carried out extensive conformational analysis including tautomerism and intramolecular hydrogen bonding effects on SU using *ab initio* MO and DFT methods (HF, B3LYP and MP2) to correlate the structural preferences with PPARγ activity of SU analogues. We compared the molecular electrostatic potential of SU and TZD moieties to show the similarity of the binding interactions to PPARγ receptor. We have also carried out computational polymorphism analysis and proposed several theoretically possible polymorphs to try to solve the problem of polymorphism preferences of SU drugs.

References:

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Synthesis and Biological Activity of Some New Triazino Indole Derivatives

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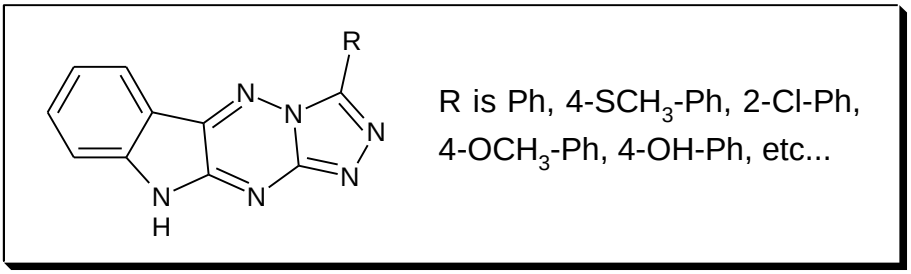
[b]Department of Chemistry, Saurashtra University, Rajkot, Gujarat, India
[c]Department of Biomedical Sciences & Technology, University of Cagliari, Italy

The current work is on the basis of our earlier findings to synthesize & evaluate several triazino indole derivatives. In continuation of angularly fused triazolo-triazino-indole derivatives some linearly fused derivatives were synthesized to find out the difference in the effect of the linear and angular fused derivatives on their biological profile.

The antiviral activity of as-triazines and clinical efficacy of methisazone were well documented. The action of isatin-3-thiosemicarbazone is known to have antiviral activity against certain poxviruses. The antiviral spectrum of 1-methylisatin 3-thiosemicarbazone, which reportedly extends to adenoviruses, may be rather broader but is still limited to several groups of DNA viruses.

The reaction scheme involves four steps for the synthesis of substituted phenyl[1,2,4]triazolo[4',5':2,3][1,2,4]triazino[5,6-b]indole in which first step deals with the condensation between isatin and thiosemicarbazide in the presence of potassium carbonate & water as solvent to yield triazine-indole-3-thione, which underwent hydrazinolysis in second step, to afford as-triazino[5,6-b]indol-3-yl-hydrazine. In the third step different substituted aromatic aldehydes were condensed with 3-hydrazino-triazino[5,6-b]indole to give corresponding bezylidiene derivatives. Cyclization of the above hydrazones using bromine and acetic acid afforded linear cyclization to give the below compound. All compounds were characterized and Antiviral properties are evaluated.



Synthesis, Characterization and Antimicrobial Screening of Some Thiazole Derivatives

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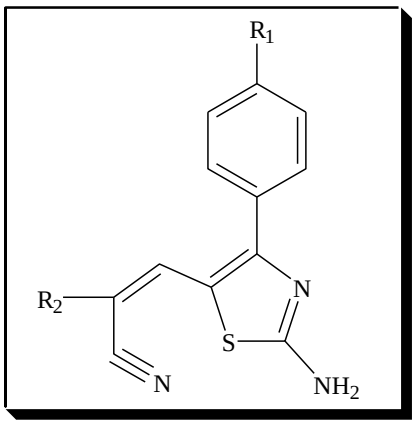
Synthesis of some 3-[2-amino-4-(4-substituted phenyl) (2H-1,3-thiazol-5-yl)]-2-substituted prop-2-enenitrile have been synthesized by conventional and microwave media. The yield and reaction time period are noticeably improved in microwave media in comparison with conventional method. The series of synthesized compounds are elucidated on the basis of their elemental analysis and spectral data and screened for their antimicrobial activities.



Where,

R_1 = H, Cl, Br, Me, MeO
R_2 = CN, $CONH_2$, COOEt

Synthesis and *in vitro* Pharmacology Studies of Some New Heterocycles Based on 1H- pyrazolo[3,4-b] pyridine

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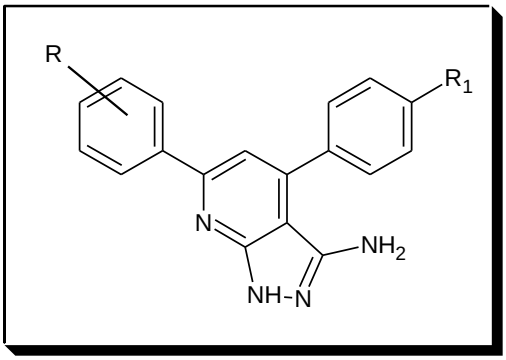
Heterocyclic compounds have great applicability in pharmaceutics because they have specific chemical reactivity and provide false symptoms in biosynthetic process or block the normal functioning of biological receptors. Heterocyclic compounds containing pyrazolo-pyridine derivatives possess important therapeutic value because of their fused ring system. The pyrazolo-pyridine exhibit wide range of biological activities such as antihypertensive [1], antibacterial [2], anti-HIV activity [3] etc. Our aim to introduce some new heterocycles based on 1H- pyrazolo[3,4-b] pyridine under microwave irradiation (MWI) and conventional heating, respectively. All structures of the newly synthesized compounds were elucidated by elemental analysis and spectral data & tested for their antimicrobial and anticancer activity.



References:

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A Convenient One-pot Synthesis of 3-(2, 6-diphenyl (4-pyridyl)-2-chloro Quinoline under Microwave Irradiation and their Antimicrobial Activity

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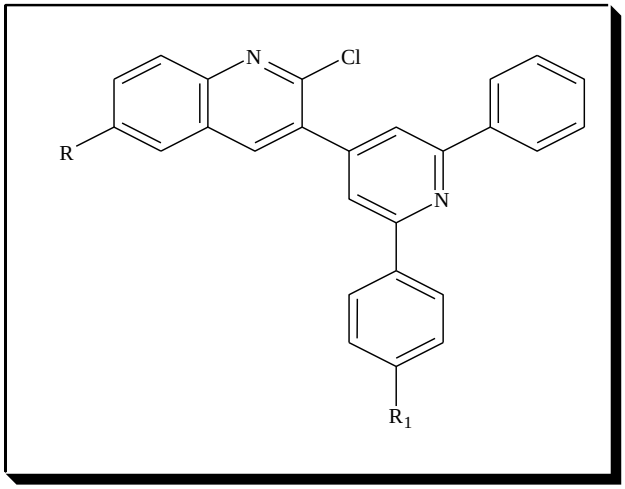
A series of 3-(2,6-diphenyl(4-pyridyl)-2-chloro quinolines **5a-x,** were synthesized in high yields by four component, one pot cyclocondensation reactions of 2-chloro-3-formyl quinolines **1a-d**, various acetophenone **2a-f,** N-phenacylpyridinium chloride **3,** ammonium acetate **4** in acetic acid assisted by microwave irradiation. All the compounds have been characterized by elemental analysis, IR, ^{1}H NMR and ^{13}C NMR spectral data. They have also been screened for their antimicrobial activities.



(5a-x)

Where,

R = H, CH_3, OCH_3, Cl
R_1= H, CH_3, OCH_3, Cl, Br, F

Synthesis and Antibacterial Activity of Some New Tetrahydro-benzo[4,5]thiazolo[[2,3-b]quinazolin-1-one and Quinoline Containing Compounds

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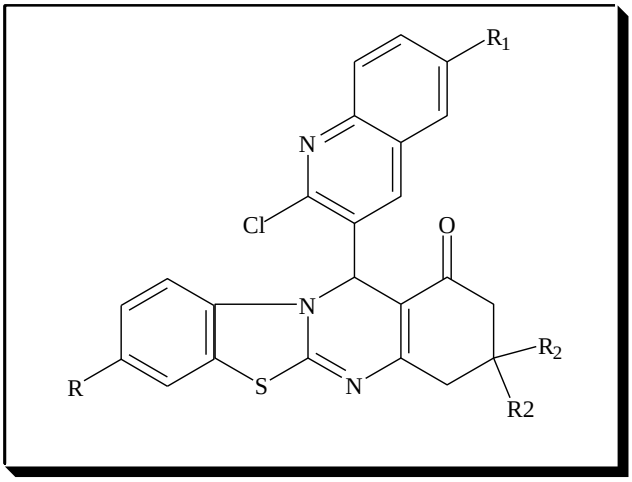
A new series of 12-(2-Chloro-6- substituted-quinolin-3-yl)-3,3,8-substituted-2,3,4,12-tetrahydro-benzo[4,5]thiazolo[[2,3-b]quinazolin-1-ones(D1-32) were prepared in one pot by condensing various 2-chloro-3-formylquinoline(A1-4), 2-aminobenzothiazole(B1-4) and 1,3-cyclohexadione(C1-2) derivatives in ethanol. All the compounds were characterized by their percentage yield, melting point, elemental analysis, ^{1}H-NMR and ^{13}C-NMR spectra and IR-spectra. All the synthesized compounds were screened for their antibacterial against some gram positive and gram negative bacteria.



D(1-32)

R=H, Cl, CH_3, OCH_3
R1= H, Cl, CH_3, OCH_3
R2=H, CH3

Extraction of Humic Acid from Bio-logical Matrix

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Humic Acid (HA), a biologically complex, colloidal, polydisperse macromolecule formed during bio-degradation is ubiquitous in environment. HA molecule is re presented by hydrophobic compound as alkanes, alkenes, fatty acids, sterols, terpenoids, quinines, phenolic groups, etc. HA is documented to interact with over 50 elements from the periodic table, nutrients, toxic metals, radionuclides and anthropogenic compounds. HA is employed in varied facets as veterinary medicine, in agriculture, chemistry, environment, and even in human health issues.

HA is known to play a vital role as a chemotherapeutic agent. It exhibits Anti-Viral, Anti-Microbial, Anti-Inflammatory and Anti-Coagulant property [1]. A substantial fraction of HA is in carboxylic acid group, imparts the ability to chelate with positively charged bivalent metal ions. Hence, it has crucial role as a Dilator, increasing cell wall permeability for minerals from blood to bones or cells. HA derivative has potent HIV-1[2], Herpes inhibiting properties.

Most of HA used is extracted from coal-lignite, marine water, soil and peat. In the present work, HA is extracted from biological matrix "DRY COWDUNG" [3]. It is naturally available bio-organic, complex, fecal matter of the bovine species. It is enriched in minerals, carbohydrates, fats, proteins, bile salt and many aliphatic and aromatic species. Hence, HA extracted from biological material would have better matrix effect than that extracted mostly from Abiotic factor. Physical as well as chemical properties of extracted HA were studied by powder XRD, TGA and FT-IR spectroscopy. The same were compared with the structure given in the literature.

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In vitro Study of Anti Tubercular Drugs against the Resident Flora of Human

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Tuberculosis is one of the stiff diseases caused by *Mycobacterium tuberculosis*. Several antibiotics and drugs are used to cure the disease. Many anti tubercular drugs and their combinations are used to treat the tuberculosis. The treatment for tuberculosis is carried out for longer duration particularly in case of patients infected with multi drug-resistant M tubculosis strains.

Attempt is made to study the effect of such agents and their combination of drugs on the resident bacterial flora isolated from the healthy human individual. The bacteria isolated form the oral cavity and fecal flora have been selected for these purpose about five isolates from gingiva, five isolates from tongue and seven isolates from throat has been selected for this study and seven isolates from fecal matter and five isolates from rectal swabes has been identified and tested against the known anti tubercular drugs and their combinations attempts have made to determine the MlC and MBC for them. The drugs selected for these purpose are Isonizaid Rifampicin, Ethamtutol, Pyrazinamide, Thiacetazone, Streptomycin and Kanamycin.

Majority of the bacteria have MIC 2-8 ug/ml which is effective concentration for M tuberculosis also.Only few isolates are having high MIC as high as 16-32 ug/ml. The bacteriostatic and bactericidal effects are determined for all the bacterial strains. Among these agents isoniazide, streptomycin, thiacetazone and kanamycin were found bacteriostatic whereas isoniazide, rifampicin, ethambutol and pyrazinamide were found bactericidal for the bacteria tested.

In silico Evaluation of Sulfaquinazolinone Derivatives Library against Antimicrobial, Antimalarial and Antituberculosis Activity

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[b]Department of Chemistry, V P Science College,
Vallabh Vidyanagar-388 120, Gujarat, India
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There are several sulfonamide-based groups of drugs. The original antibacterial sulfonamides (Formally called sulfa drugs) are synthetic antimicrobial agents that contain the sulfonamide group. Sulfaquinazolinone derivatives are basically synthesized by the grouping of sulpha and quinazolinone moiety. The sulfa-related antibiotics and drugs are used to treat bacterial and some fungal infections as they interfering with their metabolism. The first sulfa drug was prontosil. It was discovered by the Gerhard Domagk in 1935. They were the "wonder drugs" before penicillin and are still used today with the combination of other active moiety.

Present work is an assessment of novel sulfaquinazolinone derivatives against antimicrobial, antimalarial and antituberculosis activity using docking softwares . Entire library include around 100 compounds with different active group viz. azitidinone, imidazole, pyrimidine and sulfamethazone. All the compounds are screened against different biological recepter. Drylab works includes sketch of novel compound and creation of sulfaquinazolinone derivative library in the form of mol and mol2 file. Each compound was docked against several receptors available in public domains using docking softwares. Sulfamethoxazole and sulfamethazone deravitives were proved excellent against Dihydropteroate Synthetase from *Bacillus anthracis* and *Staphylococcus aureus*, indicated the prospective application as an antimicrobials agents. Our works mainly focus on problem of multi drug resistance, indicating by several groups of organism viz. plasmodium and mycobacteria against compound contains single moiety like sulfonamide derivates. Library's compounds are made up of multi group like sulfa moiety, pyrimidine moiety and quinazolinone moiety to provide a poor platform to the organisms for the resistance against compounds. Successful compounds are pipeline for synthesis in wet lab.

Effect of Berberine on the Glucose uptake in L6 Myotubes

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Diabetes mellitus is a chronic disorder characterized by increased blood glucose level and the only cause is insufficient or inefficient insulin secretary response. At present over 170 million people are living with diabetes across the globe [1] and it cause about 5% of all deaths globally each year [2]. In modern drug discovery programmes, natural products from medicinal plants form a platform for the discovery of new drug entities. Glucose uptake is the rate limiting step in the insulin targeted skeletal muscle and is mediated by GLUTs [3]. Berberine is a plant alkaloid found in the roots, rhizomes, stems, and bark. The medicinal plant containing berberine is used as hypoglycemic agent, but the molecular basis of it is yet to be elucidated [4]. This paper understands the effect and the mechanism of action of berberine in L6 rat skeletal muscle. The study reveals that berberine has enhancing effect on glucose uptake in a time- and dose-dependent manner. The 2 hour incubation with 5 μM berberine shows approx 40 % increase in glucose uptake. Interestingly berberine stimulated glucose uptake does not vary as insulin concentration increases. The effect of Cytochalasin B, an inhibitor of the hexose carrier, on the berberine induced glucose uptake has also been studied. These results suggest the beneficial effect of berberine on glucose uptake and on the insulin pathway.

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Synthesis of 2-(thiomethyl-2'-benzimidazolyl) Benzimidazole and its Derivatives as Potential Proton Pump Inhibitors

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Gastric Ulcers are caused by various factors such as mental stress, dietary habits, intake of irritable food etc. The Peptic Ulcers are mainly caused [1] due to damage of mucous membrane because of excess of secretion of gastric acid. The ulcers are treated with a variety of drugs/anti-ulcer agents. At present Proton Pump Inhibitors are gaining importance since they block the proton Pump of H^+/K^+-ATP ase, an enzyme specifically present in the parietal cells of the stomach to inhibit the gastric acid secretion [2]. Chemically these compounds as referred as "Prazoles". Structurally, these compounds consists of a "Benzimidazole ring" attached to a sulphoxide unit, an active methylene group and heteryl moiety.

In our search for new anti-ulcer agents, we have prepared new Prazoles containing a sulphoxide unit and an active methylene group attached to two "Benzimidazole" rings on opposite sides, various roots have been explored for the synthesis of title compound. Details of our study in this direction will be presented.

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Synthesis and Antibacterial Studies of s-triazine Based Novel Heterocycles

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Substituted s-triazine derivatives are an important class of compound having anticancer,[1] antitumor,[2] antibacterial, antimalarial,[3] antiviral and antifungal activities. These compounds have been used in the treatment of depression and hence received a considerable therapeutic importance. Urea derivatives possess various biological activities like antibacterial and antiHIV.[4]

Coumarin derivatives revealed new biological activities with interesting potential in therapeutic applications besides there traditional employment as anticoagulants. They have yielded important results as antibiotics, anti AIDS [5] and antitumor drugs.

With references to the above biological importance, we have synthesized s-triazine based heterocycles by condensing s-triazine with cyclopropylamine, 4-hydroxycomarin and various aryl ureas at suitable conditions. All the synthesized compounds were well characterized by spectroscopic data as IR, NMR and elemental analysis. The invitro antibacterial activities in MIC were carried out against different panel of organisms. Some of compounds displayed high in vitro antibacterial activities against tested microorganisms.

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Mechanistic Study of Oxidation of Antibacterial Agent, Norfloxacin by Alkaline Permanganate

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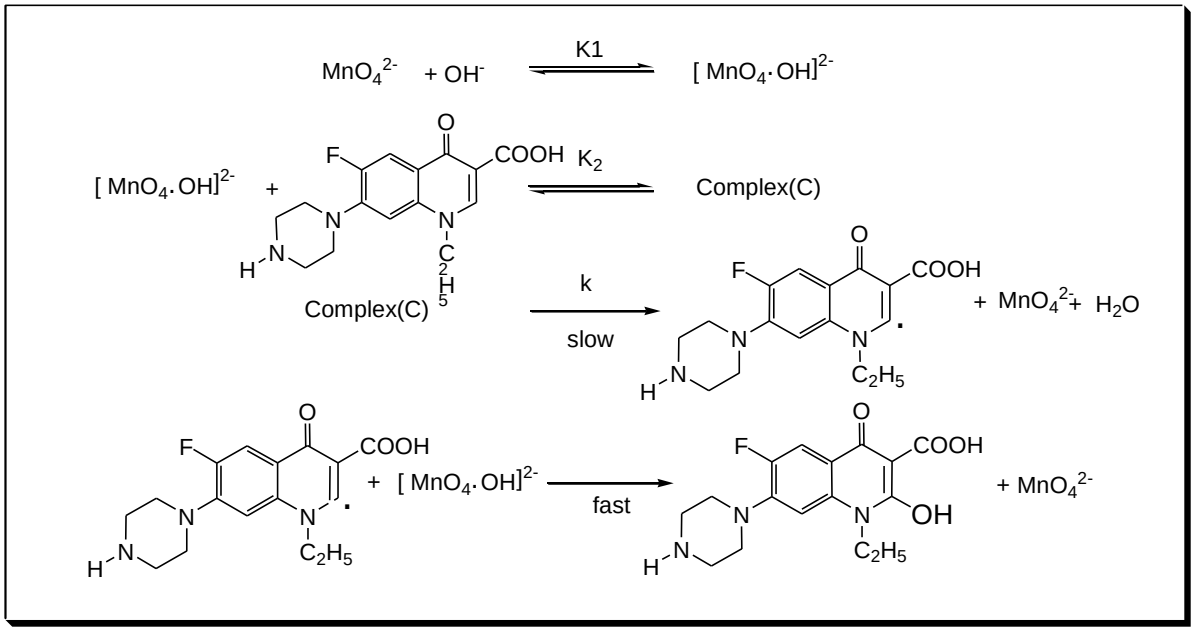
The oxidation of norfloxacin with alkaline permanganate has been studied spectrophotometrically at 25^{o}C and at constant ionic strength of 0.10-mol dm^{-3}. The oxidation products are identified by LC-ESI-MS technique and other spectral studies. The stoichiometry is found to be 1:1 i.e. one mole of manganese (VII) reacted with one mole of norfloxacin. The reaction is first order with respect to manganese (VII) concentration. The orders with respect to norfloxacin and alkali concentration are found to be less than unity. The effect of added products, ionic strength and dielectric constant of the medium is studied on the rate of reaction. On the basis of experimental results the following mechanism is proposed.



The reaction constants involved in the different steps of the reaction mechanism are calculated. The activation parameters with respect to the slow step of the mechanism are determined and discussed.

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Preparation and Screening of 3- isopropyl-4-substituted phenyl-1-phenyl-1,4,5,7-tetrahydro-6h-pyrazolo[3,4-d]pyrimidin-6-ones as Potent Antibacterial Agents

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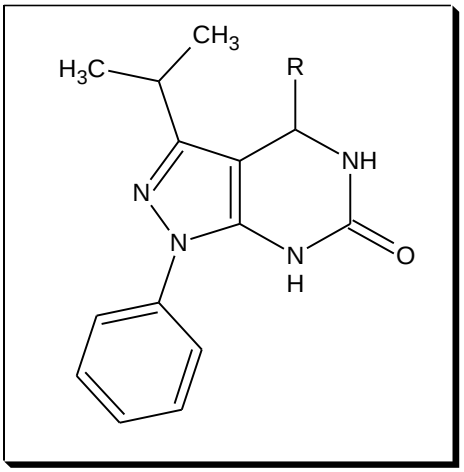
Pyrimidines represents one of the most active classes of compounds possessing a wide spectrum of biological activities viz. significant *invitro* activity against unrelated DNA and RNA viruses including Polio and Herpes *viruses*, diuretics, antitubercular**,** antihyp-ertensive etc. Some pyrimidines, which occur as natural products like nucleic acids and vitamin-B and can be used as therapeutic agents for the treatment of AIDS and anticancer. Synthesis of 3-isopropyl-4-substituted phenyl-1-phenyl-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-d]pyrimidin-6-ones (I_{a-j}) have been undertaken by the the cyclo condensation of benzaldehydes,5-isopropyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one catalytic amount of con. minerals acids.



(I) R=Substituted phenyl

The constitutions of the products (Ia-j) have been supported by using elemental analyses, IR, ^{1}H NMR and mass spectral data. The products (I_{a-j}) were assayed for their *in vitro* biological assay like antimicrobial activity towards gram positive and gram-negative bacterial strain and antifungal activity at different concentrations for their MIC values.
The biological activities of the synthesized compounds were compared with standard drugs.

Prediction of 3-Dimensional Structure of GLI2 of *Homo sapiens*

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Gli2 is a transcriptional activator, even though it is also suggested to have a weak repressing activity. Gli2 is expressed in the interfollicular epidermis and the outer root sheath of hair follicles in normal human skin.Gli2 is able to induce G1–S phase progression in contact-inhibited keratinocytes which may drive tumour development. Studies have also shown that GLI2 plays a dual role as activator of keratinocyte proliferation and repressor of epidermal differentiation. For the structure prediction with homology modeling, template protein was obtained by BLASTp, The predicted 3-D model may be further used in characterizing the protein in wet laboratory.

New Validated Stability-indicating High Performance Liquid Chromatographic Assay method for the Simultaneous Determination of Tramadol Hydrochloride and Aceclofenac in Commercial Tablet

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The present work describes development and validation of stability-indicating high performance liquid chromatographic assay method for the determination of tramadol HCl (TR) and aceclofenac (AC) in tablet formulation. The combination formulation was subjected to ICH recommended stress condition. The method has shown adequate separation for TR, AC from their degradation products. Separation of the drugs from the degradation products formed under stress condition was achieved on a C18 column using a mobile phase consisting of 0.01M-ammonium acetate buffer pH 6.5 -acetonitrile (65:35, v/v) at a flow rate of 1 ml/min and UV detection at 270nm. The method was validated to specificity, linearity, LOD & LOQ, precision, accuracy and robustness. The method was found specific against placebo interference and also during the force degradation. The linearity of the proposed method was investigated in the drug concentration range of 15–60 µg/ml (*r*= 0.9999) for TR and 40–160 µg/ml (*r*= 0.9999) for AC. The accuracy was between 98.10–98.87% for TR and 97.34– 99.49% for AC. Stress testing showed degradation product, which were well separated from parent compound, confirming its stability indication capacity.

Intramolecular and Intermolecular Charge Transfer Spectroscopy in UV-VIS and IR Region in Different Environment

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An effort to explain the ground and excited state intra/intermolecular charge transfer photophysics of Pyrrole-2-Carboxyldehyde (PCL), Pyrrole-2-carboxylic acid (PCA) and its related compounds in UV-VIS and IR region has been reported in this paper. Vibrational modes have been successfully explained with ab initio Density Functional Theory calculations. The experimental and theoretical data shows the existence of intramolecular hydrogen bonding between $H_6 \ldots O_{11}$ of pyrrole and formyl group in ground state and possibility of intramolecular and intermolecular proton transfer from pyrrole group(-NH) to formyl group (-C=O) in the excited state.

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An Efficient Synthesis of bis- and tris-indolylalkanes Catalyzed by a Brønsted Acid-surfactant-combined Catalyst in Water

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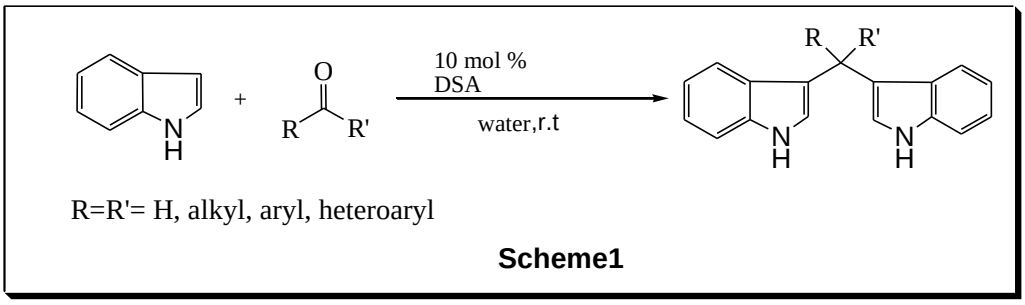
The development of simple and efficient processes for the synthesis of biologically active compounds in water is one of the latest challenges for chemists [1]. On the other hand, bisindolyl alkanes and their derivatives constitute an important group of bioactive metabolites [2]. As a part of our ongoing research interest in green chemistry [3] we want to report here a simple and efficient synthesis of bis- and tris-indolylalkanes from carbonyls (aldehydes/ketones) and indoles with excellent yields in the presence of dodecylsulphonic acid (DSA), as a catalyst in water at room temperature. The dodecylsulphonic acid acts both as Brønsted acid as well as surface-active agent in the reaction mixture.



R=R'= H, alkyl, aryl, heteroaryl

Scheme1

References:

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Enantioselective Synthesis of (+) And (-) β Conhydrine

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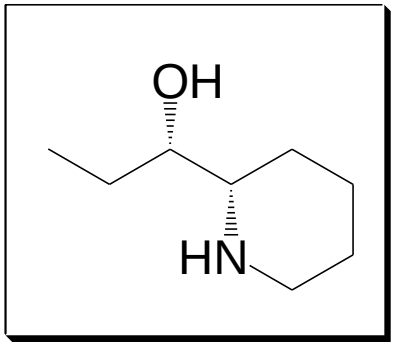
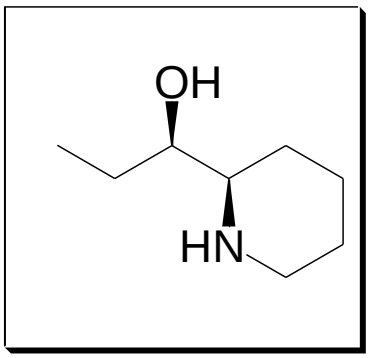
Biologically active alkaloids containing 2-(1-hydroxyalkyl)-piperidine unit are abundant in nature and have attracted much attention due to their antiviral and antitumour properties.[1,2] This class of compound includes (+) and (-) β Conhydrine which was first isolated from the seeds and leaves of the poisonous plant, *Conium maculatum L*, in 1856.[3]



(-) β Conhydrine



(+) β Conhydrine

Investigations in our laboratory over the past few years have demonstrated the utility of nitroaliphatics in the synthesis of pharmacologically important natural products.[4] In this context, we have developed a practical synthesis of this molecule. The details of the synthesis will be presented.

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Evaluation of Anti-Diabetic Activity of Extracts of *Gymnema sylvestre* in Streptozotocin Induced Diabetic Rats

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Gymnema sylvestre (*G. sylvestre*; Asclepiadaceae) is an herb native to the tropical forests of southern and central India where it has been used as a medicine for diabetes. Though its therapeutic effects are not entirely known, the herb has been reported to reduce blood sugar levels. In this context, the present study was undertaken to evaluate the anti-diabetic activity of different extracts of *G. sylvestre* in albino Wistar rats. Streptozotocin - induced (45 mg/kg, i.p.) diabetic rats were treated orally with hydroalcoholic and processed extracts of *G. sylvestre* (37.5, 75 and 150 mg/kg) or vehicle (1% carboxy methyl cellulose) or glibenclamide (0.6 mg/kg) continuously for 28 days. Changes in body weight and haemoglobin content and biochemical alterations in serum levels of glucose, cholesterol and triglycerides were assessed on 14th day of the treatment and at the end of experiment. Treatment with extracts of *G. sylvestre* showed significant ($p \leq 0.05$) reduction in the streptozotocin- induced elevated levels of serum glucose, cholesterol and triglycerides levels. The extracts also prevented the loss of body weight and reduction in haemoglobin content compared to diabetic control rats. Based on the findings of the present study, it can be stated that the hydroalcoholic and processed extracts of *G. sylvestre* possess anti-diabetic activity.

Screening and Characterization of Antibiotic Producer Actinomycetes from Saline Environment

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The pharmaceutical industry over several decades has probably isolated and screened millions of *Streptomyces* strains. However, it soon became apparent during screening programmes probability of rediscovering known compounds are getting increased, so strategies must be introduced into screening programmes to increase the chances of discovering novel isolates and which can lead to the novel compounds. In present work an attempt has been carried out to isolate and characterize the antibiotic producer haloalkaliphilic actinomyctes from the diverse and less explored saline desert (Little Rann of Kutch) and soda lake (sambhar lake Rajasthan). Isolation was carried out by enrichment isolation technique using Glucose Asparagine medium containing 10% w/v salt and 9 pH. Haloalkalitolerant actinomycetes strains were isolated from different samples collected from the various different region of the saline desert and soda lake. Antimicrobial activities were further examined from both crude and partially purified antibiotic against *S. aureus, S. typhi, S cerevesiae, A. niger* and *P. aeruginosa.* Result indicates the bright possibilities for exploration of haloalkalitolerant isolates for antibiotic production and additionally point out the need of detail study of saline environments.

Vapor phase Alkylation of Indole with Methanol over $Ni_{1-x}Co_xFe_2O_4$ (x=0, 0.5 & 1) type Ferrospinels

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Vapor phase alkylation of indole with methanol was carried out over Ni_{1-x} $Co_xFe_2O_4$ (x = 0, 0.5 & 1.0) type ferrospinel in a fixed-bed reactor. The maximum of 68.4% yield of 3-methylindole at 76.8% indole conversion was obtained under optimized conditions of temperature 598 K, indole/methanol molar ratio 7 and WHSV 0.5 h^{-1}. The activity of calcined catalysts revealed that either Bronsted or Lewis acid sites are the suitable sites for 3-methylindole formations.

QSAR of Nitrofuranyl Amides Utilizing Calculated Molecular Descriptors: Statistical and Neural Network Approach

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The global increase of multi-drug resistant *Mycobacterium tuberculosis* strains and intolerance of first line anti-tuberculosis drugs may cause major problems and necessitate modification of structural therapy regimen. In an ongoing effort to develop new and potent anti-tuberculosis agents, structure-function relationships of a second-generation series of 47 biologically active nitrofuranyl amides [1, 2] with substitution at cyclic secondary amines (Fig. 1) are reported in this study. Quantitative structure activity relationship (QSAR) models based on calculated physicochemical, topological and other groups of descriptors have been extensively used in the present investigation for predicting biological activity for these derivatives. We have developed various regression models such as ridge regression, stepwise regression and partial least squares for activity prediction. Attempt has also been made for applying more recently explored genetic (genetic function approximation) and machine learning (k-nearest neighbor and neural networks) methods for a clear understanding. Validations of models are performed utilizing training and test sets. Results based on leave-one-out (LOO) principle have been discussed in case of counter propagation neural network analysis. Finally, the relative effectiveness of the molecular descriptors in these models are compared and discussed.

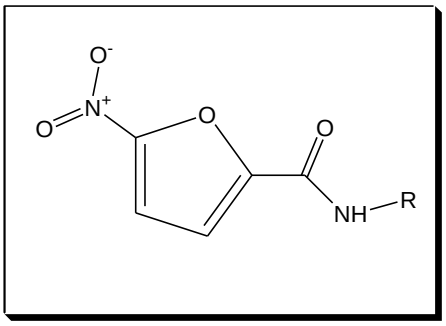

Fig. 1: Nitrofuranyl amide with substituent as R

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Synthesis of Oligosaccharides Secreted by *Lactobacillus* and *Thermophlilus* strains

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A wide variety of exopolysaccharides (EPS's) produced by Lactic acid bacteria (LAB) present in the body provide an important contribution to human health by acting as prebiotic substrates, nutraceuticals, cholesterol lowering agents or immunomodulants. The structure of a ropy strain of *Lactobacillus* spp. G-77 has been characterized recently, which contains a unique 1,2-*cis* linked branched trisaccharide. Another heat stable bacteria belong to genus *Thermus*, which are able to grow at extremely elevated temperature. In contrast to the Gram-negative bacteria the outer membrane of *Thermus* does not composed of lipopolysaccharides but some unique glycolipids. Recently, the structure of a tetrasaccharide repeating unit of the glycolipid isolated from *Thermus thermophilus* Samu-SA1, a thermohalophilic bacterium has been demonstrated in which a unique D-galactofuranosyl moiety present at the non reducing end through an α-linkage. In order to analyze and assess the role of EPS produced by *Lactobacillus* spp. G-77 and glycolipids in the adaptation process of *Thermus thermophilus*, a reasonable quantity of the tri- and tetrasaccharide corresponding to them is required. We herein report a concise synthesis of a unique trisaccharide and a tetrasaccharide as their methyl glycosides corresponding to the *Lactobacillus* spp. G-77 and *Thermus thermophilus* Samu-SA1 respectively (Figure 1).

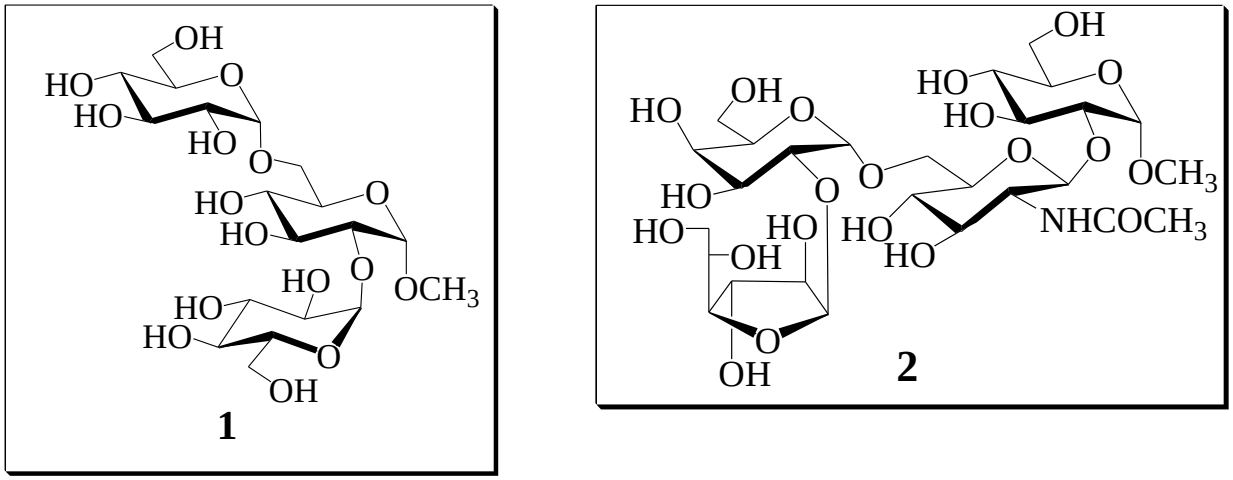

Figure 1: Structures of synthesized oligosaccharides.

References:
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Importance of Bound Phenolics in Kodo Millet (*Paspalum scrobiculatum*) and Finger Millet CO 13(*Eleucine coracana*) for Antioxidant Activity and Identification of Antioxidant Phenolic Compounds by RP-HPLC and ESI-MS

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Epidemiological studies have shown that consumption of whole grains is associated with reduced risk of chronic diseases, which are attributed in part to their unique phytochemical composition[1, 2]. Millets are semi-arid crops grown in India and Asia and form a staple food for the lower socioeconomic class. In our previous studies, we have reported for the first time higher antioxidant activity in the methanolic extracts of kodo millet and finger millet compared to other millets and cereals[3, 4]. In the present study, bound phenolics were extracted from kodo millet (KMM: market variety; KMV: vamban1) and finger millet CO13 (FMC) by alkaline hydrolysis followed by ethyl acetate extraction and the free phenolics were extracted by methanol.The total phenolics and flavonoids were estimated. The content of bound phenolics in KMM, KMV and FMC were 1013 ±27.5, 745 ± 39.2, 77.66 ±2.27 mg GAE/100 g respectively. Whereas the free phenolics of KMM, KMV and FMC were 25.81±1.74, 7.5 ± 0.24, 9.47 ±1.1 GAE/100 g respectively. The flavonoid content of bound phenolics in KMM, KMV and FMC were 501 ±50, 160 ± 12, 72.74 ± 8.3 mg C E/100 g respectively. Whereas the free phenolic fraction showed 292±8.7, 77 ± 3.0, 112.9 ±4.7 respectively**.** The content of bound phenolics and flavonoids were significantly higher in all the three millets than those of free phenolics. The antioxidant activities of free and bound phenolics were evaluated using DPPH radical scavenging assay, Trolox equivalent antioxidant capacity, superoxide anion scavenging, reducing power and iron (II) chelation assays. In all the antioxidant activity assays, the bound phenolic fraction contributed significantly higher antioxidant activities than free phenolics. Surprisingly bound phenolics did not show significant metal chelating activities.

TLC analysis of crude methanolic extracts of KMM, KMV, and FMC using hexane: ethyl acetate: acetic acid (31:14:5) solvent system showed 4, 5, 1 spots respectively. Further, RP-HPLC coupled with a PDA detector was used to identify these compounds using binary solvent system (A: 2% Acetic acid; B: MeOH). All the chromatographic profiles were well represented at 280 nm and 320 nm indicating the phenolic acids and flavonoids. A total of 11 peaks in KMM (catechin, quercetin derivative and unidentified compounds), 13 peaks in KMV and 1 major peak (catechin) in FMC was identified. ESI MS analysis revealed the presence of neochlorogenic acid quercetin derivative, myricetin derivative, caffeoyl shikimic acid, methyl epicatechin gallate, hexosyl ferulate, and mericitin galloyl glycoside and epicatechin digallate in KMM.

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Biosynthesis of Curcumin Capped Gold nanoparticles for Inhibiting Formation of Amyloid Plaques and Reduce Amyloid *in vivo*

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The panorama of finding a safe and effective new approach to both prevention and treatment of Alzheimer's disease (AD) is tremendously exciting. Studies suggest Curcumin's ability to scavenge free radicals and suppress inflammatory cytokines seems promising to prevent and treat Alzheimer's disease and other neurodegenerative disorders. We propose that Curcumin capped gold nanoparticle can be better Aβ (Beta amyloid) aggregation inhibitor and prevented Aβ oligomer formation We aim to synthesize Curcumin capped Gold Nanoparticles (NP) for more successful treatment and prevention of Alzheimer's Disease (AD) as compared to drugs currently being investigated for treatment. Gold nanoparticles have been synthesized using commercially available Curcumin. Curcumin template the reductive preparation of gold nanoparticles which is found to be <50nm. UV-Vis absorbance showed peak at 544 nm due to plasmon resonance of Gold nanoparticles. The characterization of gold nanoparticles will be done using TEM, SEM and FTIR. The effects of Gold nanoparticles against damage induced by beta amyloid will be studied in vitro and in vivo.

Spectral, Electrochemical and Theoretical Investigation of Micelle Encapsulated Copper (II) Phenolate Complexes as Models of Galactose Oxidase

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Biologically important copper containing metalloenzyme Galectose oxidase consists of a cysteine-linked tyrosyl radical which is implicated as a redox-active subunit in the stereospecific oxidation of D-alcohols to aldehydes. Surfactants micelles provide the typical hydrophobic environment in aqueous solution around active site of matelloproteins under certain physiological pH. UV-visible spectra, Cyclic voltammetry, Square wave voltammetry and ESr spectra of copper (II) phenolate model complexes are carried out surfactant medium above the cmc values. The model systems show a weak band at 500-600nm (d-d transition) and a sharp band at 320-360nm (MLCT band d Cu-ה* antibonding orbital of phenolate residue) and their cyclic volatammograms contain a reversible, one electron wave at $E_{1/2}$=0.100V (SDS) or 0.200V (CTAB) vs Ag/AgCl (Glassy Carbon electrode) which for the ligand rather than the metel-centered process to yield M^{II}-phenolate radical species. The electronically generated M^{II}-phenolate radical species are EPR silent (anti-ferromagnetic coupling between a coordinated phenoxy radical and a central metal ion) and shows a new optical absorption feature is observed at λmax=440nm, which is similar to that reported for the active forms of a coordinated phenoxy radical in that of enzyme. Theoretical calculations proved the oxidation reduction potential of the model system is through ligand rather than through metel.

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Biosorption of Copper Ions Using 'Coconut Husk Powder' in a Batch Process

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This investigation comprises the equilibrium and kinetics on biosorption of copper ions from aqueous solutions using `Coconut husk powder' in a batch process. The results indicate that biosorption of copper is increased with an increase in adsorbent dosage and decrease in adsorbent size. A significant increase in percentage removal of copper is observed as pH value is increased from 1 to 7 and the percentage removal is decreases beyond pH 7. Increased initial concentration of copper in the aqueous solution results in lower percentage of biosorption. Freundlich and Langmuir isotherm models describe the present data very well indicating favourable biosorption. The biosorption follows pseudo-second-order kinetics.

Bioremediation of Diabetes with Plant Extracts

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Diabetes mellitus is the most common serious metabolic disorder which characterized by a hyperglycemia. This can be classified in to two types. Type 1 is Insulin Dependent Diabetes Mellitus (IDDM) and type 2 is Non-Insulin Dependent Diabetes Mellitus (NIDDM). The incident of type 2 diabetes is much higher than type 1 diabetes [1, 2]. In the present study the effect of ripe and unripe fruit peel aqueous extract of *Psidium guajava (p. guajava)* has studied on normal and diabetic rats. The rats treated with unripe extract shows a significant fall ($p < 0.001$) of blood glucose level (BGL) in normal rats during fasting blood glucose levels (FBG) and ($p < 0.001$) in sub diabetic rats during glucose tolerance test (GTT) at a dose of 400 mg/kg bw. Where as the fall observed significantly in FBG, post prandial glucose (PPG) and urine sugar levels in severely diabetic rats was ($p < 0.05$) and ($p < 0.01$) respectively. Conversely the effect of ripe fruit peel aqueous extract shows a significant rise ($p < 0.01$) and ($p < 0.001$) in BGL in normal and sub diabetic rats respectively. Laser Induced breakdown Spectroscopy (LIBS) is used for the elemental analysis of fruit peel aqueous extract of Guava. Experimental results show that Mg concentration is high and K concentration is low in unripe fruit peel aqueous extract in comparison to ripe fruit peel aqueous extract. The concentrations of other minerals like (Na, N, O and C) are nearly same in both the extracts.

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Multiple labeling of Oligonucleotides and Quenching effect of Deoxyguanosine Nucleotides

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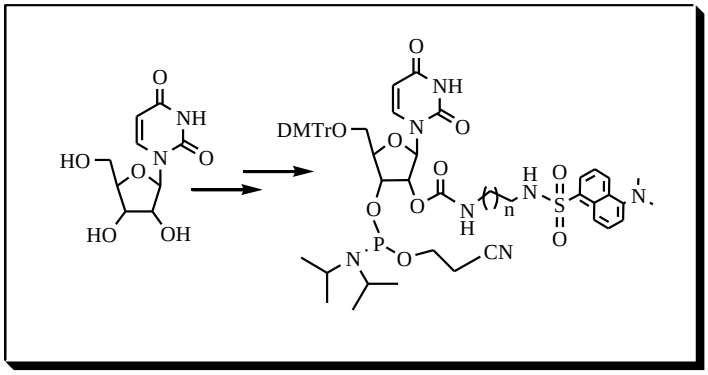
Multiple labeling of oligonucleotides using specific 2'-O-modified uridine phosphoramidite, covalently linked with 5-dimethylaminonaphthalene-1-[N-(6-aminohexyl)] sulfonamide (dansyl hexylamine) derivative through carbamate linkage has been described. The applicability of the proposed method has been made in homogeneous hybridization studies with complementary oligonucleotide strands having "G" rich telomeric unit at 3'-end. Fluorescence quenching has been observed due to inherent quenching property of deoxyguanosine moiety present at the terminal position just opposite to the 2'-O-modified analogues of uridine. The results may aid further, in rational designing of DNA probes for multiple labeling and for non-radioactive detection of telomeric target nucleic acids.



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Molecular Capsules by Ionic Interctions in Calixarenes

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The unique structure and easy functionalization at lower and upper rim of calix[4]arenes are responsible for their unique building blocks in supramolecular chemistry. The multi-calix[4]arenes have been used in self-assembly, molecular boxes, cation binding, drug delivery and many other biological processes. Molecular capsules are synthesized from the self-assembly of two or more subunits equipped with the correct molecular instructions to drive their recognition in solution and consequently the self-assembly into the desired structure. The ionic interactions are employed as an important attractive force for the synthesis of non-covalent supramolecular capsules apart from hydrogen bonding and metal ligand coordination. Calix[4]arenes with *O*-alkyl chains at their lower rims and the upper rim of one calixarene adorned with four negatively charged groups, while the upper rim of a complementary half sphere possessing four positively charged groups, both half-spheres attract each other in polar solvents owing to multiple electrostatic interactions and finally interlock like two gear wheels. Herein we report the synthesis of various anionic water soluble 5,11,17,23-tetrasulfonatocalix[4]arenes and different cationic water soluble calix[4]arenes by modified methods and their associations by ionic interactions in the formation of molecular capsules by different spectroscopic techniques in polar solvents.The required anionic water soluble 25,26,27,28-tetraalkoxy-5,11,17,23-tetrasulfonatocalix[4]arenes and cationic water soluble 25,26,27,28-tetraalkoxy-5,11,17,23-tetrakis(trimethylammonio)calix[4]arenes were synthesized by ipso-sulfonation and ipso-nitration of O-alkoxy calix[4]arenes. Their structures and conformations were identified by different spectroscopic analysis especially by ^{1}H NMR spectroscopy. The formation of self-aggregates leading to generation of molecular capsules by multiple ionic interactions between water-soluble anionic and cationic calix[4]arenes have been studied by UV-visible, ESI-MS, TGA and other spectroscopic techniques.

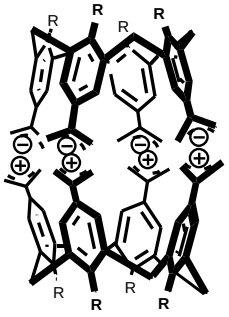

Figure: Molecular Capsule

Neem : A Potent Contraceptive

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Arishta, the cure-all is one of the Sanskrit names for Neem, *Azadirachla indica* A. Juss (Family: Meliaceae). The name is related to its multitudinal uses both in medicine and agriculture which are due to a large number of secondary metabolites found in various parts of the tree. Neem has been extensively used in Ayurveda, Unani and Homoeopathic medicine and the tree is still regarded as "Village Dispensary" in India. Its contraceptive effect has been tried through oral, vaginal and subcutaneous routes of application. Either oil as such or oil or leaf extracts have been used for both as a female and male contraceptive. Recent work on Neem seed volatile fraction has shown its importance as anti-larvicidal, anti- bacterial and has strong spermicidal activity. Looking to the extraordinary importance of volatile constituent GC- Mass analysis of steam volatile fraction of Neem seed oil has been reported along with critical review on contraceptive effect of Neem.

Synthesis and *in vitro* Biological Studies of 2-Amino-4-phenyl-1,3-thiazole Schiff Base

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A Schiff base has been synthesized by the condensation of 2-amino-4-phenyl-1,3-thiazole with 8-formyl-7-hydroxy-4-methylcoumarin. The synthesized compound has been characterized on the basis of analytical and spectral (i.r., ^{1}H n.m.r, ^{13}C n.m.r., FAB-mass and fluroscence) data. The newly synthesized Schiff base has been screened for its antibacterial (*Escherichia. coli, S. aureus, S. pyogenes and P. aeruginosa*) and antifungal activities (*Aspergillus niger, Aspergillus flavus and cladosporium*) by MIC method. The brine shrimp bioassay was also carried out to study their invitro cytotoxic properties.

Quantum Mechanical Modeling as a Supportive Tool for the Assessment of SAR: Studies on some Therapeutic Classes

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Knowledge of the electronic surface distribution is very important to understand the ligand receptor interaction. Highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) gives the electronic density surface of the molecules. This would be helpful in future to design of novel molecules. In our study we considered 34 and 23 molecules categorized as antiepileptics and antibacterials respectively were studied using quantum mechanical parameters to assess the difference in bioactivity based on electronic arrangement. A pattern based on HOMO and LUMO was developed for each class of the antiepileptic drugs and the antibacterial fluoroquinolones. Each class witnessed a common pattern of the electronic surface distribution. An effective evaluation of the activity could be done based on assessment of the pharmacophoric groups in terms of electronic arrangement. This paper emphasize the importance of quantum mechanical modeling as a tool in predicting bioactivity and could be employed as a supportive feature to SAR.

Correlation of Global Electrophilicity with the Activation Energy in Single-Step Concerted Reactions

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Experimental energy of activation (E_a) of the single-step concerted oxidation process of aliphatic primary alcohols by quinolinium bromochromate (QBC) [1] are correlated with the theoretically evaluated global electrophilicity values (w) [2]. Conceptual justification in favor of correlating w of the substrate with E_a involved in single-step concerted reaction is also discussed. The evaluated w values at HF/cc-pVTZ and MP2/6-31G(D,P) methods are found to be as expected (when we consider structural aspects), although there are some inconsistencies in other methods [e.g., HF/6-31G(D,P), B3LYP/cc-pVTZ, BLYP/dnp, PW91/dnp, PWC/dnp, VWN/dnp]. The reasons for the inconsistencies, even with superior B3LYP/cc-pVTZ method, are discussed thoroughly [3]. It is observed that higher the value of w more is the value of E_a involved in the process of oxidation of primary alcohols by QBC. The present study also makes it clear that local electrophilicity (s_k^+) values of O_{OH} (O-atom of the OH-group in primary alcohol) are unable to explain the observed E_a trend when more significant (i.e., much larger) local nucleophilicity values ($s_{O_{OH}}^-$) are compared [4-6]. This is evident from the corresponding correlation coefficient values.

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2D And 3D Qsar Studies on 4-Phenylpyridyl, 4-Phenylquinoline, 4- Phenylisoquinolinone and 1-Phenylindenes a Potent Class of AT1 Angiotensin II Receptor Antagonist

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Angiotensin II regulates the cardiovascular homeostasis and binds to a receptor known as angiotensin receptor (AT). This receptor is of two types (AT1 and AT2) and belongs to G-protein Coupled Receptor (GPCR) superfamily.AT1 antagonists are preferred over ACE inhibitors due to their selective nature and lesser side effects. Most of the AT1 antagonists have the biphenyl fragment and heterocyclic system. Among the large variety of the heterocyclic system, stereo electronic characteristics of the imidazo [4, 5-b] pyridine moiety may be considered optimal for the interaction with receptor.[2] To see the effect of substitution of the distal phenyl moiety and substitution at imidazo [4, 5-b] pyridine on the biological activity, the 2D and 3D QSAR studies have been carried out on the title compounds.[3,4]

The total set of 41 compounds was divided into training and test set of 29 and 12 compounds respectively. The best 2D QSAR model showed a moderate correlation ($r = 0.822$, $r^2 = 0.675$) of high statistical significance (>99.9%) [$F_{4,\ 24\alpha 0.001}=6.59$, $F_{4,\ 24}=12.489$]. The model described well the variation in Angiotensin II receptor antagonistic activity and it also predicted the activity of test set compounds very well ($r^2_{pred}=0.747$).

The 3D QSAR (CoMFA) studies on the same set of compounds resulted in the 3D model with the q^2 value of 0.469 which was improved to 0.747 by the application of region focusing. These models also showed good external predictivity $r^2_{pred}=0.502$ and $r^2_{pred}RF=0.566$ respectively indicating the robustness of the two generated models. These studies substantiated the 2D results and suggested that phenyl ring with electronegative bulkier substitution at ortho position and ethyl substituent at imidazopyridine moiety at R1 position may lead to the compounds with better AT1 antagonistic activity.

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Antibacterial Activity and Establishment of *in vitro* Cultures of *Lantana camara L.*

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We report here for the first time, a reproducible protocol for establishment of callus and cell suspension cultures from the leaves of *Lantana camara L*. L.camara, regarded both as a notorious weed and a popular ornamental garden plant, has a plethora of bioactive compounds that find use in folk medicine in many parts of the world [1].

The aqueous and ethylacetate extracts from leaves as well as those from in vitro raised cells were tested and have been found active against Streptococcus mutans. S. mutans is a Gram-positive, faculatative anaerobic bacteria commonly found in the human oral cavity and is a significant contributor to tooth decay.

A standardized protocol for suspension cultures will help up of biomass and isolation of medicinally important compounds [2]. Moreover, establishment of in vitro cell culture offers an efficient alternative mode of utilization of its biomass in a more effective and constructive manner with stable irrespective of seasonal variations.

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DFT-Based Reactivity and QSAR Studies on Anticancer Activity of *cis*-Platinum (II) Complexes

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Platinum anti-cancer drugs bind to DNA, forming a variety of intrastrand and interstrand adducts, the most abundant of which are 1,2-intrastrand cross-links between the N7 atoms of two adjacent guanine bases. In order to study the reaction pathway followed by the drug molecules and their binding properties, it is important to understand the reactive nature of the molecules. The structure and chemical reactivity of some selected cis-platinum(II) complexes (Fig), including clinically used drugs, cisplatin, carboplatin and oxaliplatin are investigated using the density functional theory (DFT) calculations. The calculated geometries of the complexes are in agreement with their available X-ray data. The global and local reactivity descriptors such as hardness, chemical potential, electrophilicity index, Fukui function and local philicity are calculated to investigate the usefulness of these descriptors for understanding the reactive nature and reactive sites of the complexes. Inclusion of solvent effect shows that both global and local descriptors change the trend of reactivity with respect to their trend in the gas phase. The stability of the complexes increases with the inclusion of water molecules. Simple regression analysis is applied to build up a quantitative structure-activity relationship (QSAR) model based on DFT derived electrophilicity index for the Pt(II) complexes against A2780 human ovarian adenocarcinoma cell line to establish the importance of the descriptor in prediction of cytotoxicity.

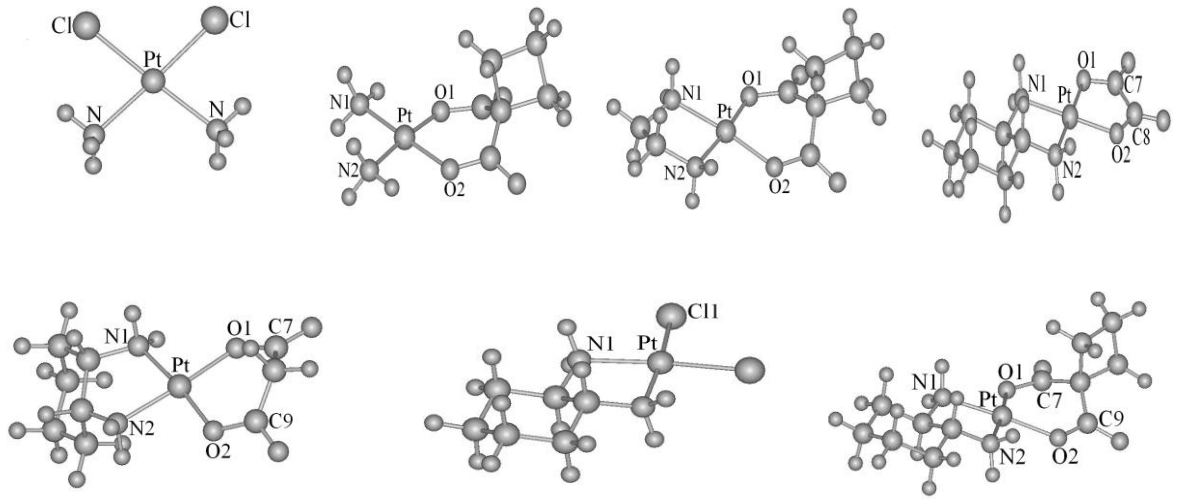

Fig 1

Novel N-(sub alkyl/aryl)-2-(sub) phenylthiazolidine-4-carboxamides: Synthesis and *in-vitro* Anti-tubercular Activity

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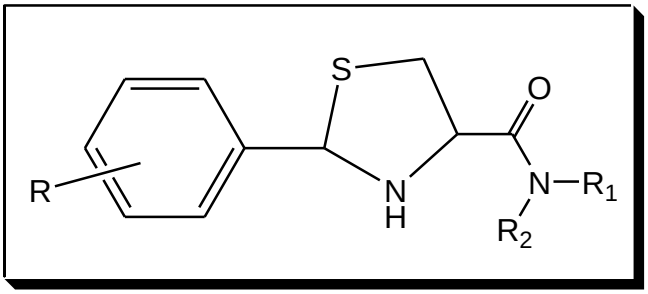
With approximately 3 million annual deaths in the 1990s, tuberculosis (TB) remains a leading cause of mortality worldwide in the 21st century. It is estimated that one-third of the world population harbor a latent infection by the causative pathogen, *Mycobacterium tuberculosis* (MTB). Long-term therapies lasting between 6 and 9 months have frequently led to patient non-compliance and in turn, contributed to the emergence of multi-drug resistant TB (MDR-TB). The cost of treating a patient carrying MDR-TB is much greater, typically running into tens of thousands of rupees per patient, than for patients carrying a drug-sensitive strain. Without effective treatments, the fear is that the number of infections caused by MDR-TB will increase out of control. In an attempt to identify novel anti-tubercular compounds we have identified 2-aryl thiazolidine carboxylic acid amide derivatives with potent antimycobacterial activities. Sixty four N-(sub alkyl/aryl)-2-(sub)phenylthiazolidine-4-carboxamides were synthesized from L-cysteine and (sub) benzaldehyde by two step reaction, evaluated for *in-vitro* antimycobacterial activities against *Mycobacterium tuberculosis* H37Rv (MTB), multi-drug resistant *Mycobacterium tuberculosis* (MDR-TB).



Most of the compounds were active against MTB and MDR-TB with MIC of <1µM. The compound (4-benzylpiperazin-1-yl)(2-(4-fluorophenyl)thiazolidin-4-yl)methanone (**KPA 25)** was found to be the most potent with MIC of 0.12µM and was three times more active than the existing first line anti tubercular drug isoniazid.

Tumorigenic Property of Cyanobacteria Isolated from Polluted Water Bodies of Pilani.

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The microalgae have significant attraction as natural source of bioactive molecules, because they have the potential to produce bioactive compounds in culture, which are difficult to produce by chemical synthesis. Under metabolic stress, these accumulated pools of intermediates and may induce subsidiary pathways to form secondary metabolites. Secondary metabolites that are identified from various strains of cyanobacteria include pigments, alkaloids, toxins, antibiotics, carotenoids, lipopeptides, etc. They are hepatotoxic cyclic peptides with Molecular weight ranging from 824 to 1,044 Da. Over 75 natural structural variants were reported and specific inhibitors of protein phosphatases. The general composition for these toxins is as follows: cyclo (-D-Ala^{1}-L-X^{2}-D-erythro-ß-methylAsp^{3}-L-Z^{4}-ADDA^{5}-D-Glu^{6}-N-methyl-dehydroAla^{7}). Demethylation can occur on amino acid number 3 and/or 7; X = leucine; (L), arginine (R), tyrosine(Y); Z = arginine and alanine(A) methionine(M) Currently combinations for XZ include recently, LR, LA, YA, YM, YR, and RR. ADDA is necessary for biological activity. Microcystins are the most widespread of the cyanobacterial toxins. The present study on biochemical analysis and Tumourgenic activities of fresh water filamentatous heterocystous formation cyanobacteria isolated from the polluted water body in the vicinity of Pilani, Jhunjhunu District, Rajasthan. Methanolic extract of isolated strain produces tumour in invivo assays model (mice). Partial thin layer chromatography purification and paper chromatography infer the presence of various proteins, pigments, carbohydrates. Further purification and characterization of these compounds is in progress.

Polysaccharide Structure of *Acrocarpus fraxinifolius* Wight. Seeds Polysaccharide by Methylation Technique

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Acrocarpus fraxinifolius Wight. plant belongs to family-Fabaceae, Caesalpiniaceae, is called as *Mandania, red cedar and pink cedar* upto 30-60 m in height and 2.14 m diameter. Plant is native of tropical Asia and distributed in India, China, Mynamar, Indonesia, Nepal, Sri Lanka, Sumatra, Vietnam, Bangladesh, Thailand, Indonesia, and tropical Africa. In India it occurs in Northern and Eastern Himalaya upto an altitude of 1000-1200 m height. Seeds extract exhibited the antimicrobial activities. Wood is commercially used for making furniture, tea boxes, doors, windows and waste word is used as fuel. Seeds contains a water soluble sugars as D-galactose and D-mannose in 1:3 molar ratio. Chemical modification of polysaccharide allow the preparation of new polymers with specific properties. The main aim of the work was to elucidate the structure of polysaccharide from *Acrocarpus fraxinifolius* Wight. seeds by methylation and study the chemical modification to improve the solubility in water. Seeds polysaccharide was subjected to structural investigation upon methylation by Haworth, Hakomari and Purdie's method using sodium hydroxide, sodium hydride, dimethyl sulphate, dimethyl sulphoxide, methyl alcohol, methyl iodide and silver oxide to give fully methylated product. It did not show any hydroxyl groups at 3500-3600 cm^{-1} absorption band in IR-spectra (KBr). It was hydrolysed with sulphuric acid (1N) afforded five methyl sugar fraction on whatman no. 3MM filter paper sheet by paper chromatography. Methyl sugars were identified as 2,3,4,6-tetra-O-methyl-D-galactose, 2,3,6-tri-O-methyl-D-galactose, 2,3,4-tri-O-methyl-D-mannose, 2,3,6-tri-O-methyl-D-mannose and 2,3-di-O-methyl-D-mannose in 1:1:1:4:1 molar ratio. Isolation of 2,3-di-O-methyl-D-mannose is triply linked with C_1, C_4 & C_6 position by (1→6)-α-type and (1→4)-β-types linkage which reveals that the one branching point occurs in the main chain. Linkage between D-galactose and D-mannose are of (1→6)-α-type at non reducing end while (1→4)-β-types at main polymer chain. Therefore, it indicated that every 8 hexoses are the repeating unit which consists of 2 hexose of D-galactose and 6 hexose of D-mannose units. On the basis of above findings methylation results a polysaccharide structure has been proposed for *Acrocarpus fraxinifolius* Wight. seeds polysaccharide.

Synthesis, Antitubercular and Antimicrobial Activity of Some Novel Imidazolinones and Thiazolidinones

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2-Arylimino-3-N-aryl-5-(1'N,3'-diphenyl pyrazolylmethino)-4-thiazolidinones and 1N-Phenyl-2-methyl-4-(1'N,3'-diphenyl-4'-pyrazolylmethino)- imidazolin-4-one have been prepared via multistep reaction. 4-thiazolidinones have been synthesised by the condensation of 1-N,3-diphenyl-4-formyl Pyrazole and 2-p-tolyl imino-3-(p-tolyl)-5H-4-thiazolidinone. Imidazolinones derivatives have been prepared by condensation of 2-alkyl/aryl-4-(1'N,3'-diphenyl-4'-pyrazolylmethino)-oxazolin-5-one with different aryl amines.

The hydrazone of phenylhydrazine and acetophenone on reaction with DMF-$POCl_3$ yielded 1N,3-diphenyl-4-formyl pyrazole (I). The Erlenmeyer azalactone products, oxazolone derivative (II) have been prepared by Perkin reaction of (I) with acyl derivative of glycine in presence of acetic anhydride and sodium acetate. The azalactone (II) on reaction with different aromatic amines in presence of pyridine produced imidazolinone derivatives (IIIa-m). The reaction of different bisarylthiourea[19] with mono chloro acetic acid furnished to 2-arylimino-3-aryl-5H-4-thiazolidinones.

The structure of all the synthesised products has been supported by IR, NMR, Mass spectral study and elemental analyses. All the compounds were screened for their *in vitro* antitubercular activity towards a strain of *Mycobacterium Tuberculosis* $H_{37}Rv$ and antimicrobial activity against different strains of bacteria and fungi.

Metal Chelates as Potential Anti-hyperglycemic Agents: studies on Some Oxovanadium (IV) Chelates Involving Biomimetic ONO-Donor Sugar Schiff bases

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The design of vanadium compounds with an optimal impact and a minimized toxicity has been a task of several research groups.[1] For any complex considered for therapeutic use it is importantto consider the intrinsic toxicity of the ligand, especially if the treatment is predicted for a long period. In this context sugars or amino sugars may be interesting ligands as normally they are non-toxic compounds. Introducing an anchoring group into a sugar molecule, which as a primary coordinating site may promote the deprotonation/coordination of the alcoholic hydroxyl groups, the complex-forming ability may be, enhanced several orders of magnitude.

There has been great interest in the past two decades in the mechanism of the insulin-like function of vanadium and in developing new vanadium compounds as potential insulin adjuvants [2] or replacement in the treatment of diabetes, most notably when administered orally. Great efforts have therefore been made to synthesize oxovanadium (IV) complexes of high biological activity and low toxicity, which are readily absorbed. Many oxovanadium(IV) complexes with various coordination modes have been prepared, viz., $VO(O_4)$, $VO(N_3O)$, and $VO(N_2O_2)$ {consistent with combination of hard acids and hard bases} and the relationship between their structures and insulin-mimetic activities has been examined by evaluating both in vivo and in vitro results.

In view of the medicinal importance of vanadium compounds, and also extending [3] our search for more efficacious compounds of vanadium with neutral charge and low molecular weight (desirable qualities of vanadium compounds to be useful as metallopharmaceutical drugs), we present here the first synthesis of VO^{2+} complexes of amino sugar-Schiff bases (H_2L) (Fig.1) having the general composition, $[VO(L)(H_2O)]$. The compounds so obtained were characterized on the basis of analytical data, vanadium determination, molar conductance and magnetic measurements, TG, IR, EPR, and electronic absorption spectral studies. Based on these studies, a square pyramidal structure (Fig.2) has been proposed for these chelates. The 3D-molecular modeling [4] (Fig.3) and analysis have also been carried out for one of the representative compounds to substantiate the proposed structure.

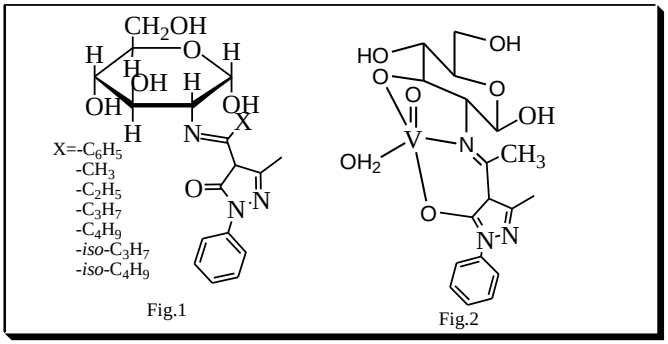

Fig.1 Fig.2

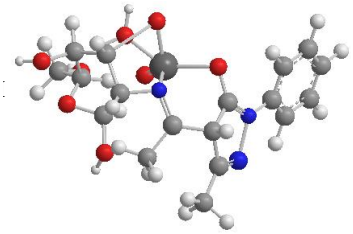

Fig.3

References:

[1] P.A.M. Williams, S.B. Etcheverry, E.J. Baran, *J. Inorg. Biochem.* **1997**, *65,* 133.
[2] K. H. Thompson, J. H. McNeill, C. Orvig, *Chem. Rev.*, **1999** ,*99*, 2561.
[3] R. C. Maurya and S. Rajput, *J. Mol. Structure*, **2006**, *794*, 24.
[4] R. C. Maurya and S. Rajput, *J. Mol. Structure*, **2006**, *79*, 89.

Analytical Quality Validation in Assessing Heavy Metal Pollution in Work Environment by Atomic Absorption Spectrophotometry

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Biological monitoring of workers can be considered to have a role to play in assessing whether protective measures at the place of work and are functioning properly. It helps in suggesting a tentative scheme which would make use of biological monitoring of chemicals in the occupational health care of exposed populations. The biopsy materials taken for quantitative analysis was human hair and nails. Data collection consisted of administrating a screening questionnaire as per recommendation of World Health Organization to establish eligibility as well as to obtain relevant personal and medical details of the subjects under study. The workers were selected basically on the criteria of potential exposure to trace toxic metals. Age and sex matched controls were selected from among those who had no exposure to metals and were apparently healthy. The biopsy materials were collected, washed with non-ionic detergent and deionized water in succession, dried and subjected to wet acid digestion using mixture of nitric and perchloric acid to make a water clear sample solution as per protocol laid down by International Atomic Energy Agency, Vienna. The quantification of metals was affected with an Atomic Absorption Spectrophotometer taking adequate quality control measures. The analytical quality validation is intended to promote the reliability and reproducibility of data by ensuring the data quality, with respect to its accuracy, integrity, completeness and clarity. It has been observed that variations due to sampling, pre-treatment errors are large compared to the variation introduced at analysis stage. Preparation of standard reference material is another step in depicting the level of deviation in the analytical results from standard value in view of non-availability and adequate supply of reference standards in the country.

A Novel Ce(III)-catalyzed Multicomponent Diastereoselective Synthesis of 3-Mercapto-2(1*H*)-pyridinones

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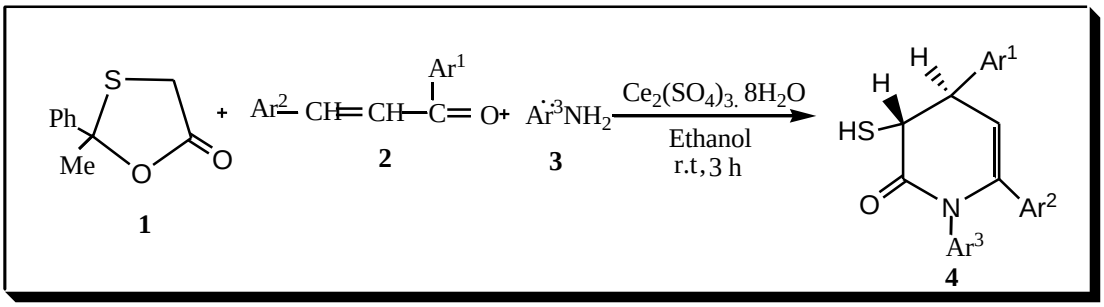
The development of simple, efficient and general synthetic routes using available reagents under environmentally friendly conditions still remain targets in modem organic chemistry. As part of our work on the investigation of novel approaches for the new bond formation through ring transformations, we have chosen $Ce_2(SO_4)_3.8H_2O$ as a promoter for efficient , stereoselective synthesis of 3-mercapto-2(1*H*)-pyridinones via a one-pot (3+2+1) multicomponent coupling reactions of chalcones, 2-methyl-2-phenyl-1,3-oxathiolan-5-one and aromatic amines. The synthesis involves sequential Michael addition, condensation, and ring transformation to afford the target molecules. Ambient temperature, operational simplicity, use of an environmentally clean catalyst, high yields, short reaction time are the key factors of the present synthetic protocol.



Synthesis and Antimicrobial Activity of 5-{4'-[(6''-aryl)-2''-hydroxy-3'',4''-dihdropyrimidine-4''-yl]-phenyl carbamido}/5-{4'-[(6''-aryl)-2''-mercapto-3'',4''-dihydropyrimidine-4''-yl]phenyl carbamido}-dibenz[b,f]azepines

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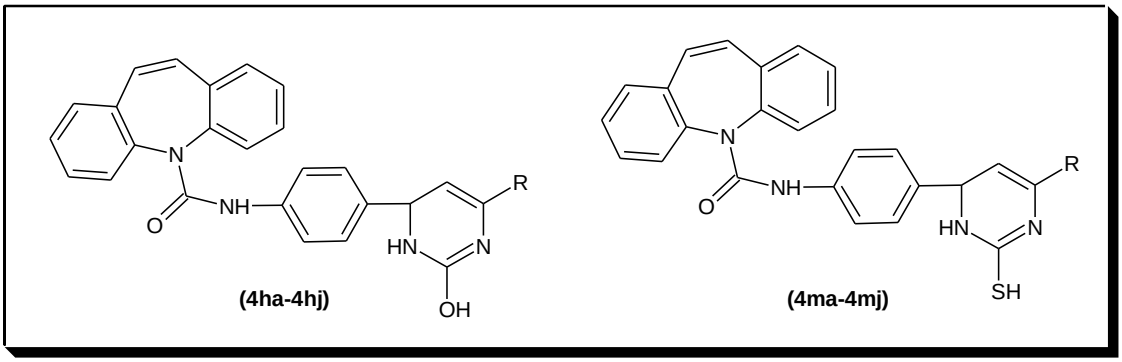
[b]Shree M. & N. Virani Science College, Rajkot – 360 005 (Gujarat) India

5-{4'-[(6''-aryl)-2''-hydroxy-3'',4''-dihdropyrimidine-4''-yl]-phenyl carbamido} dibenz[b,f]azepines **(4ha-4hj)**, 5-{4'-[(6''-aryl)-2''-mercapto-3'',4''-dihydropyrimidine-4''-yl]phenyl carbamido}-dibenz[b,f]azepines **(4ma-4mj)** have been synthesized. The products have been assayed for their antimicrobial activities. Some of the products showed moderate activity in comparison with known standard drugs viz. ampicillin, chloramphenicol, norfloxacin and greseofulvin.



The constitutions of the products have been characterized by IR, ^{1}H-NMR, Mass spectral studies and elemental analysis.

Synthesis and Characterization of Cardo bisbenzoxazines and their Thermal Polymerization

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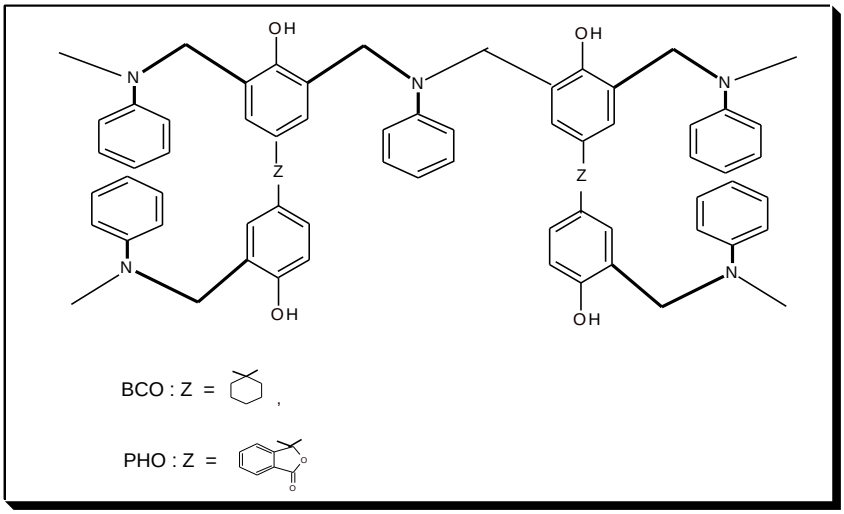
Bisbenzoxazines of bisphenol-C (BCO) and phenolphthalein (PHO) were synthesized by condensing 0.05mol bisphenol-C/phenolphthalein, 0.2mol formaldehyde and 0.1mol aniline. BCO and PHO were thermally polymerized via ring opening polymerization. Resultant cross-linked polymers (PBCO and PPHO) were characterized by solubility, IR, NMR, DSC and TGA. Bisoxazines and their polymers followed two- step degradation. Both BCO and PHO undergo selective ring opening polymerization over the temperature range 100-150^{0}C and are thermally stable up to about 250^{0}C. The % residue at 550^{0}C is substantially higher for PHO samples (56-67%) than BCO samples (20-25%) indicating highly thermally stable nature of PHO. Ring transformation reaction is also supported by DSC. New thermosetting materials may be useful for specific applications to be exploited.



Spectral and Mechanistic Investigations of Oxidation of Pentoxifylline Drug by Alkaline Permanganate

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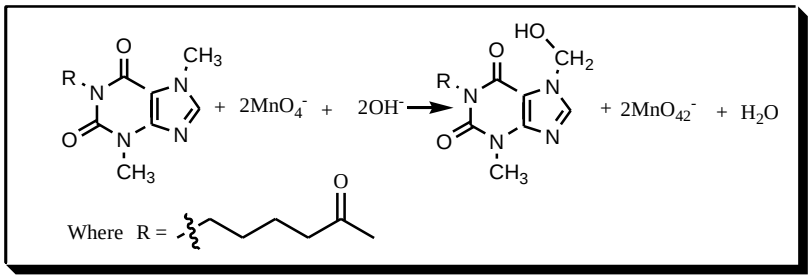
The kinetics of oxidation of pentoxifylline (PTX) by permanganate (MnO_4^-) in alkaline medium at 298 K and a constant ionic strength of 0.10 mol dm^{-3} was studied spectrophotometrically. The oxidation products are alcohol (1-Methyl-3-(5-oxo-hexyl)-dihydro-pyrimidine-2,4-dione) and Mn(VI). The stoichiometry is i.e. [PTX]:[MnO_4^-] = 1:2 as given below



The reaction is of first order in Mn (VII) concentration and is less than unit order in PTX concentration. The rate of reaction increases with increase in OH^- concentration (order =1.6). Effect of added products, ionic strength and dielectric constant of the reaction medium has been investigated. The oxidation reaction in alkaline medium has been shown to proceed via a pentoxifylline anion, which further reacts with one molecule of permanganate species in a rate determining step followed by other fast steps to give the products. The main products were identified by TLC and spectral studies. The activation parameters are computed and discussed.

Transesterification of Chromenes Employing Immobilized Lipase in Ionic Liquids

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Over the past decade green chemistry has emerged as a bright, new approach for the traditional field of chemistry as it struggles to find its place in the international drive towards global sustainability. Superior catalysis and the replacement of conventional organic solvents are key steps towards reasonable solutions to the many green issues, which have to be addressed by the chemical industry worldwide. Different studies spanning over last few years concerning the use of biocatalysts in ionic liquids have received attention due to advantages they offer such as increased solubility of organic substrates, high possibility to carry out processes which are thermodynamically unfavorable in ILs, and facilitating the recovery of both enzyme and ILs. Our quest to explore different chemo-enzymatic reactions, it was thought worthwhile to employ these ionic liquids as solvents in biocatalytic reactions. We wish to report herein the transesterification of chromene derivatives catalyzed by *Candida Antarctica* B lipase in Ionic Liquid using vinyl acetate as an irreversible acyl donor at room temperature. The parent structure, chromenes are found to possess various pharmaceutical activities. On functionalized with acyl, alkyl, halogen and other groups, these further showed increased in their bio-potentiality. Acylation plays a significant role in organic chemistry, as shown by many different methods, which have been developed for key transformations.

ICRF- 193 Treatment Interferes with Spindle Elongation in Dividing *S.pombe* Cell

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ICRF-193, a noncleavable, complex stabilizing topoisomeraseII (topoII) inhibitor has been shown to target topoII in mammalian cells. With the aim of elucidating the roles of topoII in dividing *S.pombe* cells, we examined the effects of ICRF-193 treatment on such cells. The study on double mutant ts *top2*-cs *nda3* indicated that ICRF-193 treatment delays metaphase to anaphase transition in *S. pombe* cells compared to the DMSO treated control cells. It is reported that anaphase inhibitor securin is kept stable during such delay. The spindle characteristics were severely affected by the drug treatment. Phase2 and Phase3 of spindle elongation were not distinct as previously reported for *top2-191* mutant cells but more interestingly, the ICRF-193 treated cells showed constant spindle elongation speed in Phase2 and Phase3 supporting the delay induced by ICRF-193 treatment. Using fixed cells of Top2-GFP, we could observe the dot signal of GFP in ICRF-193 treated cells compared to the DMSO treated cells, indicating the trapped topoII on the DNA after ICRF-193 treatment. In short, ICRF-193 treatment is effective in *S. pombe* cells. ICRF-193 affects the dividing *S. pombe* cells by inhibiting the spindle characteristics. This is the first report of ICRF-193 treatment in *S. pombe* cells.

Efficient Preparation of Benzylidene Acetals in Carbohydrate Derivatives

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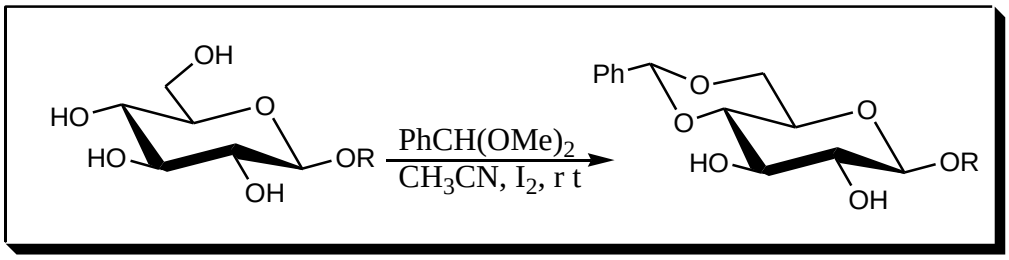
Benzylidene acetal is one of the frequently used protecting group in the oligosaccharide synthesis for the temporary protection of C-4/C-6 hydroxyl groups in carbohydrate derivatives. It can be removed easily under acidic hydrolysis or under neutral condition by hydrogenolysis. One of the two C-O bonds of the benzylidene acetal can be regioselectively opened for its application in oligosaccharide synthesis. Several methods have appeared in the literature for the introduction of benzylidene acetal in carbohydrates. Despite of their potential utilities most of the methods are time consuming and often required excess of 24 h for completion, a large excess of reagent and tedious work-up followed by chromatographic purification. In recent years, molecular iodine has been used as an inexpensive, non-metallic, non-toxic bench-top catalyst in several functional group transformations in carbohydrate chemistry. We describe herein a rapid preparation of benzylidene acetal of carbohydrate derivatives using benzaldehyde dimethylacetal in the presence of molecular iodine as catalyst (Scheme 1).



Scheme 1: Molecular iodine catalyzed benzylidene acetal formation in carbohydrate derivatives.

Reference:

[1] Panchadhayee, R.; Misra, A. K. *J. Carbohydr. Chem.* **2007**, in press.

Synthesis of 4-aryl-2-(3(5)-substituted-5(3)-trifluoromethyl-1-pyrazolyl)-thiazole as Potential Antifungal Agents

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Heterocyclic compounds bearing trifluoromethyl group play an important role in medicinal and agricultural fields. Among them, pyrazoles and thiazoles are of special interest as potential herbicides, fungicides, analgesic and antipyretic agents. Also, pyrazolylthiazoles are used for cardiovascular diseases and for agrochemical lead. Our focus is to synthesize pyrazolylthiazoles derivatives bearing trifluoromethyl group on 3 and or 5 positions of pyrazole ring as potential antifungal agents. A perusal of literature revealed that the most common route to synthesis pyrazolylthiazoles comprised of the reaction of 2-hydrazinothiazoles with β-diketones. But, the reaction suffers with the draw-back of regioselectivity and affords non-separable mixture of products. So, in the present investigation, an alternate route was explored to prepare some new trifluoromethyl substituted pyrazolylthiazoles involving the reaction of 3(5)-trifluoromethyl-5(3)-substituted-1-thiocaboxamidepyrazole **1** with α-halocarbonyl compounds. Synthesis of the starting material **1** was accomplished by the reaction of thiosemicarbazide with trifluoromethyl-β-diketones. However, the reaction yielded mixture of two products namely 3-trifluoromethyl-5-substituted-1-thiocaboxamidepyrazole and 5-hydroxy-5-trifluoromethyl-3-substituted-1-thiocarboxamidepyrazoline. Later on, 4-aryl-2-(3-substituted-5-trifluoromethyl-1-pyrazolyl)thiazoles were obtained exclusively by cyclization and simultaneous dehydration of 5-hydroxy-5-trifluoromethyl-3-substituted-1-thiocarboxamidepyrazolines with phenacyl bromides in the reaction conditions. Also, 3-trifluoromethyl-5-substituted-1-thiocaboxamidepyrazole on reaction with phenacyl bromides yield expected 4-aryl-2-(3-trifluoromethyl-5-substitutedpyrazol-1-yl)thiazoles along with formation of α-thiocyanatoketones. Title compounds are expected to have potential antifungal activity and are under trial. Formation of these compounds was confirmed on the basis of their IR, ^{1}H, ^{13}C, ^{19}F NMR, mass and elemental analysis.

Mechanistic Study of Ruthenium (III) Catalysed Oxidation of L-Lysine by a New Oxidant, Diperiodatoargentate(III) in Aqueous Alkaline Medium by Stopped Flow Technique

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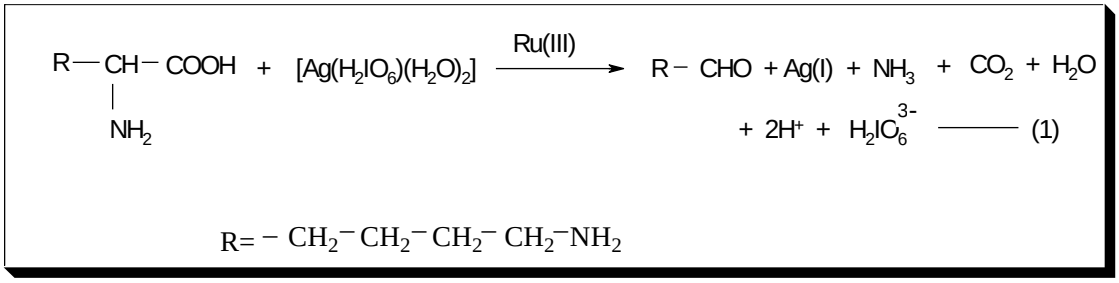
The kinetics of Ru(III) catalysed oxidation of L-lysine by diperiodatoargentate (III) (DPA) in alkaline medium at 298K and a constant ionic strength of 0.50 mol dm^{-3} was studied spectrophotometrically. The oxidation products are aldehyde (5-aminopentanal) and Ag (I). The stoichiometry is i.e. [L-lysine]:[DPA] = 1:1. as given below



Scheme 1

The reaction is of first order in [Ru (III)] and [DPA] and is less than unit order in both [L-lys] and [alkali]. Addition of periodate had a retarding effect on the reaction. Effect of added products, ionic strength and dielectric constant of the reaction medium have been investigated. The oxidation reaction in alkaline medium has been shown to proceed via a Ru(III)-L-lysine complex, which further reacts with one molecule of monoperiodatoargentate(III) (MPA) in a rate determining step followed by other fast steps to give the products. The main products were identified by spot test, IR, GC-MS studies. The catalytic constant (K_c) was calculated at different temperatures. The activation parameters with respect to slow step of the mechanism are computed and discussed and thermodynamic quantities are also determined. The active species of catalyst and oxidant have been identified.

Discovery of Spiro-piperidin-4-ones as Antimycobacterial Agents

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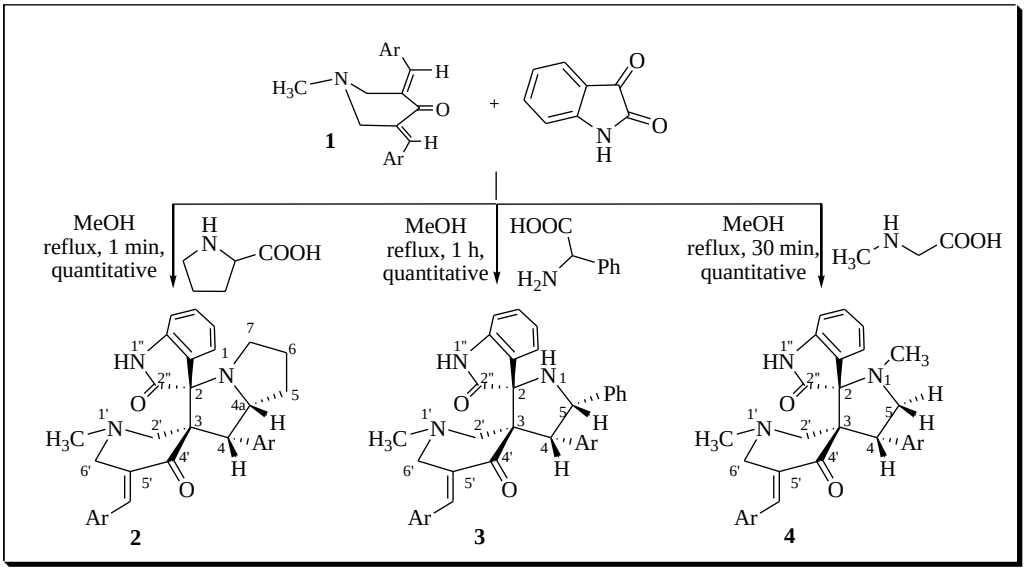
1,3-Dipolar cycloadditions constitute a versatile protocol for the construction of five membered ring heterocycles [1]. The cycloaddition of azomethine ylides to exocyclic olefins furnish spiro-pyrrolidines, which display important biological activities [2]. In general, spiro compounds have drawn considerable attention of the chemists in view of their very good antimycobacterial activity [3]. In the present investigation, an atom economic protocol for the stereoselective synthesis of several spiro-pyrido- pyrrolizines and pyrrolidines **2–4** through 1,3-dipolar cycloaddition of azomethine ylides, generated *in situ* from isatin and α-amino acids, to various 1-methyl-3,5-bis[(*E*)-arylmethylidene]tetrahydro-4(1*H*)-pyridinones is described. The compounds **2–4** were screened for their *in vitro* antimycobacterial activity against MTB and MDR-TB by agar dilution method for the determination of MIC in duplicates. The MDR-TB clinical isolate was resistant to isoniazid (INH), rifampicin, ethambutol and ciprofloxacin. Most of the compounds displayed excellent *in vitro* activity wherein **3e** with *p*-F aryl rings was found to be the most active compound *in-vitro* with a MIC of 0.05μg/mL against MTB equivalent to isoniazid and 31 times more potent than ciprofloxacin. Compound **3e** was also the most active one against MDR-TB with MIC of 0.1 μg/mL which is 16 and 125 times more potent than isoniazid and ciprofloxacin respectively.



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A Green Microwave Induced Decarboxylation of Indole and Nitroaryl Substituted Carboxylic Acids

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A clean decarboxylation protocol has been developed for various indole acids by using aq. $NaHCO_3$-piperidine reagent combination in PEG under microwave irradiation. The obtained indole derivatives possess a number of important pharmacological properties. The role of various substituents at the aromatic ring towards the decarboxylation reactions has been investigated. Resonance effects play an imperative role for carrying out the decarboxylation reactions. The developed protocol provides a green alternative to the hitherto indispensable multistep approaches involving toxic quinoline/copper salt combination.

Synthesis of 1-(2,6-dichlorophenyl)-3-methylene-1,3-dihydro-indol-2-one Derivatives and *in vitro* Anticancer Evaluation Against SW620 Colon Cancer Cell Line

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[b]Dabur Research Foundation, Ghaziabad-201010, India.
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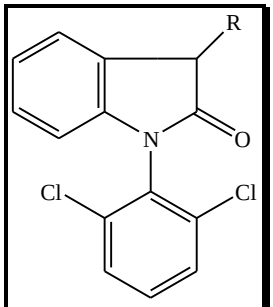
[e]Ara healthcare, Ghaziabad

A small library of 2-indolinone derivatives with the 2,6-dichlorophenyl ring at the N_1 position and with varying substitutions including aryl groups at the 3-position were synthesized, and their structures were confirmed by spectral analysis. All molecules were screened for their *in vitro* cytotoxic activity on SW620 colon cancer cell lines. Among the designed series compounds **4c**, **4f** and **4j** were found to be active at concentrations of 2-15 μg/ml. Some 3D-QSAR models were also built to understand the structure activity relationship.



4a-t

Highly Chemoselective S-methylation Reactions using Trimethyl orthoformate

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In recent years, an increasing interest has been focused on trimethyl orthoformate as a reagent for safer and selective methylation protocols. Common methylating agents are toxic and dangerous. Although ortho esters are most commonly used for the preparation of ketals and acetals through transacetalation, transetherification, and reduction reactions, some successful Trimethyl Orthoformate-mediated N-methylations of aromatic amines and imidazole-like compounds have also been claimed. In the present work, we have described chemoselective S-methylation reaction using trimethyl orthoformate.

Synthesis, Anti-inflammatory and Anticancer Activity Evaluation of Some Sulfonamide and Amidine Derivatives of 2-iminothiazolines

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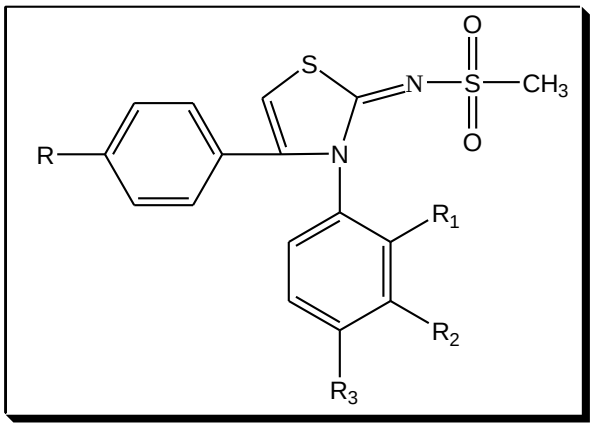
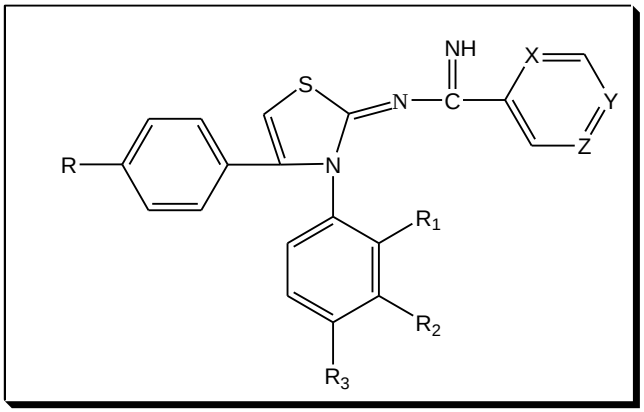
Sulfonamide (I) and amidine (II) derivatives of various 2-iminothiazolines have been synthesized and characterized by spectroscopic means & elemental analysis. These well characterized derivatives have been screened for anti-inflammatory & anticancer activity. Some of the compounds exhibited good anti-inflammatory & anticancer activity.



[**I**]



[**II**]

Where: R, R_1, R_2, R_3, X, Y & Z are various substituents

Protein Tandem Repeats: Distribution, Function, Evolution and Association with Diseases

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About 14% of the protein sequences in the SwissProt database contain repetitive region, viz., tandem repeats, multiple copies of motifs/profiles, multiple copies of domain. Our main focus is only on tandem repeats. Tandem repeat can be defined as contiguous repeat pattern of two or more copies. These copies can be exact or approximate.

Eukaryotic proteins are more likely to have repeats compared to Viruses, Bacteria and Archaea, because eukaryotic proteins are involved in some unique functions. Incidence of repeats is independent of protein length. Proteins with higher incidence of repeats are involved in functions like transcription, translation, protein-protein interaction. Tandem repeats in proteins are correlated with tri-nucleotide repeats at genome level, and various secondary structure repeats of alpha-helices and beta strands at structure level. Proteins with tandem repeats, especially Single Amino Acid Repeats have medicinal importance and are involved in various neurodegenerative diseases like Huntington's disease. These proteins are also found to occur in sequences which are poorly conserved in evolution.

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Design, Synthesis and Biological Activity of Dipeptidic Compounds Exhibiting Antimicrobial Activities

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A series of small cationic peptides having two to six amino acids, which exhibited encouraging antibacterial activities have been recently reported.[1,2] Since these peptides don't have specific receptor and possess microbial cell membrane lysis activity due to the presence of amphiphilic structure, we considered only the hydrophobic and positive ionisable features for the generating a hypothesis using hip-hop module of CATALYST software. Top ranked hypothesis showed the presence of distinct hydrophobic and hydrophilic regions on different faces of appropriate conformation taken by the active molecules (Fig.1) in accordance with the accepted mechanism of antimicrobial peptides.[3] Based on this hypothesis, we proposed two series of dipeptides having required structural features fitting into the pharmacophore model. Apart from arginine and tryptophan, histidine and 2-alkyl-L-histidines were found to be important for antimicrobial activity. The synthesis of dipeptides involved: (i) the synthesis of 2-alkyl-L-histidines by regiospecific alkylation of protected L-histidine via silver catalyzed radical decarboxylative oxidation; [4] (ii) conversion of C-terminal carboxylic acid to either methyl ester or benzyl amide; [5] (iii) peptide coupling using DIC and HONB. These dipeptides have been biologically screened for antibacterial activities against *Escherichia coli, Stapylococcus aureus, Staphylococcus Epidermis, Pseudomonas aeruginosa, Klebsiella Pneumoniae* and for antifungal activities against *Candida albicans.* The results show encouraging correlation with the theoretical studies. The presentation will highlight all aspects of synthetic strategies, pharmacophore mapping, mechanism of action and biological activity of these dipeptidic compounds.

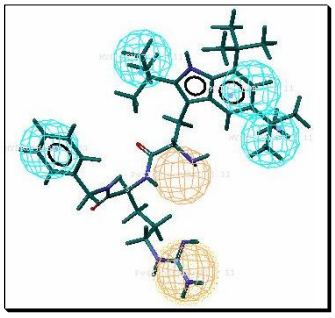

Figure 1

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Computational Study of Folylpolyglutamate Synthetase Enzyme from *Mycobacterium tuberculosis*: Implications for Structure-based Drug Design

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Mycobacterium tuberculosis (Mtb) overcomes the numerous challenges presented by the immune system of the host. In the last 40 years few anti-TB drugs have been developed, while the drug-resistance problem is increasing; there is thus a pressing need to develop new anti-TB drugs active against both the acute and chronic growth phases of the mycobacterium. In *Mycobacterium tuberculosis*, Folylpolyglutamate synthetase (FPGS) catalyzes the ATP-dependent addition of a glutamate residue via an amide linkage to the γ-carboxylate group of the folate or folate polyglutamates. FPGS is essential for folate biosynthesis in *Mycobacterium tuberculosis* and therefore is a potential target for antitubercular chemotherapy. In the absence of its crystallographic structure, our aim was to develop a structural model of MtFPGS. This will allow us to gain early insight into the structure and function of the enzyme and its likely binding to ligands and cofactors and thus, facilitate structure-based inhibitor design. To achieve this goal, initial models of MtFPGS were generated using MODELER. The best quality model was refined using a series of minimizations and molecular dynamics simulations is further assessed by PROCHECK, PROFILE-3D and PROSTAT, which show that the refined model is reliable. With this model, molecular docking studies were performed to elucidate the probable binding mode of folate substrates, glutamate and ATP. The knowledge gained from the current study should prove useful in the design and development of inhibitors as potential novel therapeutic agents against tuberculosis by either de novo drug design or virtual screening of large chemical databases.

Antihepatotoxic Effect of *Hygrophila auriculata* Against CCl_4 -induced Hepatic Damage in Albino Rats

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Hygrophila auriculata (K. Schum) Heine (syn.) *Asteracantha longifolia* Nees, Acanthaceae are described in ayurvedic literature as Ikshura, Ikshugandha and Kokilasha "having eyes like the Kokila or Indian Cuckoo". The roots, seeds and ashes of the plant are extensively used in traditional system of medicine for various ailments like jaundice, hepatic obstruction, rheumatism, inflammation, pain, urinary infections, edema and gout. It is classified in ayurvedic system as seethaveeryam, mathuravipaka and used for the treatment of premeham (diabetes), athisaram (dysentery), etc.

The hepatoprotective activity of the ethanol extract and methanol fraction of the arial part were studied on CCl_4-induced (2 ml/kg, s.c.) liver toxicity in albino rats. The oral administration of extracts of *Hygrophila auriculata* (K. Schum) Heine, to albino rats for 5 days. The activity on albino rat was monitored by several liver function tests, viz glutamic oxalacetic transaminase (SGOT), glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALKP) total protein (TP) and total albumin (TA) in serum.. Furthermore, hepatic tissues were subjected to histopathological studies.The observations reveled that, the ethanolic extract and methanolic fraction obtained from *Hygrophila auriculata* showed significant antihepatotoxic activity, where as in methanolic fraction was found to be most active.

Network Properties of Repeat Proteins

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Protein Contact Network is a graph-theoretical representation of the protein structure, where each amino acid is a node and the spatial proximity of amino acids is considered as a link between them. The Protein Contact Networks can thus be considered as a set of closely connected amino acids falling within a range of interaction distance (8A). These Network Graphs have been used to study proteins that display repetitive patterns belonging to different repeat families *viz.* Ankyrin Repeats, HEAT Repeats, TPR Repeats and Armadillo Repeats collected from Pfam Database. The degree distribution observed for the Network Graph of these proteins reveals a significant pattern that can be used for the identification of proteins with repeats. Graph spectral analysis also yields potential ways in which such proteins can be identified against the non repeat proteins. Proteins belonging to particular repeat families are seen to form distinct clusters when compared on parameters such as Characteristic Path Lengths and Clustering Coefficients.

Clustering of Adenosine Kinase Inhibitors-Study for their Different Binding Modes

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Adenosine Kinase (AK) is an enzyme which converts adenosine to adenosine monophosphate in an ATP dependent manner. Recently, studies have been performed on analogues of tubercidin as potent adenosine kinase inhibitors possessing antiseizure activity [1, 2, 3]. So far, several highly potent AK inhibitors were identified but none of them suitable for further development. Here we took a set of active ligands (tubercidin analogues) which possess common core but differ in side chain substitution. This study combines the pharmacophore analysis and docking calculations to derive binding mode of tubercidin analogues (different clusters in the active site). The docking studies prove the existence of diverse binding modes of analogues as presumed by a workgroup, based on the SAR of these molecules [1]. This pattern of clustering was also analyzed by the clustering based on topological descriptors which represent 2d structural information and 3D pharmacophoric fingerprints. Clustering based on the basis of ligand structure alone also gives clue for their different binding pattern. Characteristics of the active site such as size or volume, hydrophobic interactions and amino pi interactions are likely to be fundamental determinants of the difference in their binding modes.

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Application of *Cassia grandis* Seed Gum-graft Poly(methylmethacrylate) on Pb^{2+} Removal from Industrial Wastewater

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In the present research work *Cassia grandis* seed gum-graft-poly(methylmethacrylate) samples was synthesized by using persulfate/ascorbic acid as a redox system. The copolymer samples were evaluated for lead(II) removal from the aqueous solutions where the sorption capacities were found proportional to the grafting extent. The conditions for the sorption were optimized using copolymer sample of highest percent grafting. The sorption was found pH and concentration dependent, pH 2.0 being the optimum value. Adsorption of lead by the grafted seed gum followed a pseudo-second-order Kinetics with a rate constant of 4.64 ×10−5 g/mg/min. The equilibrium data followed the Langmuir isotherm model with maximum sorption capacity of 126.58 mg/g. The influence of electrolytes NaCl, Na_2SO_4 on lead uptake was also studied. The adsorbent was also evaluated for Pb(II) removal from battery waste-water containing 2166 mg/L Pb(II). From 1000 times diluted waste water, 86.1% Pb(II) could be removed using 0.05 g/20 ml adsorbent dose, while 0.5 g/20 ml adsorbent dose was capable of removing 60.29% Pb from 10 times diluted waste water. Optimum Pb (II) binding under highly acidic conditions indicated that there was a significant contribution of nonelectrostatic interactions in the adsorption process.

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Pictet-Spengler Reaction towards Synthesis of New 1,4-Disubstituted-1,2,3,4-Tetrahydro-β-Carbolines And 1,4- Disubstituted –β–Carbolines. Formation of γ-Carbolines-A Novel Observation.

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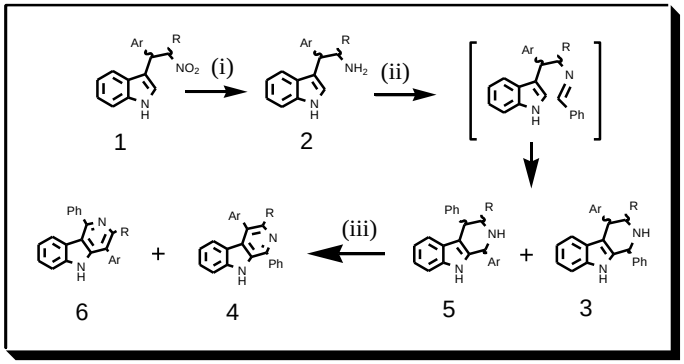
Tetrahydro-β-carbolines (THβCs) are potent neuroactive alkaloids. THβCs as pharmacophores have exhibited a wide range of pharmacological properties. They have been shown to inhibit monoamine oxidase A and bind with nanomolar affinity to serotonin receptors. THβCs also bind to GABA, a receptor ion channel and modulate molecular mechanisms controlling anxiety, convulsions, and sleep. B- Cabolines exhibit many important biological activities like mutagenic and co-mutagenic properties, significant anti-tumor and anti-HIV activities, and inhibition of topoisomerase. The pictet-Spengler condensation is most widely used and extensively studied method for the synthesis of tetrahydro-β-carbolines. Amongest the variously substituted tetrahydro-β-carbolines, very few reports are available typically for the 1,4-disubstituted tetrahydro-β-carbolines and also 1,4- disubstituted -β-carbolines.

Microwave-asisted conjugate addition of indole on nitro-olefins furnished nitro compounds, which were reduced to tryptamines. Further. By using Pictet-Spengler condensation, new 1,4-disubstituted-1,2,3,4-tetrahydro-β-carbolines were synthesized in diastereoselective manner. Dehydrogenation of the tetrahydro-β-carbolines produced new 1,4- disubstituted -β-carbolines. As a new observation, in some of the cases, Pictet-Spengler condensation and dehydrogenation gave two products, namely 1,4- disubstituted -β-carbolines and 1,4-disubstituted-γ-Carbolines. A mechanism is proposed for this observation.



Where: **1a,2a,3a,4a**: Ar = phenyl, R = H; **1b,2b,3b,4b,5b,6b**: Ar = 3,4-dimethoxyphenyl, R=H; **1c,2c,3c,4c,5c,6c**: Ar = 3,4-dimethoxyphenyl, R=H; **1d,2d,3d,4d**: Ar = 2-furyl, R=H; **1e,2e,3e:** Ar = p-aminophenyl, R=H; **1f,2f,3f**: Ar = 2-thienyl, R=H; **1i,2i**: Ar = 2-furyl, R = methyl.

Scheme1: Reagent and conditions: (i) Raney- Nickel/methanol; (ii) trimethylsilylchloride, PhCHO, DCM, 88h, 0-25^{o}C; (iii) Pd/C (5%), Xylene.

Mechanism of Rotenone Induced Cell Death in Glial Cells

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Rotenone, a pesticide has been reported to induce the destruction of dopaminergic neurons and cause various degrees of Parkinsonism in rats. We investigated effect of rotenone on glial cells comprising about 90% cells of the brain. C6 rat glial cell line was used to evaluate its noxious effects. Treatment of rotenone significantly reduced the viability of cells in concentration dependent manner. Rotenone treatment led to increased LDH release in media, increased reactive oxygen species (ROS) production, decrease in mitochondrial membrane potential, altered nuclear morphology and DNA fragmentation. Results suggested rotenone mediated apoptotic death of glial cells.

Synthesis and Biological Activity of Some New N-aryl-1,4-Dihydropyridines containing Furan Nucleus

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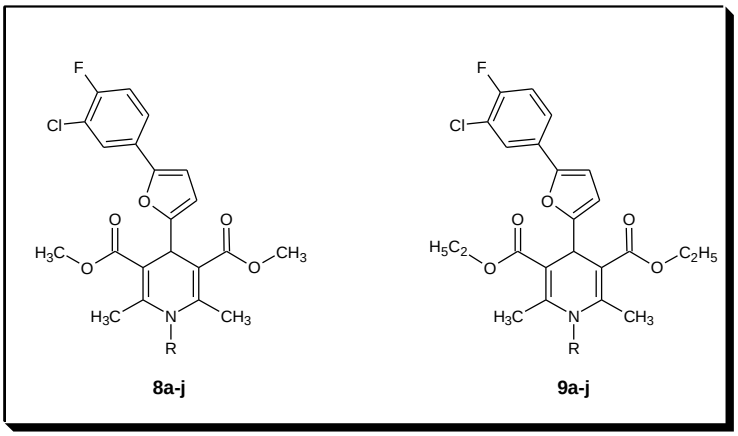
Among a wide variety of heterocycles that have been explored for developing pharmaceutically important molecules 1,4-dihydropyridine have played an important role in medicinal chemistry. 1,4-Dihydropyridines possess a broad spectrum of biological activities, such as the ability to control the influx of calcium into cells, as well as enzymatic,[1] antitubercular,[2] antifungal and antimicrobial,[3] antihypertensive,[4] and many other properties. 4-Aryl-1,4-dihydropyridines of the nifedipine type (DHPs, *e.g.* 2–4) are the most studied class of organic calcium channel blockers [5] and, since their introduction into clinical medicine in 1975, have become almost indispensable for the treatment of cardiovascular diseases such as hypertension, cardiac arrhythmias, or angina.[6]



Where R = Aryl

Furan nucleus containing different 1-N-aryl-2,6-dimetyl-3,5-dicarbmethoxy-4-[5'(*m*-chloro-*p*-flourophenyl)-2'-furyl]-1,4-dihydropyridines **8a-j** and 1-N-aryl-2,6-dimetyl-3,5-dicarbethoxy-4-[5'(*m*-chloro-*p*-flourophenyl)-2'-furyl]-1,4-dihydro-pyridines **9a-j** were synthesized. The newly synthesized compounds were fully characterized on the basis of elemental analysis, IR, ^{1}H NMR, and mass spectral data. The antitubercular activity and antimicrobial activity of all compounds have been evaluated.

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Synthesis Characterization and Biological Features of Oxazine and Phthalazines

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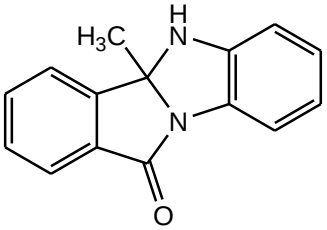
The synthesis, characterization and anti-microbial activity of Oxazine and Phthalazines formed by the condensation reaction of 2-acetyl benzoic acid with different nucleophiles viz. hydrazine, hydroxylamine, semicarbazide, phenylhydrazine and 1,2-diaminobenzene have been described. The reaction have been carried out under thermal and microwave conditions and the product selectivitynoticed under microwave irradiation has been highlighted. 4b-Methyl-4b-11-dihydro-5H-benzo[4,5]-imidazo[2,1-a]isoindol-11-one seems to be very active towards all the tested species, particularly towards pseudomonas aervsinosa.



4b-Methyl-4b-11-dihydro-5H-benzo[4,5]-imidazo[2,1-a]isoindol-11-one

Ionic Liquid Mediated Cyclization of 2'-Hydroxychalcones and 2'-Aminochalcones: Synthesis of Flavanones and 2-Aryl-2,3-dihydroquinolin-4(1*H*)-one

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Flavanones and 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones are widely distributed compounds in nature that serves as valuable precursors for the synthesis of many medicinally important compounds of diverse biological activities (hypertensive, antibacterial, antitumor, antifungal, anti-inflammatory) [1]. The traditional method for the preparation of flavanones and 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones comprises an intramolecular cyclization of 2'-hydroxychalcones and 2'-aminochalcones, respectively in presence of corrosive reagents, expensive catalysts, involving flammable and toxic organic solvents [2]. In recent past, the use of ionic liquids continues to spread unimpeded in organic synthesis as a reaction solvent and catalyst due to their many advantages for facilitating chemical reactions [3]. These neoteric solvents are nonflammable, non-volatile, recyclable, commercially available, thermally stable, and possessing high polarities and broad miscibilities. We have developed a facile, efficient and green synthesis of biologically potent flavanones and 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones utilizing ionic liquid as reaction medium. Results of this synthetic procedure will be presented in the conference.

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Hydroformylation-Oxidation-Hydrolysis Route for Synthesis of Hydroxy Propionic Acids

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Hydroxy propionic acids viz 3-hydroxy propionic acid and 2-hydroxy propionic acid (lactic acid) are important bifunctional compounds for pharmaceutical as well as polymer industry [1,2]. Lactic acid is a commodity chemical important mainly in polymer industry whereas 3-hydroxy propionic acid is a specialty-important for pharmaceutical/biochemical industry [3]. Both the hydroxy propionic acids are currently synthesized by enzymatic catalysis – bio route which suffers from problems of high dilution and lower rates.

We report in the present study a new catalytic route for hydroxy propionic acids from vinyl acetate (VAM) comprising three steps viz. hydroformylation, oxidation and hydrolysis. VAM is hydroformylated to acetoxy propanals (2 and 3). Rh-catalyzed hydroformylation of VAM preferentially gives 2-acetoxy propanal (> 95 % selectivity) whereas Co-catalysts found to produce both 2- and 3-acetoxy propanals with 50 % selectivity to each. Effects of solvents and physical parameters were studied for hydroformylation of VAM using Co2(CO)8 as catalyst. The oxidation of hydroformylation product i.e. 2-and 3-acetoxy propanal was carried out using supported TM catalyst with high yields of corresponding carboxylic acids, which after hydrolysis using Amberlite IR-120 resin give hydroxy propionic acids Thus a new route for simultaneous synthesis of hydroxy propionic acids is demonstrated.

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Antibacterial Peptides from the Haemolymph of Crabs

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Marine crabs are potential sources of new antibiotics. The search for antimicrobial agents has taken a definite direction in developed countries. The present investigation was taken up to study the antibacterial activity of crude haemolymph extracts from six different species of crabs. Two positive controls Amphicillin and Erythromycin were also used. Investigation against a range of 10 different bacterial strains was used. The result demonstrated that the crab haemolymph of crude samples tested against gram positive and gram-negative pathogenic bacterial strains and two antibiotic resistant strains were used. In antibacterial activity the highest zone of inhibition was observed in the haemolymph against *Vibrio cholerae* and lowest zone of inhibition was observed in the haemolyph of *M. depressus* against *S.paratyphi-B* and *S.typhi*. On the basis of TLC and 1HNMR profile both, chloroform soluble and methanol fractions of the haemolymph showed ninhydrin positive spots indicating the presence of peptides. Chloroform soluble fraction was selected for further studies by ESI/MS analysis. The present study indicates that the haemolymph of crabs would be a good source of antimicrobial peptide agents and would replace the existing inadequate and cost effective antibiotics.

Oxoketene Dithioacetal Chemistry: Facile Synthesis of Triarylmethanes from α-Aroylketene dithioacetals *via* 2,3,4-Trisubstituted Pyrroles

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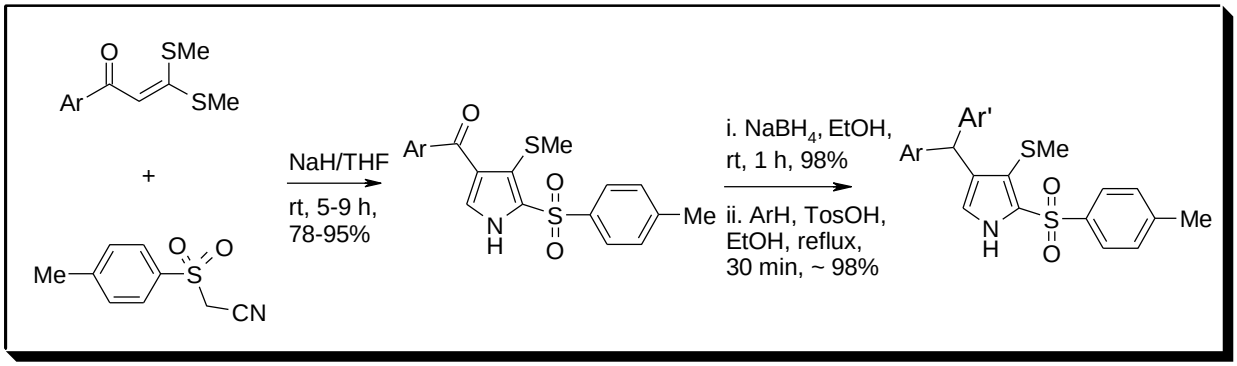
The α-aroylketene dithioacetals (AKDTA) are versatile synthetic intermediates, which are well exploited for the preparation of a variety of heterocyclic compounds. Generally, they behave as α,β-unsaturated carbonyl compounds having two methylsulfanyl leaving groups. Both the carbonyl carbon and the olefin carbon can be attacked by appropriate nucleophiles to furnish 1,2- or 1,4-addition products. The 1,2- or 1,4-addtions are dependent on hard or soft nature of the nucleophiles. For example, the AKDTAs can be used for synthesis of a combinatorial library of coumarins [1]. In spite of their popularity as three carbon synthones the AKDTAs have seldom been exploited for 1,3-dipolar cycloaddition reactions. We have shown that the reaction of a AKDTAs with TosMIC takes place smoothly when NaH in dry THF to furnish 2,3,4-trisubstituted pyrroles [2]. These 2,3,4-trisubstituted pyrroles were further transformed to triarylmethanes via reduction of the carbonyl group to tert-alcohol and substitution of alcohol moiety with electron rich aromatic compounds. The triarylmethanes prepared in this study could have application in pharmaceutical / material science. Details of the study and spectral characterization of the products will the presented in the seminar.



Ar = C_6H_5, 4-$CH_3C_6H_4$, 4-ClC_6H_4, 4-$C_6H_5C_6H_4$, 1-$C_{10}H_7$, 2-$C_{10}H_7$, pyrene, ferrocene
Ar' = Indole, *N*,*N*-diethyl aniline etc.

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Mechanism of Interaction and Conformational Studies on the Binding of Buzepide Methiodide to Bovine Serum Albumin

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The binding of an antihypertensive drug, buzepide methiodide (BZP) with bovine serum albumin (BSA) was investigated using fluorescence, circular dichrosm (CD), UV-vis absorption and FTIR techniques under simulative physiological conditions. The Stern-Volmer plot indicated the presence of static quenching mechanism. Binding constant and the number of binding sites were calculated based on fluorescence data and were found to be 3.73×10^3 M^{-1} and 0.99 at 302 K. The thermodynamic parameters, ΔH^0, ΔS^0 and ΔG^0 were evaluated by carrying out the interactions of BZP with BSA at different temperatures. These results indicated that the hydrophobic force played a major role in the binding of BZP to BSA. In order to locate the binding site in BSA for the drug, displacement experiments were carried out using different site probes. Based on these results coupled with thermodynamic parameters, it was proposed that the BZP bound to Site I (subdomain IIA) of BSA. The distance, *r* between the donor (BSA) and acceptor (BZP) was determined based on the FÖrster's theory of non-radiation energy transfer. CD results showed that the α-helicity of BSA decreased from 59.1 % (in free BSA) to 53.7 % (in bound BSA). Absorption and FTIR results also supported the change in conformation of BSA upon binding to BZP. The decreased binding constant of BZP-BSA in presence of some common ions revealed the availability of more amounts of free drug in plasma. This necessitated for the readjustment of dose limits of BZP in presence of common ions.

Twisted Intramolecular Charge Transfer Probe Induced Formation of α-cyclodextrin Nanotubular Suprastructures

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Complexes of organic compounds with cyclodextrins (CDs) are appropriate models to study the process of molecular self-assembly. The hydrophobic inner cavity of the truncated cone-like structures of the CDs have 4-8Å diameter. It is well known that cyclodextrin and its derivatives can incorporate appropriately sized guest molecules selectively through weak interactions like hydrophobic interaction, van der Waals force and hydrogen bonding. Depending on the relative sizes of the cyclodextrins and the guest molecules, more than one guest can be accommodated inside a single CD cavity. If the guest molecule is long enough, several cyclodextrins can be threaded along its length. α-CD nanotubes could only be developed either on well-defined surfaces or using polymeric molecules to hold them together. Unlike β-, and γ-CDs, formation of molecule induced stable α-CD nanotubes could not be observed so frequently, probably because of the size factor and consequently the thermodynamic instability of the complexes. Our attempt is to explain the method of construction of α-CD nanotubular suprastructures with the aid of a twisted intramolecular charge transfer (TICT) molecule named as trans-2-[4-(dimethylamino)styryl]benzothiazole (DMASBT). DMASBT is known to have dual fluorescence due to the existence of the locally excited (LE) state (stable in nonpolar environments) and TICT state (stable in environmnets of higher polarity). The dipolar nature of the TICT form of DMASBT helps to bring the 1:2 probe-CD complexes together. The –OH groups on the rim of the CDs form hydrogen bonds to form the nanotubes. These nanotubes, in turn, because of the same charged nature of DMASBT trapped inside the tubes, come together to develop bigger tubes through lateral hydrogen bonding. Steady state anisotropy and atomic force microscopy confirm the formation of the α-CD suprastructures.

Synthesis, Screening for Antitubercular Activity and 3D-QSAR Studies of Substituted *N*-Phenyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxamide

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Multi-drug resistance to commonly used Antitubercular drugs has propelled the development of new structural classes of Antitubercular agents. This paper reports the synthesis, evaluation and 3D-QSAR analysis of a set of substituted N-phenyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamides as Antitubercular agents. Substituted acetoacetanilides were reacted with various aromatic aldehydes and urea which yielded the tetrahydropyrimidine derivatives with a phenyl carbamoyl group at C5 position, and with various substitutions on the 4-phenyl and the N-phenyl aromatic rings. All compounds were screened for Antitubercular activity against Mycobacterium tuberculosis H37Rv strain. The QSAR models were generated on a training set of 23 molecules. The molecules were aligned using the atom-fit and field-fit techniques. The CoMFA and CoMSIA models generated on the molecules aligned by the atom-fit method show a correlation coefficient (r^2) of 0.98 and 0.95 with cross-validated r^2 ($q^{2)}$ of 0.68 and 0.58, respectively. The 3D-QSAR models were externally validated against a test set of 7 molecules for which the predictive r^2 (r^2 pred) is recorded as 0.41 and 0.32 for the CoMFA and CoMSIA models, respectively. The CoMFA and CoMSIA contours helped to design some new molecules with improved activity.

Synthesis and Antimicrobial Screening of 1, 6-Dihydropyrimidine Derivatives

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Such 1,6-dihydropyrimidines are associated with wide spectrum of biological activities like antimicrobial, anti-inflammatory, antidepresent, anti HIV, antitubercular, anticancer and fungicidal properties. This kind of compounds has been synthesized and the constitutions of the products have been elucidated on the basis of IR, ^{1}H NMR and mass spectral data. The products were assayed for their biological assay.

A Synthesis of Quinazolin-4-one Derivatives Their Characterization and *in-vitro* Biological Activity

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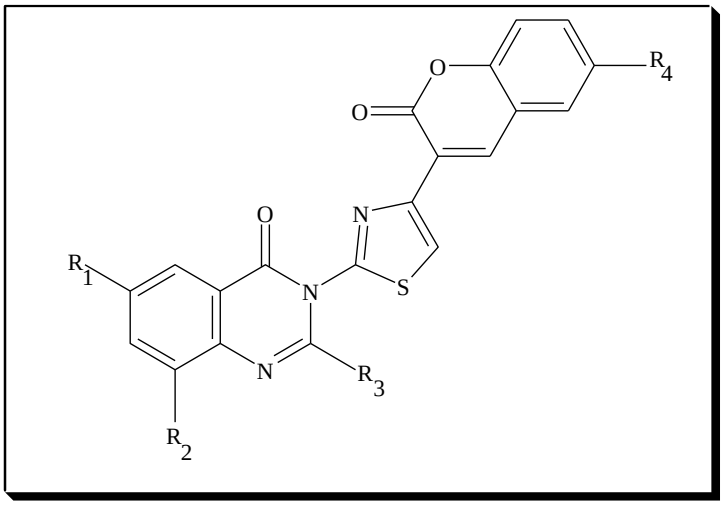
Twelve new quinazolin-4-one derivatives of 3-[2-(4-oxo-2-phenyl-3-hydroquinazolin-3-yl)-1,3-thiazol-4-yl]chromen-2-one have been synthesized by reaction of 3-(2-amino-1,3-thiazol-4-yl)chromen-2-one with 2-phenylbenzo[d]1,3-oxazin-4-one in dry pyridine. All the compounds have been screened for their in-vitro anti-bacterial studies. They have been characterized by elemental analysis, IR, NMR spectral data.



Where: R_1 = H, Br; R_2 = H, Br; R_3 = Ph, CH_3; R_4 = H, Br

Biochemical Characterization of *P. yoelii* Adenosine Deaminase

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Malarial is a serious public health problem in tropical countries. The emergence and spread of resistance to the existing antimalarial drugs have highlighted the need for discovery of new antimalarial molecules. *Plasmodium* and other parasitic protozoa lack the de-novo pathway of the purine biosynthesis and rely on either purine salvage pathway or on host for their purine requirement. This reliance of the parasite on the salvage pathway can serve as target for the chemotherapeutic attack. In malarial parasite, the purine salvage pathway utilizes hypoxanthine, formed by the phosphorylation of the inosine, as the major source of nucleotide synthesis. Inosine is formed by the deamination of adenosine deaminase, which is one of the important enzymes of the purine salvage pathway. The enzyme (adenosine deaminase) from rodent malarial parasite *P.yoelii* was purified by gel filtration and ion exchange chromatography. The kinetic properties and the effect of known inhibitors of the enzyme viz., 6-thioguanosine and 2' deoxyinosine, were studied on the activity of the purified enzyme. The inhibitors significantly inhibited the activity.

Alternative Reaction Media: Synthesis and Suzuki Reaction of Biologically Important Heterocycles in Aqueous Medium

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In continuation of our earlier interest on molecular diversity and search for new leads in drug-designing program aimed at achieving simple and environmentally compatible synthetic methodologies,[1] we have synthesized wide variety of various biologically important scaffolds incorporating various nuclei in which pyrimidine or pyran ring is annulated in aqueous medium emphasizing utility of nitriles and Multi-component reaction (**MCR**) methodologies in heterocyclic synthesis of biological importance.

Further the potential of aqueous medium is also studied for Suzuki reaction of various heterocycles synthesized in our laboratory for the first time because the use of water should be one of the priority issue in modern organic chemistry and a basic challenge in view of the green approach to organic compound transformation.

Regioselectivity was observed in case of halogenated pyrimido[2,1-b] benzothiazole derivatives, arylation occurs at thiazole ring exclusively and halides survey showed that rate of reaction is maximum in case of iodine. Antimicrobial and cytotoxic activities of representative compounds were studied.

Detailed synthetic approach and biological screening studies presented in the conference.

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Synthesis and Antimicrobial Activity of Some Hexahydropyrimidine Derivatives

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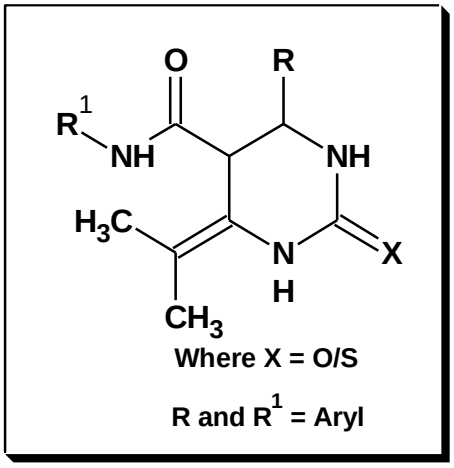
Interesting biological activities of a heterocycle like tetrahydropyrimidine have been extensively explored for their applications in the field of pharmaceutical chemistry. Antimicrobial agents are continuously in the process of modification to exhibit broader spectrum, greater potency and lesser toxicity. Significant biological properties associated with pyrimidine derivatives have focused considerable interest to design the compounds in which pyrimidine ring system associated with sulphur or oxygen atom is incorporated.



The title compound have been synthesized by condensation of different aryl aldehydes and 1,3-dicarbonyl compound with urea/thiourea in acidic media.

The constitution of all the compounds have been supported by Elemental analyses, IR, ^{1}H NMR and Mass spectral studies. Purity of all the compounds have been checked by thin layer chromatography. The products have been screened for their *in vitro* biological activity like antibacterial activities towards Gram *+ve* and Gram *–ve* bacterial strains and antifungal activity towards Aspergillus niger.

Histopathology and Biochemical Alterations in the Liver and Kidney of the *Chianna punctatus* (Bloch) Exposed to Folidol.

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Pesticides have been widely used all over the world to control insects, pests and disease vectors. The Pesticides are useful tools in agriculture and forestry, but their contribution to the gradual the degradation of the aquatic ecosystem cannot be ignored (Konar, 1975 and Basak, 1977). The pesticides pollute the aquatic ecosystem were they carried by rain water. From here they pass into the food Chain, ultimately produce toxicity to fish, birds, wild life and in turn to man. Due to the residual effect of pesticides, important organs like the 1iver, kidney, brain, gill, stomach and mussels are damaged. Toxic effect of organochlorine and carbamate pesticides have been studied by many authors, but the prevalence of organophosphate pesticide in the environment has became a matter of great concern (Sulodia and Singh 2004). The present investigation evaluates the toxicity of the folidol on the histopathology and Biochemical of the liver and kidney of the *Channa punctatus* (Bloch.) after sub- lethal exposure to for 75 and 90 days was investigated. The result showed that the histopathological change induced in the liver and kidney presented by cytoplasmic vacuolization, necrosis, hypertrophy, pyknotic, hemorrhage, and. degeneration of kidney tubules were recorded at the 20 ppm and 40 ppm. Sub-lethal concentration. The biochemical observation revealed marked in liver and kidney total protein and glycogen are altered with the control. These changes were time dependent

Synthesis of Highly Functionalised 1,4-Thiazines as A New Class of Antitubercular Agent

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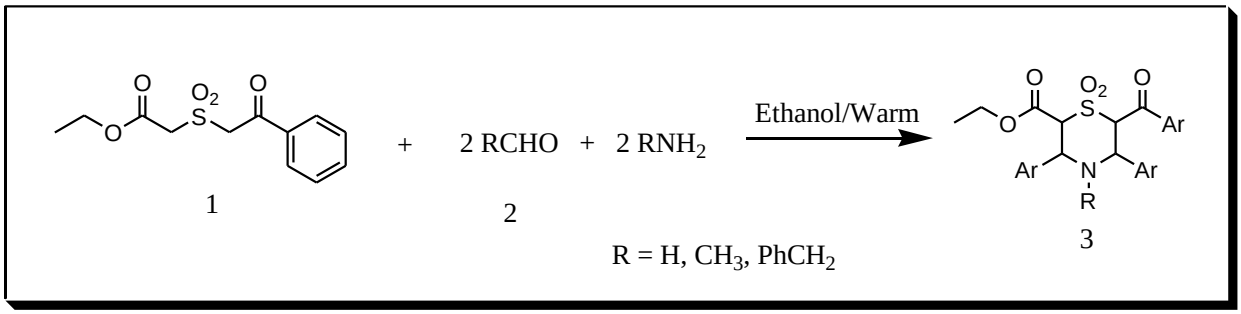
A series of ethyl 6-(4-chlorobenzoyl)-1,1-dioxo-3,5-diaryl-1,4-thiazinane-2-carboxylates **3** were prerared in the good yields (75-95%) from the reaction of ethyl 2-[(2-oxa-2-arylethyl)sulfonyl]acetate **1**, substituted aromatic aldehydes **2** and amines. The compounds were evaluated for their in vitro antibacterial activity against Mycobacterium tuberculosis H37Rv (MTB), multi-drug resistant tuberculosis (MDR-TB) and mycobacterium smegmatis using agar solutuion method. Ethyl 6-(4-chlorobenzoyl)-3,5-di(4-nitrophenyl)-1,1-dioxo-1,4-thiazinane-2-carboxylate was found to be the most promising compound (MIC: 0.4 μM) active against MTB and MDR-TB.



In vitro Anti Cancer Activity of Siddha Drug Shapthajala in Different Cell Lines

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Cancer is a disease that affects a person not just physically, but psychologically too. The pain involved, the immense cost of treatment and the suffering created are so high that many cases of suicide are reported when the disease is confirmed. Present medical options utilize expensive drugs and treatment is held at a premium. Further, these drugs have a number of side effects making life, living hell. These drawbacks make it necessary to explore alternative treatment options. Siddha drugs are a viable alternative as they remove many of these obstacles. Being of plant origin, they have very few side effects. These drugs when used along with a strict dietary regimen promise excellent results.

The studies carried out on the RD (Rhabdo myosarcoma) VERO Cells (primary monkey kidney) HEP 2 (human epithelial cell line of the larynx) drugs, Shapthajala (liquid) have confirmed its anti-tumor and anti-proliferative activity by the method of MTT Assay for cell viability and Cytotoxicity Assay. A suitable dilution level exists between the cytotoxic activities of the drug on normal and cancerous cells, which can be utilized for formulating the drug's dosage. The drug being a formulation and not just a single compound has the ability to induce cell death in a number of pathways. Further study is thus required to confirm their mechanism of action on the cancer cells.

Antibacterial Activity of Partially Purified Leaf Extract of *Acacia senegal* Collected from Regions Near to Pilani.

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The Indian Thar Desert, has specific characteristics with respect to endemic and medicinal plants. There are about 200 species of plants with recognized medicinal uses in the desert, some of them include *Commiphora wightii, Withania somnifera* and *Urginia indica* The medicinal usefulness of others is yet to be established. Extracts of many plants like *Calotropis procera, Tecomella undulata, Acacia senegal* have been used by local people for the treatment of various diseases, but the active ingredients present in most of the medicinal plants have not been characterized. Currently the research aims at screening plants of desert origin for antibacterial compounds. Seven plants, which include *Calotrpis procera, Acacia senegal, Acacia nilotica, Salvadora persica, Prosopis cineraria, Calligonm polygonoides* and *Aloe vera* were collected from regions near to Pilani (Rajasthan) and screened for their antibacterial activity by disc diffusion method. Highest antibacterial activity was demonstrated by *Acacia senegal* and Acacia nilotica followed by Aloe vera. Ethanolic extract of *Acacia senegal* showing highest activity was purified further by solvent extraction method and then by column chromatography using silica gel of mesh size 60/120 and mobile phase comprising butanol and methanol mixture. Thin layer chromatography on silica plates was done after each purification step to confirm the level of purity. Similarly bioautography study was also done to localize antibacterial activity on the chromatogram.

Comparison of Elemental Concentration of Normal Uterus and Uterus Fibroids by Neutron Activation Analysis

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Occupational and environmental exposure to large amount of toxic and non toxic elements may pose both short- term and long-term health risks. The present work involves evaluation of these trace elements in Uterus and Uterus fibroids employing Neutron Activation Analysis.

Fibroids (myomas) are noncancerous growths in or on the uterus. There are different types of fibroids namely Submucous, Intramural, Subserous and Pedunculated myoma.

Samples of normal uterus and uterus fibroids were collected directly from the operation table of various hospitals, into pre-treated vials. Vials were stored at -10°C to -70˚C. The tissue samples were dried by lyophilization and ground to a fine powder using agate mortar and pestle. The samples and the certified reference materials/ elemental standards were then packed in polyethene and sealed. The samples and standards were co-irradiated for short and long durations in different reactors at BARC (having different neutron flux) for short and medium or long lived nuclides. The activity of the desired isotopes was determined by counting the samples and the standards at their respective photopeaks on HPGe detector. The concentration of the elements was found out by relative method and compared with the normal uterus values. There was a variation noticed in concentration of trace elements like Sc, Mn, K, Fe, Br and Zn in uterus and uterus fibroids.

This work will help in evaluating the carcinogenic potential of trace elements in uterus. This work will also provoke to search the sources of hazardous chemicals and metals and research on effective remediation for them.

8-Azastetoid Structural Motifs: Synthesis and Stereochemical Investigation on Substituted Perhydro-1-quinolinol and Perhydrocyclopenta[*b*]pyridin-1-ol

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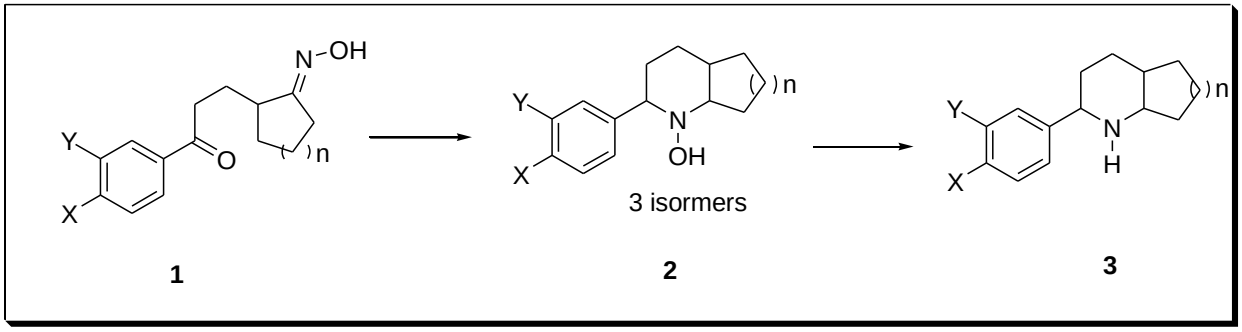
Hydroxylamines derived from secondary amines find use in the synthesis of nitrones and nirtroxides, applicable in 1,3-dipolar cycloaddition reaction. They are also used as bioantioxidants, spin-traps and in magnetic resonance imaging. Moreover, hydroxylamines, in general, exhibit enhanced biological activity compared to free amines. We became interested in the studies on hydroxylamines incorporated into 8-azasteroidal framework. Reduction of the mono-oxime **1,** from 1,5-diketones, with sodium borohdride/AcOH conveniently provided cyclic hydroxylamines **2**, that fit into 8-azasteroidal framework. Thus, a non-chiral mono-oxime **1** from 1,5-diketone was efficiently transformed in stereoselective manner to two sets of three isomeric cyclic perhydro-1-quinolinol and perhydrocyclopenta[*b*]pyridin-1-ol **2**. The structure and stereochemistry of **2** was assigned on the basis of extensive application of NMR spectroscopic techniques and X-ray crystal structure analysis. Reduction of hydroxylamine **2** with H_2/Pd/C provided corresponding secondary amines **3**. Both hydroxylamines **2** and free – secondary amines **3** fit into the enzyme fragments derived from acetylcholine receptor-ion channels. Details of synthesis, stereochemical assignments and QSAR studies will be presented in the symposium.



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3D- QSAR Studies of AcetylCholine Esterase (AChE) Inhibitors for the Treatment of Alzheimer's Disease

Shailendra S. Chaudhaery, Anshuman Dixit and Anil K. Saxena
Medicinal and Process Chemistry Division, Central Drug Research Institute,
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Alzheimer's disease (AD) is an irreversible, progressive disorder in which brain cells (neurons) deteriorate resulting in the loss of cognitive function. The two most significant physical findings in the cells of brains affected by Alzheimer's disease are neuritic plaques and neurofibrillary tangles. One possible approach to treat this disease is to restore acetylcholine levels by inhibiting acetylcholinesterase (AChE) with reversible inhibitors [1,2,3,4]. These Acetylcholinesterase inhibitors (AChEI) include tacrine [5], donepezil [6], galanthamine [7] and rivastigmine [8], which have been shown to induce a moderate improvement in memory and cognitive function but do not appear to prevent or slow the progressive neuro-degeneration. Hence, the systematic QSAR studies (CoMFA and CoMSIA) [12] have been carried out on a series of 1,2,3,4 tetrahydroisoquinoline [9] and meta Carbamate derivatives[10] in order to identify the essential structural features of AChE inhibitory activity. A pharmacophore model for AchE inhibitors was selected on the basis of highest ranking in HipHop module of Catalyst [11]. This model contained one hydrophobic, three hydrogen bond acceptors, two ring aromatic and one positive ionizable feature. All the compounds in dataset were aligned onto this model and this alignment was used to generate CoMFA and CoMSIA models. The satisfactory models were obtained with LOO q^2=0.50, r^2 = 0.904, $r^2_{predictive}$= 0.57; q^2= 0.60, r^2=0.89, $r^2_{predictive}$= 0.65 for CoMFA and CoMSIA models respectively. The derived contour maps revealed that steric, electrostatic, hydrophobicity, hydrogen bond acceptor features are important for AChE inhibition activity. It is also pertinent to note that the CoMFA and CoMSIA results are in strong agreement with each other and with pharmacophore model. Thus the generated 3D-QSAR models may be useful for the design of new potent AChE inhibitors.

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Microwave Assisted Rapid Synthesis of 1-Alkylated-2-thiohydantoin and Arylmethylene-2-thiohydantoins using easily Accessible N-Alkylglycine Ethyl ester

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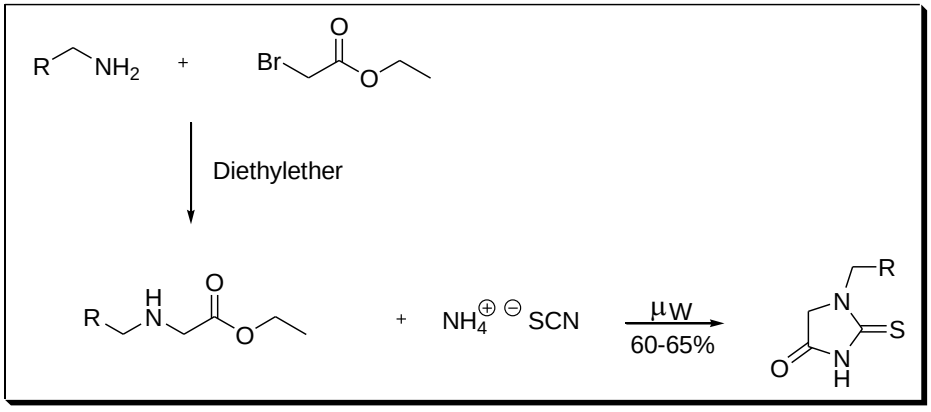
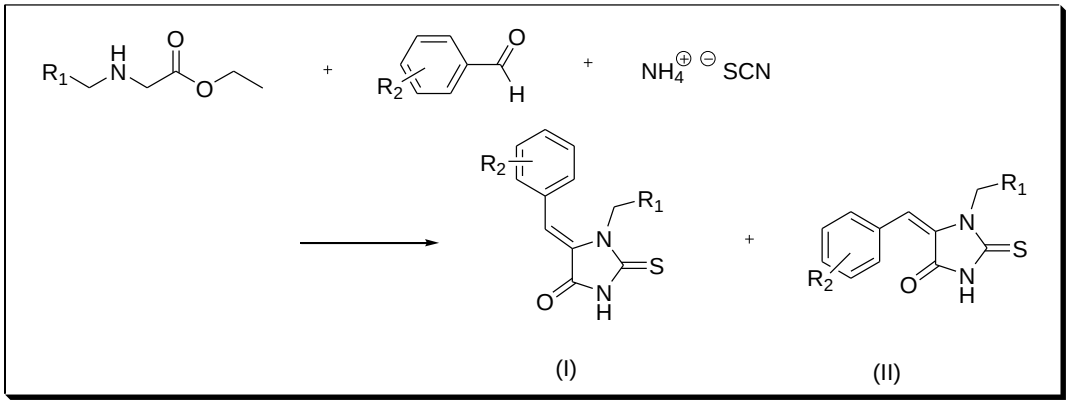
Depending on the nature of substitution, hydantoin ring posses a number of pharmacological properties, e.g. fungicidal, herbicidal, antitumor, antiinflamatory, anti HIV, hypolipidemic, and antihypertensive activities. In our program of synthesis of aplysinopsin analogues to generate lead for antimalarial and antileishmanial activity we found it necessary to synthesize 1-alkylated arylmethylenehydantoin derivatives.

We describe here a microwave assisted rapid synthesis of 1-alkylated hydantoin from easily accessible N-alkylatedglycine etyl ester. This protocol avoids tedious synthesis of N-alkylated glycines and their time consuming cyclization through fusion.



Scheme 1

Above reaction can be extended to combinatorial generation of library of 1-alkylated arylmethylene-2-thiohydantoin.



Scheme 2

Microwave Mediated Synthesis of Fluorine Containing Bioactive Spiro-(indoline-isoxazolidines)

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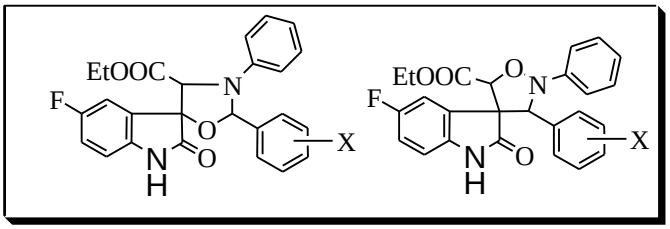
The 1,3-dipolar cycloaddition of nitrones with alkenes has received considerable attention over the past few years in the synthesis of isoxazolidines. Isoxazolidines belong to an important class of heterocyclic compounds having a wider range of biological activities. They are known to possess anti-inflammatory, antiviral and antifungal activities [1,2]. Recently, a number of publications and reviews have advocated the use of microwave technology in organic synthesis [3]. Microwave radiation generally results in enhanced reaction rates and higher product yields as compared to those by conventional heating.

In view of above, we have earlier investigated the reaction of indolylidene acetate with a series of nitrones yielding a large number of novel isomeric spiro-(indoline-isoxazolidines) in a one pot reaction sequence using environmentally benign microwave technology [4].The compounds showed good antitubercular and anti-invasive activities.

In continuation of our previously reported work, we have now synthesized novel fluorine containing analogues of regioisomeric spiro-(indoline-isoxazolidines) in moderate yields by the microwave mediated cycloaddition reaction between ethyl(5-fluoro-3-indolylidene) acetate and various substituted α,N-diphenylnitrones. The synthesized compounds were found very potent in inhibiting TNF-α induced expression of ICAM-1.



Detailed results will be presented in the symposium.

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Protective Effect of *Emblica officinalis* Seed against STZ Induced Oxidative Stress

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The oxidative stress is a crucial etiological factor implicated in several chronic human diseases such as diabetes mellitus, cancer, atherosclerosis, arthritis and neurodegenerative diseases and also in the ageing process [1,2]. The present study is an extension of our previous research work [3]. The aim of study was to determine the effect of the extract of seed from *E. officinalis* on antioxidant enzymes and osmotic fragility of erythrocytes membrane in normal as well as STZ induced severely diabetic albino Wister rats. The results revealed that the untreated diabetic rats exhibited increase in oxidative stress as indicated by significantly diminished activities of free radical scavenging enzymes such as catalase (CAT) and superoxide dismutase (SOD) by 37.5%, ($p<0.001$) and 18.6%, ($p<0.01$), respectively. However, the *E. officinalis* seed extract treatment showed marked improvements in CAT and SOD activities by 47.09% ($p<0.001$) and 21.61% ($p<0.001$), respectively. The enhanced lipid peroxidation (LPO) by 30.87% ($p<0.001$) in erythrocytes of untreated diabetic rats was significantly accentuated in the extract treated animals by 23.72% ($p<0.001$). The erythrocytes showed increased osmotic fragility due to diabetes in terms of hemolysis. It attained the normal level in diabetic treated group. The findings thus suggest that the *E. officinalis* seed extract has the potential to be exploited as an agent to boost the antioxidant system in the diabetic animal model.

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Analysis of Dihydrofolate Reductase (DHFR) and Dihydropteroate Synthase (DHPS) genes in P. falciparum and P. vivax from Bikaner, Rajasthan

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Malaria remains one of the most prevalent infectious diseases. More than 800 million cases with 2-3 million consequent deaths are estimated to occur annually. The goal of eradicating malaria has received a major setback due to the development of resistance to the various drug regimens used to treat the disease. Due to increased resistance, a regular monitoring in the field is required for effective malaria control strategies. With the parasite becoming resistant to chloroquine, in many countries, pyrimethamine - sulphadoxine combination is used as a first line antimalarial treatment for *P.falciparum* and can be used against *P.vivax* as both have the same target enzyme.

For checking the pattern of pyrimethamine - sulphadoxine resistance, *dhfr* and *dhps* genes were sequenced and analysed. Although DHFR and DHPS mutations have been described separately for *P.vivax* and *P. falciparum* from various countries, there are no reports showing both DHFR and DHPS from the same region at a given time point. This study is an effort to predict the profile of the cross species effect of antifolate treatment of the parasites in population of Bikaner, Rajasthan, India, where unstable episodes of *P. vivax* and *P. falciparum* malaria are seen after every rainy season. The data was evaluated on the basis of reported mutations as well as checked for any novel mutation. Different resistance patterns were seen for both the drugs. Both single and double mutations were seen in DHFR genes for the parasite. Both DHFR and DHPS genes showed variations in the repeat region along with some novel changes.

Studies in Synthesis of Substituted Piperidine Carboxamide Derivatives as Potent Antipsychotic Agents

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The term psychosis is categorized as a group of mental disorders, which are considered to be endogenous in origin. The most important types of psychosis are schizophrenia, affective disorders and organic psychosis. Schizophrenia is a devastating mental disorder that affects about 1% of the human population worldwide. Over the last decade basic and clinical research has considerably increased the understanding of the pathophysiology of schizophrenia, as well as the mechanism of action of antipsychotic agents. However, the pharmacological intervention does not effectively treat all the symptoms of the disease, and there is still a need for new, more effective antipsychotic compounds.

The substituted benzamides are used clinically both as antipsychotics and as stimulants of gastric motility. Clebopride is a substituted benzamide that although marketed for its stimulatory effect on gastric motility, is also a potent central dopamine antagonist. It is seen that the corresponding anilide, lacked the gastric stimulatory activity while retaining the potent central dopamine antagonist activity. This indicates that anilide analogs would be specific antipsychotic agents in comparison to the corresponding benzamide analogs.

The present work is concerned with the synthesis of N-substituted piperidine carboxamide derivatives taking clebopride as a lead molecule. We aim to alter the benzamide function to benzanilide for achieving better selectivity & biological profile. In attempt to increase antidopaminergic activity of clebopride, a series of substituted benzanilide, with N-substituted piperidine nucleus were prepared. Final compounds were recrystallized and structures of compounds are confirmed by IR and ^{1}H NMR spectroscopy.

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Distribution of Serine/Threonine Protein Kinase Genes in Pathogenic and Non-Pathogenic Mycobacteria

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Signal-transduction pathways in both prokaryotes and eukaryotes often utilize protein phosphorylation as a molecular switch in regulating different cellular activities such as adaptation and differentiation, immune response and cell division. The *Mycobacterium tuberculosis* genome encodes 11 eukaryotic-like serine/threonine kinases. Out of these, nine kinases (pKnA, pKnB, pKnD, pKnE, pKnF, pKnH, pKnI, pKnJ, pKnL) are predicted to be transmembrane proteins and two (pKnG and pKnK) kinases lack such transmembrane region. In this study we have looked for the presence and the absence of these kinases in different pathogenic and non-pathogenic mycobacteria (*M. tuberculosis* H37Rv, *M. tuberculosis* H37Ra, *M. bovis* BCG, *M. fortuitum*, *M. gilvum*, *M. smegmatis*, *M. aurum*, *M. habana*, *M avium* and *M. asiaticum*). Primers specific to STPKs genes were designed from the genome sequence of *M. tuberculosis* H37Rv and have been used to PCR amplify homologous genes using genomic DNAs of all the mycobacterial species as template. The PCR product profile has shown significant differences between pathogenic and non-pathogenic mycobacteria. These genes were further blasted for the comparative polymorphism. The data have shown that the partial homology of most of the serine-threonine kinase could be observed among the species, however full length genes were found to be species specific. A further study with the phylogeny of these kinases in mycobacteria is underway and would be discussed during the meeting.

Topological Descriptors in Modelling the Antimalarial Activity: N^1-(7-Chloro-4-Quinolyl)-1,4-Bis(3-Aminopropyl)Piperazine as Prototype

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Malaria, the most deadly parasitic disease continues to engulf millions of people in the tropical and subtropical regions of the world; reemergence of resistance strain fostered the interest in the development of antimalarial activity. The QSAR of antimalarial activity of two distinct N^1-(7-chloro-4-quinolyl)-1,4-bis(3-aminopropyl) piperazine analogues are investigated with DRAGON descriptors in order to rationalize their activity. Of these two series of compounds, one is embedded with amide characteristics and the other is with that of amine characteristics. Both the analogues have shared the radial centric information (ICR) as common modelling descriptor with increased centricity in the molecules as preferred feature for antimalarial activity. Apart from this, the models of amide analogues have suggested in favor of distantly placed nitrogen(s) and unfavorable nature of carbonyl moieties adjacent to nitrogen in the varying portion of the molecule for the activity. Moreover, for these analogues, the regression models have preferred the lone pair electrons on heteroatoms (N and O) for purposes other than H-bonds for better activity. In case of amine analogues, the models have suggested in favor of compact structural moieties in the varying parts of the molecule for improved activity. Also, for these analogues, hydrophobicity of the compound is an important factor for influencing the activity. The variations in the models of amide and amine analogues are attributed to the characteristic functional differences of these analogues. The methodical approach to get hold of these results will be presented in detail.

To Understand the Multiple Drug Resistance in Viruses with the Help of Phylogenetic Profiling and Finding Novel Drug Targets for Antiviral Therapy

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Till date 2396 viral genome are completely sequenced, but biggest challenge in front of computational biologists is the functional annotation of viral proteins and understanding the complex molecular mechanisms of viral.

Pathogenic viruses have two key features – Short generation time, and high mutation rate in our living system, so that they intelligently find the way to invade our immune system. In case of HIV type 1 genomes have been phylogenetically divided into three main groups, M, O and N.The most widespread viruses of Group M have been further divided into nine distinct subtypes, A-D, F-H, J and K, and into 11 circulating recombinant forms (CRFs). Every day it produces 10 billion progenies in our system and each progeny DNA undergoes certain variation, which helps HIV to discover new strategies to infect neighboring cells in our body.

Our main aim is to perform high throughput screening of proteome sets of viruses and find the functionally co-related proteins, which evolved simultaneously during the evolutionary process. Following this, we will study specific functionally co-related viral proteins. We are using phylogenetic profiling [1,2] and machine learning methods for that purpose.

After obtaining results from the previously described technique, we will do extensive analysis for two co-related concerns – Immune evading mechanisms and multiple drug resistance in viruses, at genomic as well as proteomic level. Central focus of our study is the role of evolution to create variation among viral progeny and find out the novel target site for antiviral drugs.

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Phytochemical Screening and Antimicrobial Activity of the Extracts from the Sida Rombifolia Linn

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The petroleum ether(C_2H_5-O-C_2H_5), chloroform($CHCl_3$), and ethylacetate(CH_3-CO-O-C_2H_5) extracts of Sida Rombifolia leaves & stem were studied for antimicrobial activity against the both, Gram positive (Bacillus subtilis, Bacillus megaterium, Staphylococcusaureus, Sarcina lutea) and Gram negative (Escherichia coli, Klebsillea species, Pseudomonas aeruginosa, Shigella shiga) micro–organism. The zones of inhibition produced by the test materials were found to be between 9 to 24 mm. phytochemical screening of the extracts indicated the presence of alkaloids, steroids, triterpenoids, tannins, flavonoids, carbohydrates and absence of cardiac glycosides**.**

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5,7-Dihydroxy-6,8,4'-trimethoxyflavone: A Potent Antibacterial Agent

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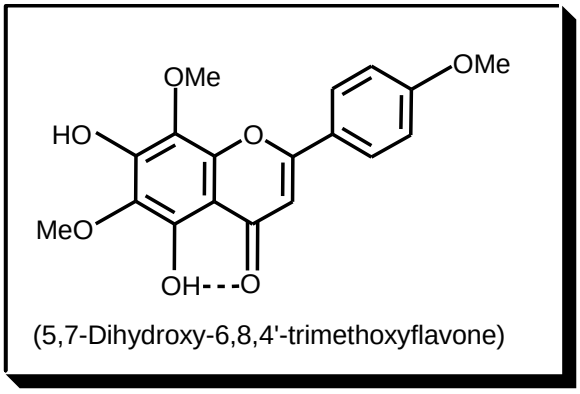
At the present scenario of drug research, bioflavonoids are being considered as useful and promising leads due to their potentials to exhibit a wide range of biological activities [1,2]. A multidirectional therapeutic uses of vast number of plant species in traditional medicine systems are known for thousands of years in many countries including India. In this new millennium, it may be urged that interest in herbal medicines and natural products in general is at an all time high. This phenomenon has been mirrored by an increasing attention to phytomedicines as form of alterative therapy by the health professions.

In continuation of our works on medicinal plants, we have found *Limnophila heterophylla* (a locally available important Indian medicinal plant; family: Scrophulariaceae) [3] as new and rich source for 5,7-dihydroxy-6,8,4'-trimethoxyflavone — a well-known natural bioactive flavonoid [4]. The petrol extract of the air-dried plant materials (aerial parts and roots) afforded the flavonoid characterized on the basis of detailed spectral studies (UV, IR, PMR, CMR, 2D-NMR, EIMS). Our studies revealed the significant antibacterial efficacies of the flavonoid against some bacterial strains, very particularly against the Gram-negative *Escherichia coli* MTCC68. It showed a strong cidal effect on the microorganism; the rate of growth of *E. coli* as well as the morphological change by bursting of cells as revealed by scanning electron microscopy on application of MIC dose of the compound clearly indicated its bacteriocidal nature rather than its bacteriostatic mode of action. Reduction in number of colony forming units (CFU) was also observed in the treated culture of *E. coli*.



(5,7-Dihydroxy-6,8,4'-trimethoxyflavone)

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Prediction of MHC Class Binding Nonamers from *Soybean mosaic virus*

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The potyvirus coat protein (CP) is involved in aphid transmission, cell-to-cell movement and virus assembly, not only by binding to viral RNA, but also by self-interaction or interactions with other factors [1]. Aphids are the vectors that spread the disease during a growing season. Sometimes, portions of the soybean seed coat have a black discoloration as a result of infection by Soybean mosaic virus (SMV). Peptide fragments of genome polyprotein can be used to select nonamers for use in rational vaccine design and to increase the understanding of roles of the immune system in infectious diseases [2]. Analysis shows MHC class II binding peptides of coat protein from SMV are important determinant for protection of many plants form viral infection. In this assay we predicted the binding affinity of SMV genome polyprotein having 3178 amino acids, which shows 3171 nonamers. In this analysis, we found the MHCII-IAb peptide regions 992-YKTAKDLLT, 2689-PILAPDGTI, 1550-KVTKVDGRT, 2759-TWLYDTLST, (optimal score is 1.506); MHCII-IAd peptide regions 2191-GSFIITNGH, 2023-FIHLYGVEP, 1418-GSSNIVVMT, 807-AAYMLTVFH, (optimal score is 0.893); MHCII-IAg7 peptide regions 3074-SDAAEAYIE, 24-EINANIANI, 3003-WYNAVKDEY, 1656-FIATEAAFL (optimal score is 1.915); MHCII- RT1.B peptide regions 1226-KTATQLQLE, 525-STAENASLQ, 274-TKERRATSQ, 1224-QAKTATQLQ, (optimal score is 1.807); which are represent predicted binders from genome polyprotein. These peptides are from a set of aligned peptides known to bind to a given MHC molecule as the predictor of MHC-peptide binding. MHCII molecules bind peptides in similar yet different modes and alignments of MHCII-ligands were obtained to be consistent with the binding mode of the peptides to their MHC class, this means the increase in affinity of MHC binding peptides may result in enhancement of immunogenicity of coat protein nonamers [3, 4]. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from Soybean mosaic virus [5].

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The Efficacy of Novel Benzimidazoles Drugs against *Plasmodium falciparum in vitro*

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Compounds with the structure of -C=N- (azomethine group) are known as Schiff bases, which are usually synthesized from the condensation of primary amines and active carbonyl groups. Schiff bases are an important class of compounds in medicinal and pharmaceutical field. They show biological activities including anti-microbial and anti-malarial activity. Similarly benzimidazoles derivatives have been used for a long time for a variety of biological activities such as CNS depressant, anti cancerous, antibiotic, antihistaminic, anticonvulsants and many others.

The sensitivities *in vitro* of *Plasmodium falciparum* to the benzimidazoles (fully characterized through spectroscopic methods) were investigated and compared to those of the commonly used ant malarial drugs chloroquine and quinine. Quinine and chloroquine were the most potent drugs tested (EC_{50} values of 8×10^{-9}–6×10^{-8} mol/L and 5–7×10^{-9} mol/L, respectively). The activity of glyoxal derivatives was found pH dependent, as was that of chloroquine, and variable. Given the variable activity of pyridine based schiff base analogues and its rapid metabolism *in vivo* into compounds through biodistribution and blood kinetics study, it appears unlikely that this benzimidazoles will be useful in the treatment of malaria. The rapid activity and different stage-specific profile of the more soluble benzimidazoles requires further investigation

Isoniazid Induced Oxidative Stress Causes Apoptosis in Hep G2 Cells by Altering Bcl2 Expression

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Isoniazid (INH) introduced in 1950s, continues to be the drug of choice in the chemoprophylaxis and treatment of tuberculosis however it has a serious limitation of being hepatotoxic. Delineating the mechanism underlying INH induced hepatotoxicity may be beneficial in devising ways to counteract toxic manifestations. Attempts have been made in this direction using various *in vivo* and *in vitro* test systems. In the present study Hep G2 cells have been used as a test system to elucidate INH induced hepatotoxicity mechanisms. Being hepatoma cell line of human origin this cell line displays many genotypic and phenotypic characters of normal human liver cells and thus it is better test system in terms of resemblance to humans. Previous studies indicated that INH exposure causes induction of apoptosis in Hep G2 cells. The present study was conducted with an aim to identify the key components/pathways of the INH induced apoptotic pathway in Hep G2 cells. Results indicated that INH exposure causes increased ROS generation along with alteration in levels of enzymatic antioxidants such as Superoxide dismutase, Catalase and Glucose-6-Phosphate dehydrogenase. Altered Bcl2/Bax ratio and characteristic DNA fragmentation emphasized involvement of apoptosis as a mediator of toxicity. We observed that there was considerable translocation of cytochrome-c from mitochondria to cytosol indicating loss of mitochondrial integrity and permeability. In addition to this, increased initiator and effector caspase activity were observed. Results indicated that INH induced aopotosis in Hep G2 cells involves disruption of delicate pro-apoptotic/anti-apoptotic regulators in the favour of pro-poptotic proteins. Collectively these results led us to conclude that INH induced apoptosis in Hep G2 cells was being mediated through intrinsic pathway that involves mitochondria as a central component.

One-into-Many Model: An Approach on DFT Based Reactivity Descriptor to Predict the Regioselectivity of Large Systems

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The present work consists of the development of a new model (named as "one-into-many") to predict the regioselectivity of large chemical and biological systems. Large chemical and biological systems with multiple reactive sites are proposed to be broken into small fragments having at least one reactive site in each fragment. The environment around each reactive site is mimicked by incorporating some buffer zone. Local reactivity descriptor (i.e., local hardness), originally proposed by Berkowitz *et al.*[1] and later on implemented by Langenaeker *et al.*[2], is evaluated for each reactive site adopting a new modified approach (i.e., without neglecting kinetic energy and exchange energy parts). When the model is applied to predict the regioselectivity (towards an electrophilic attack on it) of the base-pairs in DNA (PDB ID: 1BNA)[3] the generated results are found to be satisfactory in most cases.

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Synthesis of Biodegradable Nanoshells for Target Specific Use in Living Beings

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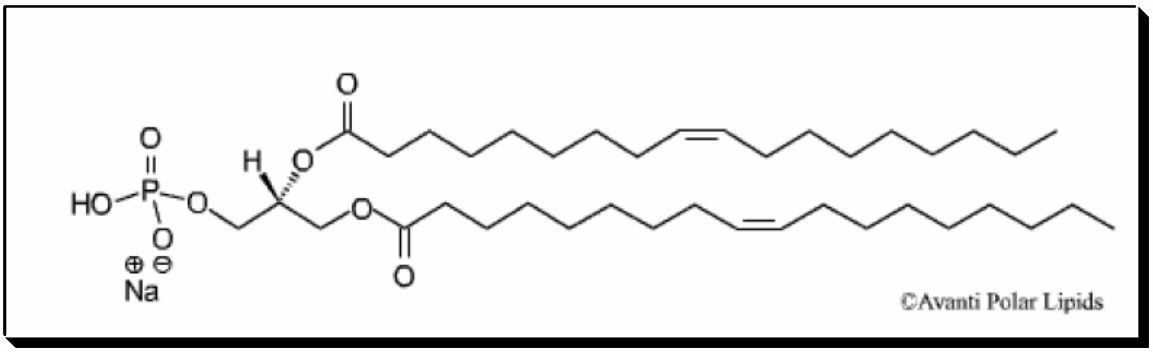
The field of nanotechnology has interspersed use in various fields. In this paper we synthesize calcium phosphate nanoshells with DOPA, phosphocholine compound forming the inner core. This chemical is preferred for the synthesis because it is having an overall negative charge and hence binds well with the calcium phosphate outer layer. Calcium Phosphate is used for preparing the outer core since it is very rigid and is present in the body and performs various functions in the body. The various processes involved in the synthesis are mixing, sonication, one step synthesis and multistep saturation synthesis. The core is imbibed with ginkgo biloba extract which is a high antioxidant supplier and reduces the free radicals concentration of the body. These nanoshells can be efficiently used for the treatment of Alzheimer's disease. This disease is mainly caused due to excessive production of free radicals. These nanoshells are approximately of 100 nm hence it can pass through the blood brain barrier and effectively work for the treatment of Alzheimer's disease. There are few molecules like tau proteins and beta amyloid plague proteins which can be adhered to the nanoshell and directed to the brain.
DOPA-1, 2-dioleoyl –sn-glycero-3phosphate



Hybrid Macrocyclic Receptors Based on Lower Rim Functionalised Thiacalix[4]arene and Amino acids: Synthesis, Structure and Binding Properties

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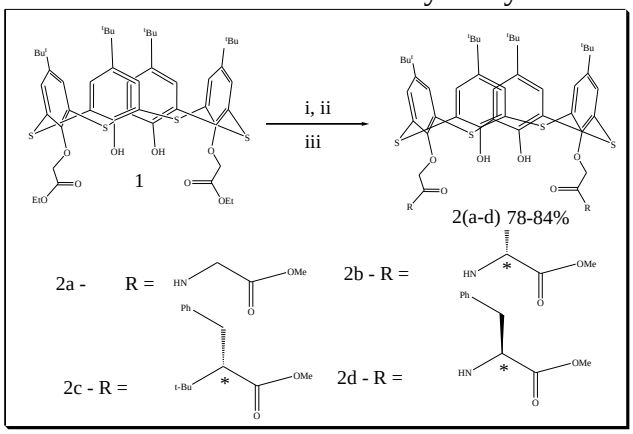
Hybrid macrocyclic receptors as characterized by the simultaneous presence of different binding groups, for example:-polar groups and hydrophobic groups which cooperates in recognition, are receiving much attention in supramolecular chemistry. [1] Calixarenes [2] have been extensively studied in recent years as topological templates in combination with amino acids or peptides as organizational elements for the complexation of sugars, amino acids and anions. Thiacalixarenes [3] have recently appeared as new members of the calixarene family. Thiacalix [4]arenes exhibit a broad range of interesting functions such as different size and conformational behavior, different complexation ability, easy oxidation of -S- bridges etc., which make them good candidates for many applications in supramolecular chemistry. Amino acids play an important role in several recognition processes of natural and artificial systems, [4] in chiral discrimination and stereoselective synthesis.

Thiacalixarenes bearing amino acid moieties were prepared by the reaction of carboxyl protected amino acid with the acid chlorides of O-carboxymethylthiacalix[4]arenes.



Scheme 1. Synthetic pathways for hybrid receptors 2(a-d) Reagents and conditions: (i) KOH/H_2O, Δ, HCl, 5 h. (ii) $(COCl)_2$, CCl_4, Δ, 3 h. (iii) 4 equiv. amino acid methyl ester hydrochloride, Et_3N/CH_2Cl_2, 0 °C – rt, 3 h.

The binding ability of these hybrid receptors towards neutral molecules, anions and cations were investigated. These new receptors showed selective binding towards Hg^{2+}ions, which increased in the order 2c< 2b< 2d< 2a. The details of the binding studies will be presented.

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Synthesis of Some 3-(Arylideneamino)-2-Phenylquinazolin-4(3H)-ones and QSAR Study Based on their Antibacterial Activity

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Some 3-(Arylideneamino)-2-phenylquinazolin-4(3H)-ones are synthesized. The compounds contained a common phenyl group at the 2-position, while the substituents on the arylideneamino group were varied. Antibacterial activity of quinazolones were studied against both Gram-positive (*Staphylococcus aureus* 6571and *Bacillus subtilis*) and Gram-negative bacteria (*Escherichia coli* K12 and *Shigella dysenteriae* 6. It was observed that incorporation of 3-arylideneamino substituent enhanced the anti-bacterial activity of the quinazolone system. Some selectivity of antibacterial effect on Gram-Positive and Gram-Negative type of bacteria was also noted. The compounds were also tested against antibiotic resistance bacteria. The QSAR studies indicated that low solubility is the major hindrance to achieve lower MIC values.
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Synthesis and Biological Evaluation of Novel Pyrimidines

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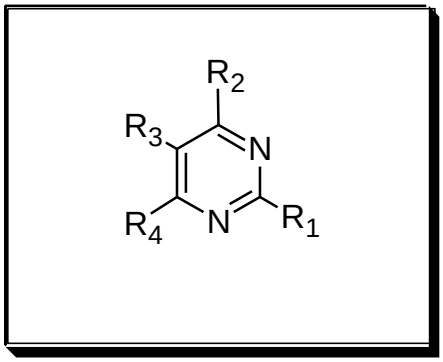
The key biochemical signal transduction pathways and transcription proteins have been explored and targeted to modulate the expression of the inflammatory proteins. One such protein that is highly expressed and plays a critical role in the pathogenic mechanisms of a number of chronic inflammatory conditions such as RA (rheumatoid arthritis), IBD (inflammatory bowel disease) and psoraisis (1) is the Tumor Necrosis Factor (TNF-α). From the discovery perspective, biological drugs targeting TNF-α have demonstrated to be effective in the treatments of patients with RA, IBD and psoriasis. Due to their potential adverse effects (1), developing orally active, small molecules that target TNF-α pose a great challenge. Herein we report the synthesis and biological activity of a series of pyrimidine analogs.



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Highly Efficient and selective Enzymatic Acylation: Separation of the Furanosyl and Pyranosyl Nucleosides

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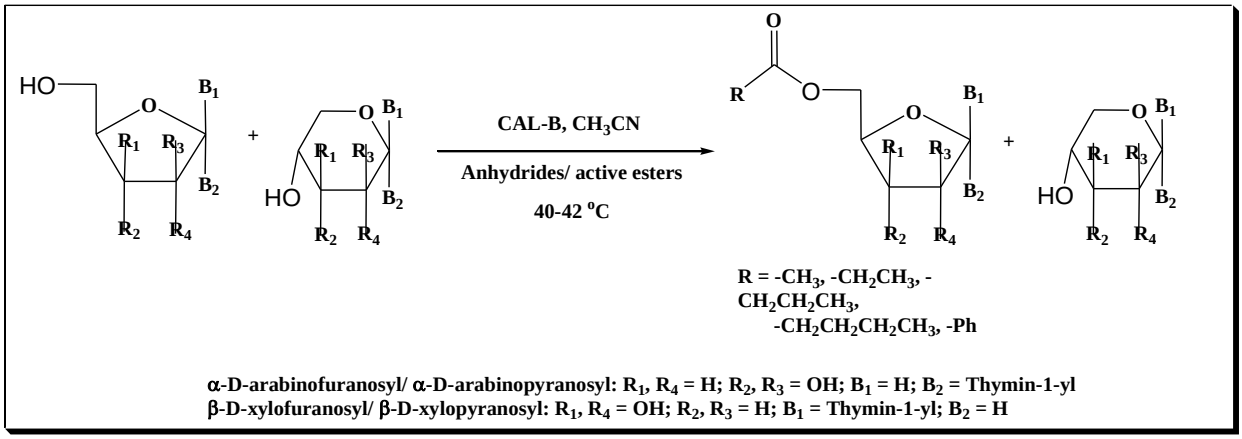
Modified nucleosides of arabinofuranosyl moiety have attracted much attention as antiviral, anticancer, antimicrobial, antitumor, anti-DNA viral, anti-hepatitis B virus agents. Arabinonucleosides with pyranosyl configuration have been used as nucleoside monomer in oligonucleotides synthesis for the evaluation of their importance in etiology of nucleic acid structure.



Scheme 1

Candida antarctica lipase-B immobilized on lewitite regioselectively acylated the primary hydroxyl group of the furanosyl nucleoside from a mixture of 1-(α-D-arabinofuranosyl)thymine and 1-(α-D-arabinopyranosyl)thymine. This selective biocatalytic acylation of furanosyl nucleoside has enabled us an easy separation of arabinofuranosyl thymine from an inseparable mixture with arabinopyranosyl thymine. Same methodology has also been successfully used for the separation of 1-(β-D-xylofuranosyl)thymine and 1-(β-D-xylopyranosyl)thymine from a mixture, which demonstrate the generality of the enzymatic methodology for separation of furanosyl and pyranosyl nucleosides.

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An Improved Chemo-Enzymatic Synthesis of *xylo* Configured Locked Nucleic Acids

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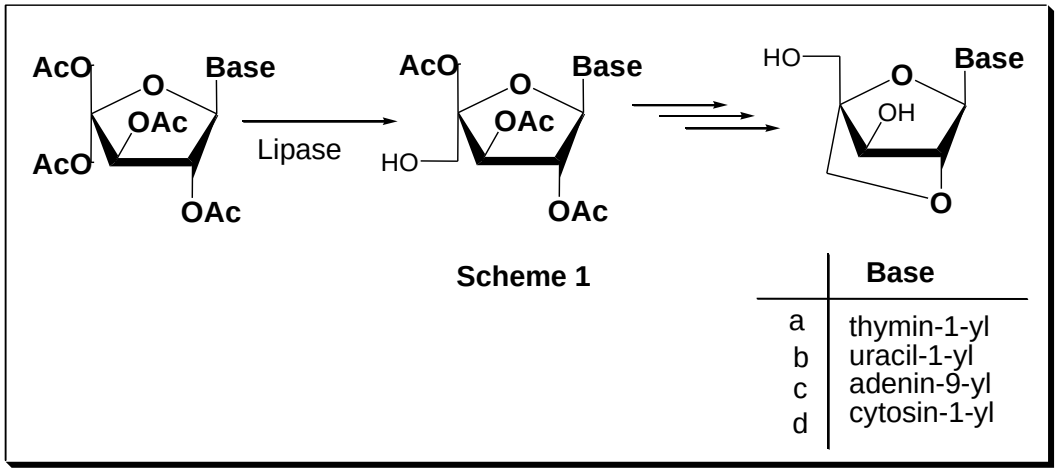
Among the most prominent structures that arise from the survey of the molecules from the nature are the nucleosides. The synthesis of the novel nucleosides analogues has become important because of their applications as therapeutic agents particularly as antiviral and also because of their use as precursor for the synthesis of the modified nucleosides [1]. During the synthesis of the targeted nucleosides and their analogues selective manipulations of the hydroxyl function in the sugar part is highly desired. It is the juncture that nature catalyst "ENZYMES" come into the picture. The use of the enzyme in the synthetic sequences provide unique advantages over the chemical synthesis viz, efficiency, regioselectivity, stereoselectivity and environment friendliness [2-5].

We have used lipases for the daistereoselective deacylation of the 4'-C-acyloxymethyl-2',3',5'-tri-*O*-acyl-*β*-L-threo-pentofuranosylnucleosides, which is an important precursor for the synthesis of the locked nucleic acids [Scheme 1].



Scheme 1

	Base
a	thymin-1-yl
b	uracil-1-yl
c	adenin-9-yl
d	cytosin-1-yl

Detailed results will be presented in the symposium.

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Fluorescence Studies of 1-nitroso-2-naphthol in Surfactant Micelles

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The fluorescence and absorption spectra of 1-nitroso-2-naphthol have been studied in presence of different surfactant solutions at room temperature with special reference to solubilization and micellization. The nonionic surfactants employed were Triton X-100, Tween-80, Tween-40 and the anionic were DBSS, DSSS, SLS and the cationic were CTAB, CPB, CPC. Fluorescence intensity for nonionic surfactants continuously enhanced with 5 to 10 nm red shift in peak position. The red shift in λ_{em} appears to be due to the hydrogen bonding capability of hydroxyl group of the compound to the surfactant micelles. Among nonionic surfactants Triton X-100 showed maximum effect. For anionic surfactants the emission intensity initially decrease and on further addition of surfactants emission intensity was increased, whereas the emission intensity with all cationic surfactants initially showed an enhancement and at higher concentration , a small lowering occurred. The explanation for the result could be that nonionic surfactants form micelles in aqueous solution above the critical micellar concentration (CMC) which increase the solubility of species with hydrophobic nature. Solubilization phenomenon is one of the important properties of micelles industrially as well as biologically. The dual nature of surfactant micelle is responsible for the occurrence of surface activity, solubilization and micellization. The maximum solubilization is attributed with the high absorbance as well as fluorescence intensity and it has also been confirmed by theoretically calculated spectral parameters, like empirical fluorescence coefficient (K_f), quantum yield (Φ_f), molal extinction coefficient (log ε) and Stokes'shift.

Evaluation of Antifungal Activity of *Diospyros kaki* Roots

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Diasoyros Kaki(Ebenaecae) is a small deciduous, monoceious or dioecious tree with a rounded crown, native of northeastern India, and extending to japan. It attains a height of 40-50 ft and a girth of 2-3 ft . It is a valuable sub tropical fruit tree and is cultivated in some parts of India.

MIC of crude ethylacetate extract and plumbagin,isodiospyrin and diospyrin in μg/ml

Fungi	crude	plumbagin	isodiospyrin	diospyrin
Aspergillus flavus	62.5	.78	6.26	12.5
Aspergillus fumigatus	125	1.57	6.26	12.5
Fusarium oxysporum	62.5	1.57	6.26	25
Cryptococcus neoformans	125	3.12	25	50
Soprothrix shenkii	250	1.57	25	50
Trichophyton mentegrophytes	250	1.57	12.5	50
Microsporon gypseum	125	1.57	6.25	12.5
Curvularia lunata	125	.78	12.5	25
Candida krusei	500	1.57	12.5	50
Candida tropicalis	250	1.57	25	50
Candida albicans	250	3.13	25	100
Rhizomucor pussilus	500	6.26	50	100
Pseudaresheria boydii	250	3.13	50	50
Phialophora verrucosa	1000	6.26	100	100

The ethylacetate extract of *Diospyros Kaki* exhibited a wide spectrum of antifungal activity against 14 pathogenic fungi – *Aspergillus flavus*(ITCC 5290),*Aspergillus fumigatus* (ITCC 4880), *Curvularia lunata* (ITCC 5248),

Candida albicans (MTCC 227), *Candida tropicalis* (ATCC 750)and *Candida krusei* (ATCC 6258) , *Fusarium oxysporum* (ITCC4998), *Cryptococcus neoformans* (ITCC 5290) and *Soprothrix shenkii* (ITCC 2317) , *Trichophyton mentegrophytes* (ITCC 3572), *Microsporon gypseum* (ITCC 5277), *Rhizopus pussilus* (W-14), *Pseudaresheria boydii* (W-48), *Phialophora verrucosa* (MCCL 320006) .The bioassay guided fractionation of the crude extract afforde 3 dimeric napthaquinones – plumbagin, isodiospyrin diospyrin. Plumbagin being the most active with MIC ranging from 6.26 μg/ml to 0.78 μg/ml while isodiospyrin and diospyrin also showed remarkably good activity exhibiting MIC from 100 to 6.26 μg/ml to 100 to 12.5 μg/ml respectively. The hyaline fungi on average had lower MIC value against all the three compounds then dematacеous fungi and yeast like fungi exhibiting the highest susceptibility . This is the first report of antifungal activity of isodiospyrin and diospyrin which could be considered as good antifungal agents.

Neuroprosthetics: An Update

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This paper is based on the development, selection, operation and support of neuroprosthetics as a part of biomedical instrumentation. The benefits of a interdisciplinary study that can ensure the safe and effective use of medical technology for the betterment of healthcare system is discussed. The neuroprothetics are broadly classified as follows:

Sensory prosthetics, comprises of visual, auditory, pain relief prosthetics. The researchers now aim to develop a visual prosthetic device which would stimulate the electrode embedded in the LGN (Lateral Geniculate Nucleus), a relay station in the visual pathway. Spinal cord stimulator is used to treat neurological pain using RF wave stimulation.

Motor prosthetics comprises of the heart/brain pacemaker which may be self/ auto/ person regulated depending on the need. Another type is the bionic arm/ limbs for conscious control of movement. Developments continue to feature sensors for detecting pressure and temperature artificially.

Cognitive prosthetics: These try to take over the function of all the different regions of the brain to restore memory and learning. The researchers are exploring the creation of biologically realistic mathematical models of brain function, the production of microchips and the brain function through neuron silicon interfaces termed as *The Blue Brain Project*. There are also developments in the Movable probe technology using MEMS (micro electro mechanical system), that continually and autonomously adjusts the electrode positions in brain for fluid delivery. Brain Machine Interface (BMI) is another example of Neuroprosthetics where the brain talks to the computer and vice-versa. Cortical activity can be modulated voluntarily even years after spinal cord injury based on which a technology was developed which would assist paralyzed person in performing simple day to day activities

Neuroprosthetics are expected to provide a solution for the people with damaged neurological functions. Their use in areas of drug delivery, treatment and human functional enhanzcement has recently been recognized, though its use depends on the cost and their availability to the common man.

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Study on Chitosan-Casein Microparticles for Biomedical Applications

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The sustained release of drug from microparticles is one of the main objectives of drug delivery systems. The successful formulation to control drug release for the required duration of time with optimum release mode depends on various factors, such as the physiochemical properties of the drug, the nature of the drug carrier matrix, the type of dosage form and the route of administration. For this research area, microparticle carrier systems made from the naturally occurring proteins have attracted considerable attention for several years as a matrix for controlled and time bound release delivery of many drugs.

This work entitled "Study on Chitosan-Casein Microparticles for Biomedical Applications" is intended to study the preparation and sustained release of a hydrophilic drug like chloroamphenicol from chitosan-casein through colloidal coacervation technique.

The proposed method can offer a simple technique for microparticle preparation in an aqueous system. The interaction between cationic chitosan and anionic casein solution was the basis of the polymer formation. The microparticle system has been studied by various methods such as FT-IR, morphological, swelling studies and drug release studies in varied pH.

Search for New Bromotyrosine Alkaloids from the Marine Sponge *Psammaplysilla purpurea* using Electrospray ionization-Tandem Mass Spectrometry (ESI-MS/MS)

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Bromotyrosine derivatives from the marine sponge *Psammaplysilla purpurea* have been investigated by electrospray ionization-quadrupole time-of-flight tandem mass spectrometry (ESI-QTOF MS/MS). In the ESI-MS spectra, predominant cluster of pseudomolecular ions in the positive ion have been observed for molecular mass information. Two new bromotyrosine alkaloids, purpurealidin-I and purpurealidin-J along with five known bromotyrosines were identified. The structural information was obtained by performing MS/MS on the precursor ions. The peaks pattern of the fragment ions is inherently related to the number of the bromine atoms on the aromatic ring. Characteristic fragmentation observed suggests the formation of the hydroxyl amine or isoxazole ring moiety in the molecule. Among those diagnostic ions and patterns, a homologous series of characteristic bromine isotope pattern is the most valuable structural indicators. These structural features facililate the rapid identification of the bromotyrosine in *P. purpurea* avoiding tedious separation and also help in detecting similar compounds in a specific genus. These observations suggest that ESI-MS/MS can provide a selective method for the analysis and characterization of bromotyrosine derivatives.

Self-Organizing Molecular Field Analysis on a New Series of Protein Tyrosine Phosphatase 1B (PTP1B) Inhibitors: 1, 2-Naphthoquinone

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Self-organizing molecular field analysis (SOMFA), a simple three-dimensional quantitative structure activity relationship (3D-QSAR) method is used to study the correlation between the molecular properties and the anti-diabetic activities of a new series of 1, 2-Naphthoquinone that acts as selective PTP1B inhibitors**.** Protein tyrosine phosphatase 1B (PTP1B) is an enzyme plays an important role in the negative regulation of insulin signaling and is involved in the insulin resistance associated with Type 2 diabetes. Thus, PTP1B inhibitors could potentially ameliorate insulin resistance and normalize plasma glucose and insulin without inducing hypoglycemia, and could therefore be a major advance in the treatment of Type 2 diabetes. Recently, a new series of 1, 2-naphthoquinone compounds has been reported to selectively inhibit protein tyrosine phosphatase 1B [1] and SOMFA studies has been performed on this series which is divided into training set and test set.

The self-organizing molecular field analysis (SOMFA) method has similarities to both comparative molecular field analysis (CoMFA) and molecular similarity studies [2]. Like CoMFA, a grid-based approach is used; however, no probe interaction energies need to be evaluated. Like the similarity methods, it is the intrinsic molecular properties, such as the molecular shape and electrostatic potential, which are used to develop the QSAR models. SOMFA calculations for both shape and electrostatic potentials were performed, the master grid maps derived from the best model is used to display the contribution of electrostatic potential and shape molecular field. The master grid maps give a direct visual indication of which parts of the compounds differentiate the activities of compounds in the training set under study. The master grid also offers an interpretation as to how to design and synthesize some novel compounds with much higher activities. The statistical results, cross-validated r^2_{CV} and non cross-validated r^2, show a satisfied predictive ability. All analysis of SOMFA model may provide some useful information in the design of new PTP1B inhibitors.

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A Novel and Convenient Synthesis of Naturally Occurring Indolylazoles

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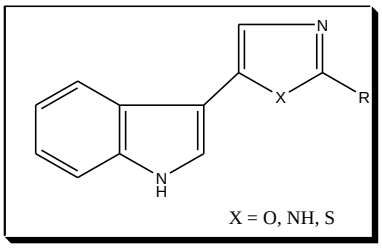
The Indolylazoles are important heterocyclic scaffold of medicinal and therapeutic interests that can be found in various natural products [1]. Various indolylazoles have been isolated from different microorganisms and are known to display interesting biological activities [1]. Most of the reported methods [2] for the syntheses of indolylazoles involve multisteps, toxic and costly reagents, and affords products in moderate yields. In view of immense biological significance of indolylazoles, we have developed a facile and high yielding protocol for the synthesis of variety of indolylazoles from readily available starting materials. The key steps in the synthesis of indolylazoles involve the formation of 3-tosyloxyacetyl-1-benzenesulfonylindole and α-acylaminoketones. Detail syntheses of 5-(3-indolyl)-oxazoles, 5-(3-indolyl)thiazoles, 5-(3-indolyl)imidazoles will be presented in the conference.



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Analytical Investigation of Cisapride, Application of Boyland-Sims Oxidation

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The application of Boyland-Sims Oxidation is described for the determination of Cisapride in pure and the dosage forms. The redox reaction involves the treatment of Cisapride with peroxidisulphate in alkaline medium. A yellow coloured product is obtained on heating which has â max at 308nm.The results obtained are compared with those obtained by reference method and subjected to acute statistical treatment.

Efficient Synthesis of 2-aminothiazoles in Water at Ambient Conditions: A Practical Approach Towards the Synthesis of the Anti-inflammatory Drug Fanetizole

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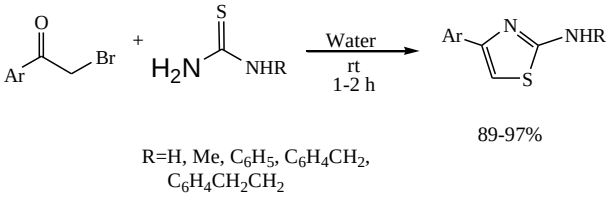
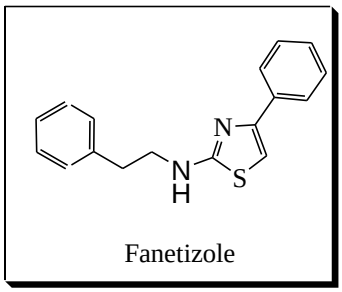
The thiazole ring system is a useful structural motif found in numerous biologically active molecules. The 2-aminothiazoles ring system is a useful structural element in medicinal chemistry having application in drug development for the treatment of allergies, hypertension, inflammation, schizophrenia, bacterial, and HIV infections.[1] Aminothiazoles are known to be ligands of estrogen receptors [2] as well as a novel class of adenosine receptor antagonists.[3]
In view of the importance of thiazole derivatives due to its pharmacological activities, we became interested in its synthesis. We have developed an efficient method for the synthesis of substituted 2-aminothiazole derivatives by condensing aromatic α-bromoketones with thioureas in water. The developed process does not require any added catalyst or co-organic solvent and was carried out at room temperature. Besides this, excellent yields have been achieved.



Scheme 1. Synthesis of 2-aminothiazoles

2-Phenylethylamino-4-phenylthiazole, commonly known as fanetizole is an anti-inflammatory agent that has been reported to have reached phase II clinical trails for the treatment of rheumatoid arthritis.[4] We have applied the developed protocol for the synthesis of fanetizole and its other analogue.



Fanetizole

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Oxidation of Ranitidine Drug by Diperiodatocuprate(III) in Aqueous Alkaline Medium

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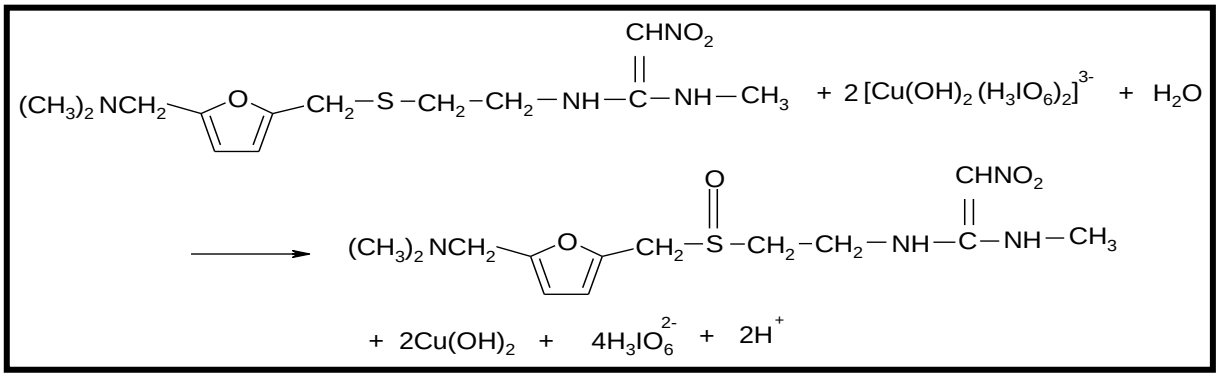
The kinetics of oxidation of anti-ulcer drug, ranitidine hydrochloride(RNH) by diperiodatocuprate(III) (DPC) in alkaline medium at a constant ionic strength of 0.24 mol dm^{-3} was studied spectrophotometrically. The reaction between DPC and ranitidine in alkaline medium exhibits 1:2 stoichiometry (ranitidine: DPC) is given below. The reaction is of first order in DPC and has less than unit order in RNH concentrations and negative fractional order in alkali concentration. Intervention of free radicals was observed in the reaction. The oxidation reaction in alkaline medium has been shown to proceed via a DPC- ranitidine complex, which decomposes slowly in a rate determining step followed by other fast steps to give the products. The main products were identified by spot test and spectral studies. The reaction constants involved in the different steps of the mechanism are calculated. The activation parameters with respect to slow step of the mechanism are computed and discussed and thermodynamic quantities are also determined. The title reaction follows the rate law:

$$k_{obs} = \frac{k\,K_1\,K_2[RAN]}{[OH^-]+K_1+K_1K_2[RAN]}$$



Stoichiometry

Synthesis and Anion Binding of Azothiacalix[4]arenes

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The development of new receptors for anions has attracted a great interest in recent years due to the fact that anions plays numereous fundamental roles in biological and chemical process. One of particular interest in this regard involves the construction of colorimetric anions sensors, since they allow "naked eye" detection. The octamethylcalix[4]pyrroles [1], calix[4]arenes and thiacalix[4]arenes are an important binding agent for various cations, anions and neutral substrates.

Calix[4]arene represent a unique three dimensional structure with almost unlimited derivatisation abilities. Thiacalix[4]arene has been described as a new member of the calixarene family. The presence of four sulfur atoms instead of methylene groups imposes many new properties on the thiacalixarene skeleton when compared with the chemistry of classical calix arenes.

Azothiacalix[4]arenes have been synthesized by electrophilic substitution with aryldiazonium salts under different reaction conditions. The binding abilities of azothiacalix[4]arenes for anions have been investigated by naked eye, UV-visible, ^{1}H NMR and other spectroscopic techniques. Presence of azophenol chromophores and diferent binding sites were found to allow not only for high selective and sensitive colorimetric detection but also easy colorimetric differentiation of various anions of similar basicity, depending upon the azothiacalix[4]arene structures and guest basicity.

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WO_3- Catalyzed Selective Oxidation of Alkylarenes and Acetophenones to Benzoic Acids With 70% TBHP

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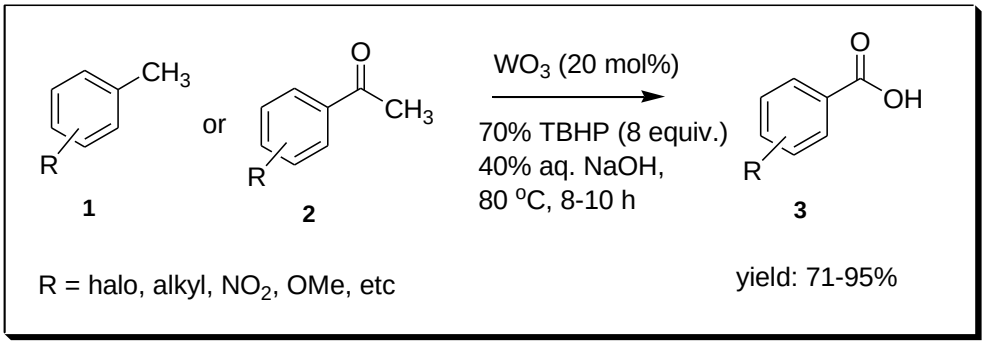
The oxidation of methylarenes to the corresponding alcohols, ketones, carboxylic acids is of industrial importance since such carbonyl derivatives constitute versatile building blocks in pharmaceutical and polymer industries. We have found that WO_3 oxidizes selectively and efficiently the substituted methylarenes (**1**) or acetophenones (**2**) to the corresponding benzoic acids (**3**) in high yields with 70% TBHP in the presence of 40% aq. NaOH. Both electron withdrawing and electron donating aromatic substrates underwent this oxidation. The catalyst WO_3 could be readily recovered and reused without any deterioration.



Scheme-1

Self-Organizing Molecular Field Analysis on a New Series of Protein Tyrosine Phosphatase 1B (PTP1B) Inhibitors: 1, 2-Naphthoquinone

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Self-organizing molecular field analysis (SOMFA), a simple three-dimensional quantitative structure activity relationship (3D-QSAR) method is used to study the correlation between the molecular properties and the anti-diabetic activities of a new series of 1, 2-Naphthoquinone that act as selective PTP1B inhibitors**.** Protein tyrosine phosphatase 1B (PTP1B) is an enzyme plays an important role in the negative regulation of insulin signaling and is involved in the insulin resistance associated with Type 2 diabetes. Thus, PTP1B inhibitors could potentially ameliorate insulin resistance and normalize plasma glucose and insulin without inducing hypoglycemia, and could, therefore, be a major advance in the treatment of Type 2 diabetes. Recently, a new series of 1, 2-naphthoquinone compounds has been reported to selectively inhibit Protein Tyrosine Phosphatase 1B [1] and SOMFA studies has been performed on this series which is divided into training set and test set.

The self-organizing molecular field analysis (SOMFA) method has similarities to both comparative molecular field analysis (CoMFA) and molecular similarity studies[2]. Like CoMFA, a grid-based approach is used; however, no probe interaction energies need to be evaluated. Like the similarity methods it is the intrinsic molecular properties, such as the molecular shape and electrostatic potential, which are used to develop the QSAR models. SOMFA calculation for both shape and electrostatic potentials were performed, the master grid maps derived from the best model is used to display the contribution of electrostatic potential and shape molecular field. The master grid maps give a direct visual indication of which parts of the compounds differentiate the activities of compounds in the training set under study. The master grid also offers an interpretation as to how to design and synthesize some novel compounds with much higher activities. The statistical results, cross-validated r^2_{CV} and non cross-validated r^2, show a satisfied predictive ability. All analysis of SOMFA model may provide some useful information in the design of new PTP1 B antagonists.

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Antimalarial Activity of 1,2,4 triamino azole Derivatives and their Pre-Radio Studies with ^{99m}Tc

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Malaria continues to be a major cause of mortality and morbidity especially throughout the developing world. In the last 25 years or so a number of significant advances have been made that have the potential to make a major contribution to the control of this disease. Some triamino azoles analogues with quinazoline, pyridine, indole and quinolines have been shown to possess significant anti-malarial activity against a multi-drug resistant strain of *Plasmodium falciparum* with IC_{50} in the range of 0.35–1.3 μM.. Structure- activity relationships in this series of compounds are discussed and possible mechanisms of action considered.

The pharmaceutical aspect of these compounds are also studied through ^{99m}Tc .Serum stability studies shows that labeled complex was stable for 20 hrs and only 1-2% dissociation of ^{99m}Tc was observed under physiological condition. The pharmokinetics of ^{99m}Tc indole complexes revealed biphasic pattern. Biodistributin studies in mice showed the major accumulation of activity in liver, kidney and tumor.

These derivatives were labeled with ^{99m} Tc by direct labeling method using stannous chloride as reducing agent. at optimized conditions of pH, stannous ion concentration and incubation time to achieve the maximum labeling efficiency (>95%).It forms stable complex with ^{99m} Tc with high radiochemical purity(98%) and showed significant accumulation at liver. Blood kinetic study showed a quick wash out from the circulation and biological half life was found to be t½(F) ¼ 1 h 15 min to 2.5h; t½(S) ¼ 10 h 05 min to 18 h.Fast clearance rate from kidneys analogue which was further evidenced in biodistribution studies, shows that this compound is potential candidate for further studies.

Potential Therapeutic Agent for Lactose Intolerant Patients by Immobilization of β galactosidase on concanavalin A Layered Calcium Alginate-Cellulose Hybrid Beads

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Department of Biochemistry, Faculty of Life sciences
Aligarh Muslim University, Aligarh, U.P, India

In the present manuscript an attempt has been made to develop a novel therapeutic agent in the form of β galactosidase immobilized on the surface of concanavalin A layered calcium alginate-cellulose hybrid beads. The stability of β galactosidase immobilized on the surface of these hybrid beads was studied against various conditions of digestive system such as pH, salivary amylase, pepsin and trypsin. Soluble and immobilized β galactosidase exhibited same pH optima. In the presence of salivary amylase and bile salts, these alginate starch beads were considerably stable without any side effects. This immobilized β galactosidase showed nearly 67% activity even after its sixth repeated use. Thus we have tried to focus on the aspect that if these beads were taken orally as a drug it will greatly help the lactose deficient subjects in consuming milk, as these beads would hydrolyze lactose present in milk into glucose and galactose in the small intestine. The size of these beads is spherical in shape which would remarkably help in the hydrolysis of lactose as they can easily enter the lumen of the small intestine and would target the lactose present inside the body.

Rate Enhancement in Coupling Reaction by Using Lewis Acids as a Promoter

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Coupling reactions like Suzuki and sonogashira are the most important reactions in organic synthesis for the synthesis of pharmaceutically important products and biologically active molecules. Alkynes are important skeleton in some natural products, pharmaceuticals, biologically active molecules, and non-linear optical materials [1, 2]. Of the various approaches to synthesize symmetrical dienes and substituted alkynes, Sonogashira cross-coupling of terminal alkynes are the most efficient route for the synthesis of such pharmaceuticals active compounds, herbicides, polymers, new materials, liquid crystals and ligands, among the various method known to synthesize biaryls [3,4]. The transition metal catalyzed Suzuki miyura cross coupling reaction of biaryls halide and aryl boronic acid has emerged as an extremity power full methods in organic synthesis for the formation of C (sp2)-C (sp2) bonds under mild condition.[5] .A number of the catalytic system has been developed for these coupling reaction, but palladium complexes are found to be the best catalyst for this reaction [6.] Palladium catalyzed Sonogashira reaction is typically catalyzed by palladium complexes in the presence of a copper salt as a co-catalyst and an amines and copper salts has attracted more and more attentions recently due to the environment constraints [7] . The problems with many of these copper- free methodologies however are that either high palladium catalyst loading have to be used or else the reaction have to be performed under anaerobic condition using palladium complexes or ligands that are expensive or hard to make.

In present study, we reported an easy, quick copper- free methodology for the sonogashira reaction that uses readily available palladium complexes and can be run in air and without having to pre-dry reagents and without the need for any solvent in presence of Lewis acid as a promoter. It was observed that rate of reaction enhance due to addition of Lewis acids like $FeCl_3$, $NiCl_2$, $SbCl_2$ etc in presence of trace amount of water. The detailed parametric investigation was carried out using standard Hermann Palladacycle and $FeCl_3$ as Lewis acid in ethanol as a solvent. The effects of different parameters like catalyst concentration, substrate concentration, base concentration were carried and the rate enhancement in Suzuki and Sonogashira was observed.

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Structural Analysis and Motif Mining of Recurrent RNA Motifs– a-Minor Motif and C Loops

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Even in this genomic era RNA is a molecule that is less understood. Motif mining in RNA molecules will lead us towards a better understanding of structures and functions of the recurrent motifs present in these molecules. The two very important recurrent RNA motifs that we have studied are A-Minor Motif and C-loops. A-Minor Motif is responsible for the global RNA architecture and the fidelity of Protein synthesis, regarding both structural and functional aspects respectively and the C loop motif has tendency to bind solely proteins. After analyzing the structure and sequence of the motifs we have looked for Torsion angles (our inbuilt tool Torsion Processor) and Base pairing edge interaction (BasePair Finder) of a base pair that happens to be present in these motifs. We have then calculated the C1'-C1' distance of the participating residues and torsion angles were classified into bins. After that correlation between the values of Torsion angles (Eta with Alpha and gamma and Theta with Delta and Zeta), were found out. The outlier was marked by using Normalization, range- +1 to -1. Following all these steps we have derived a pattern for C-Loops and A-Minor Motifs, and now we are able to mine these motives from a huge database of RNA structures. One interesting finding is that A-Minor motifs could be present within the C-loops motifs as well. We have validated our results (structural pattern for the motifs) from RASMOL and a tool RNAView present on NDB server. This has its insight into deciphering the function of RNA motifs at a higher level and to find the structural deviation, if any, from the defined pattern of a particular motif. The deviation could be due to mutation or some changes incorporated due to binding of drugs or any other such phenomenon.

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A Facile and Regioselective Synthesis of 1,4-Disubstituted 1,2,3-triazoles using Click Chemistry

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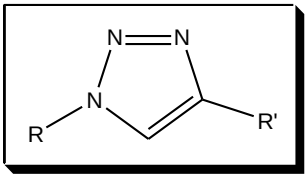
Multi-component condensation reactions constitute an especially attractive synthetic strategy since they provide easy and rapid access to large libraries of organic compounds with diverse substitution patterns [1]. In recent past, click chemistry has been explored as a newer approach for the synthesis of drug-like molecules that can accelerate the drug discovery process by utilizing a few practical and reliable reactions [2]. The 1,2,3-triazoles are important heterocycles for their widespread use in pharmaceuticals and agrochemicals [3]. In our efforts to develop one-pot multi-component condensation reactions using click chemistry, we have discovered that the reaction of α-tosyloxyketones, sodium azide and alkynes in presence of copper(I) regioselectively affords 1,4-disubstituted 1,2,3-triazoles in excellent yields at ambient temperature. More details about this synthetic procedure will be discussed in the poster presentation.



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Synthesis and Antimicrobial Evaluation of 1,3,4-oxadiazole, thioacetamide and 4-thiazolidinone Contained Novel Heterocycles

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1,3,4- Oxadiazole, thioacetamide and 4-thiazolidinone containing compounds and their derivatives attracted considerable attention from organic and medicinal chemistry due to their promising bio-activity.

1,3,4,-oxadiazole possess antibacterial [1], anticancer [2], antidepressent and anticonvulsant activities. Thioacetamides are unique class of compounds possessing various pharmaceutical applications such as treatment of parkinsonian disease and other neurological diseases [3]. Thiazolidinone derivatives also show various activities like antitubercular [4] antibiotic and hypnotic.

With reference to the above biological importance, we have synthesized various compounds which contains above mentioned three biologically active moieties. The invitro antibacterial activity in MIC were carried out against different panel of organisms. Some of the compounds displayed high in vitro antibacterial activity against tested microorganisms.

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Novel Synthesis, Characterization and Antimicrobial Activity of Some Nitrogen Containing Heterocyclic Moiety

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A series of 3-[(2,4-Dinitro-Phenyl)-(substituted amino)-1-ylmethyl-amino]-2-(un)substituted phenyl-5-(3,4,5-trimethoxy benzylidene)-3,5-dihydro-imidazol-4-one derivatives were synthesized by the condensation of 2- (un) substituted phenyl-4- (3,4,5- trimethoxy benzylidene)- 4H-oxazol-5-one and 2,4-Dinitro Phenyl hydrazine in Pyridine. which was further carried out by Mannich reaction using different secondary amines to afford title compounds. The synthesized compounds have been characterized on the basis of elemental analysis and spectral studies like IR, ^{1}H- NMR, etc. Further they were assayed for their antimicrobial activity against *E.Coli, B.Substilis* bacterial species and *A.niger* fungal microorganism.

Computational Studies of the Deracemisation of α hydroxy Esters Catalysed by *Candida parapsilosis*

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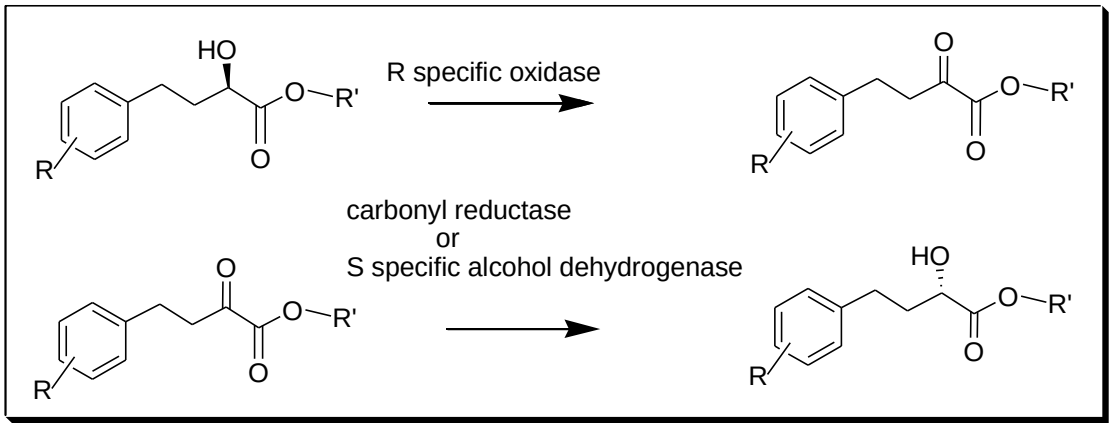
Biocatalytic deracemisation using *Candida parapsilosis* of α hydroxy esters to produce enantiomerically pure 'S' ester, as shown in the figure, has been reported [1-5]. The process can theoretically confer 100% enantiomeric excess (ee), since it involves the conversion of one enatiomer to the other while the second enantiomer remains intact (Scheme 1). But the ee of the products varied widely among them (ranging from 3% to >99%) To describe the difference in preference of various α hydroxy esters in deracemisaton reaction catalysed by *Candida parapsilosis*, target and structure based studies were carried out. Target based studies comprise of the enzyme- substrate docking studies while the structure based studies include the quantitative structure activity relationship (QSAR) studies. In both the studies we divided our compounds into training and test set, so as to test the validity of our studies. The fit obtained for the QSAR studies was excellent (r^2>0.82) with high predictive ability (q^2>0.7). The docking studies also showed a good fit (r^2>0.6) with good predictive ability (q^2>0.5). Docking studies were also able to explain the preference of the enzyme towards the 'S' enantiomer.



Scheme 1: Deracemisation reaction carried out by *Candida parapsilosis*

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Experimental Evaluation of Suitable Solvents for Studying Triclosan, a Hydrophobic Drug, in Cell Culture

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Triclosan, a broad-spectrum antibiotic, is currently being evaluated by us for its anti-cancer property [1]. A difficulty that we encountered was the choice of appropriate solvent for solubilizing this lipophilic organic compound in the culture medium. Here we present our experimental approach to identify a suitable solubilizing agent, for studying the hydrophobic drug in two cell culture systems (Y79- retinoblastoma, and MCF-7 - breast cancer cell lines).

To solubilize Triclosan, five different solvents were selected: DMSO (dimethyl sulphoxide), Absolute ethanol, 1N NaOH, Acetone [2], and PEM (55% Polyethylene glycol-400 + 45% Ethanol Mixture) [3], and diluted with the culture medium (final concentration of 1mg/ml). Triclosan dissolved completely in all the five solvents. However on dilution with culture medium, turbidity was observed in the DMSO, Absolute Ethanol, and 1N NaOH groups. Also, triclosan in 1N NaOH added to culture medium showed an unfavorable pH of 8.5 (optimal pH 7.4). On the other hand, triclosan dissolved well in PEM, and in acetone, when added to the medium, showing optimal pH. Cell viability MTT assay was performed with Y79 and MCF-7 cells that were treated with (a) different concentrations of solubilized triclosan, and (b) respective solvent controls (that is, without drug) for 48 hours. Substantially lower cell viability with PEM solvent control (64%) in comparison with the acetone control group (95%), indicated the cytotoxicity of the PEM solvent in both the cell lines. This was further confirmed by cell morphological changes (phase contrast microscopy) and by DNA fragmentation analysis. Further, comparison of the IC_{50} (50% Inhibitory Concentration of the drug over the cell viability) of triclosan in acetone versus triclosan in PEM suggested a 2.3 fold increase in drug-concentration is required to induce cytotoxicity in Y79 when PEM is used as the solvent. This implies a decreased drug-sensitivity in PEM solvent, which may be due to the large molecular size of polyethylene glycol (PEG 400) known to form micelle-like structures. These may bind with the triclosan molecule, thus rendering it less available for biological activity [4].

To conclude, acetone demonstrated favorable physico-chemical and biologic characteristics for solubilizing triclosan, enabling further investigations on the hydrophobic drug in cultured retinoblastoma and mammary tumor cells.

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Design and Synthesis of Inhibitors for *Plasmodium falciparum* Enoyl-acyl Carrier Protein Reductase (P*f*ENR).

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Malaria causes more than 1 million deaths and more than 400 million clinical cases are reported world wide annually. Due to the acquired resistance of *Plasmodium falciparum* to the anti-malarial drugs, searching for new anti-malarial drugs is necessary in modern days. Recently, an improved understanding of the biochemistry of malarial parasites has identified many potential targets for new drugs and helped shed light on the mode(s) of action of older drugs. Targets those are common to the parasite and its human host offer opportunities for chemotherapy if structural differences can be exploited. Recent studies have shown that the *P.falciparum* synthesizes fatty acids using a fatty acid synthase type II (FAS-II) instead of a type-I fatty acid synthase (FAS-I) that is present in other eukaryotes. *P. falciparum* enoyl reductase (*PfENR*) FabI is located within the apicoplast, a plastid-like organelle, responsible for several important metabolic pathways, including fatty acid biosynthesis. It is responsible for the last step of fatty acid biosynthesis in the parasite. Because of its indispensable role in the parasite's fatty acid pathway, FabI has been recognized as one of the most promising structure-based antimalarial targets, few molecules have been identified as inhibitors of FabI enzyme, namely triclosan, thiendiazaborines, diazaborines, and thiolactomycin. *PfENR* can be exploited as a novel drug target for development of new antimalarial agents[1]. Therefore, using molecular modeling methods, we have designed *in silico* derivatives of the above mentioned compounds and docked and scored them in the active site of targets, using the program GOLD (GOLD 3.0.1 CCDC, UK). Based on the docking scores we have focused attention on synthesis of some of compounds using conventional synthetic methods[2]. All synthesized compounds were confirmed by NMR and IR spectroscopy. Results for the anti-malarial activity are awaited.

PfENR : *P. falciparum* enoyl-acyl carrier protein reductase (FabI).
FAS-I : Associative or type-I fatty acid synthase.
FAS-II : Disociative or type-II fatty acid synthase.
GOLD : Genetically optimized ligand design.

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$CeCl_3.7H_2O$/NaI-Catalyzed Expeditious Synthesis of Fused 1,3-Oxazine *N*-Nucleosides from D-Glucose

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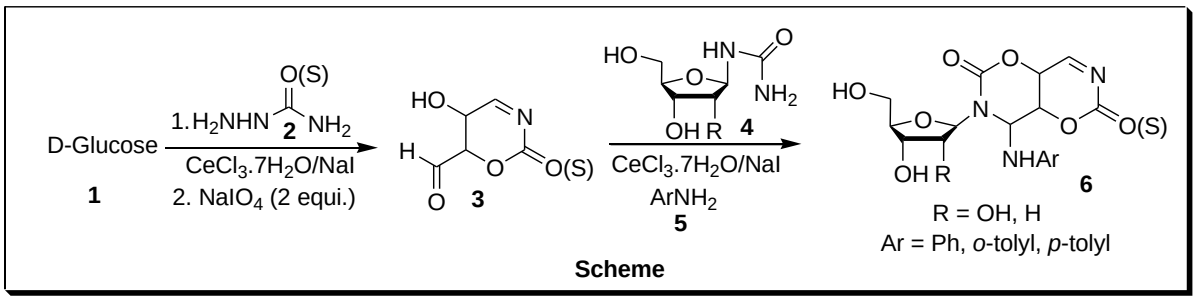
1,3-Oxazin-2-one is an important six-membered heterocyclic ring system which is present in many biologically important natural products like maystansine, maystanprine, maystanbutine and colubrinol which are known to exhibit of variety of biological activities, e. g. Antiulcer, analgesic, antihypertensive and antidepressant. Owing to the activity of $CeCl_3.7H_2O$-NaI system towards the cleavage of carbon-oxygen and silicon-oxygen bonds under neutral condition, new reactions for nitrogen-carbon and oxygen-carbon bond formation promoted by this system have been developed.

Keeping these valid points in mind and our ongoing efforts to devise new MW-assisted solvent-free cyclization processes[1,2] especially using carbohydrates as starting material,[2,3] we disclose herein a new synthetic protocol for 1,3 oxazine *N*-nucleosides from D-glucose. In this synthetic strategy, D-glucose with semi(thiosemi)carbazide and catalytic amount of $CeCl_3.7H_2O$/NaI afforded 5-hydroxy,6-polyhydroxy-1,3-oxazin-2-ones(thiones), which on Malaprade reaction yielded 5-hydroxy-2-oxo(thioxo)-1,3-oxazine-6-carbaldehyde **3**. Furthermore, by irradiating an intimate mixture of compounds **3**, ribosyl-/deoxyribosylureas **4** and aromatic amines **5** in a chemical laboratory microwave oven, we obtained 4,4a-dihydro-3-(β-D-ribo or β-D-2′-deoxyribofuranosyl) [1,3]oxazino[6,5-*e*][1,3]oxazine-2,6(3*H*,8a*H*)-diones(6-thioxo-2-ones) **6** in excellent yields (82-91%) via cycloisomerization of an aldimine intermediate under solvent-free conditions.



Scheme

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One Pot Synthesis of Novel Axially Chiral Quateraryls through Ring Transformation Strategy

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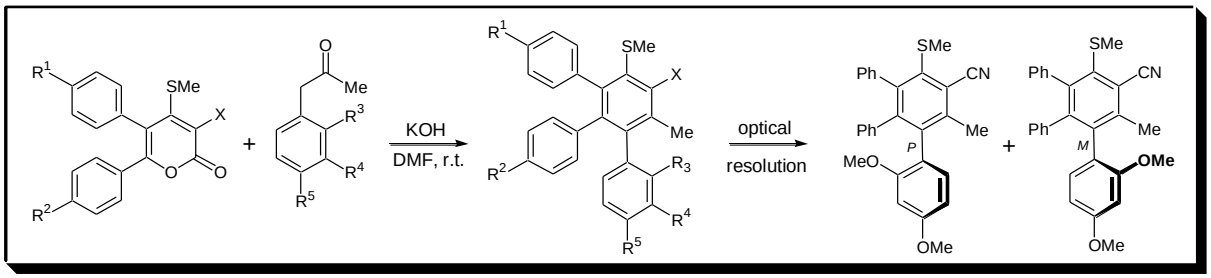
The demand for new axially chiral, atropisomerically pure biaryls for the use as efficient chiral ligands or auxiliaries in asymmetric synthesis, [1] has triggered vigorous efforts to develop new synthetic strategies [2] to architect novel aromatic scaffolds with the desired degree of conformational flexibility. Limited procedures are known for the synthesis of such biaryls in which one of the aromatic rings is functionalized with two or more aryl substituents in a juxtaposed manner. The palladium-catalyzed aryl-aryl cross-coupling between electrophilic aromatic halides $Ar(X)_n$ and organometallic species Ar-M is a versatile synthetic method for the preparation of diverse arylated benzenes. However, these coupling reactions normally require elevated temperatures and are susceptible to steric hindrance, which restricts their application in asymmetric biaryl synthesis.

During our recent studies on the chemistry of 2*H*-pyran-2-ones, we observed that lactones have promising structural topology as useful substrates for ring transformation reactions.[3] In this presentation, we will describe a general synthesis of highly functionalized quateraryls through carbanion-induced, base-catalyzed ring transformation of 5,6-diaryl-2*H*-pyran-2-ones and core-substituted phenylacetones. These conversions were found to give diversely functionalized benzenes bearing peripheral aryl rings, some of which possess inherent atropisomerism. A general method for the optical resolution of the atropo-enantiomers and the assignment of their absolute axial configurations by LC-CD coupling in combination with semiempirical CNDO/S and TDDFT CD calculations will be demonstrated. This synthetic approach offers in a transition metal-free environment a high flexibility in the construction of quateraryls with the desired conformational freedom along the molecular axis, which may help in exploring and developing new potential ligands for asymmetric synthesis.



Scheme 1

References:

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Validated HPLC Method for Determination of Aspirin and Clopidogrel in Combined Dosage form in presence of Degradation Product formed under ICH Recommended Stress Condition

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The present work describes development and validation of high performance liquid chromatographic assay method for the determination of Aspirin and Clopidogrel in tablet formulation. The combination formulation was subjected to ICH recommended stress condition. Separation of the drugs from the degradation products formed under stress condition was achieved on a C8 column using a mixture of 0.3% ortho phosphoric acid(v/v) -acetonitrile (65:35, v/v) as mobile phase. The method was validated to specificity, linearity, LOD & LOQ, precision, accuracy and robustness. The method was found specific against placebo interference and also during the force degradation. The response was linear in the drug concentration range of 3.0-12.0 µg/ml for aspirin and 1.5-6.0 µg/ml for clopidogrel with a correlation coefficient 0.9999 for both. The RSD values for intra-day and inter-day precision were less than 1.0%. The accuracy was between 99.12–99.83 % for aspirin and 98.20– 100.35% for Clopidogrel. Stress testing showed degradation product, which were well separated from parent compound, confirming its stability indication capacity.

A Novel Inbuilt Mucoadhesivity of Guava Biomaterial

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The aim of our research work is to characterize novel mucoadhesivity property of the biomaterial isolated from *Psydium gujuava* fruit. The biomaterial was isolated from guava fruit pulp by a simplified economic process. It was subjected for performing various *in vitro* and *ex vivo* studies like Shear stress method, Park and Robinson method, Wilhelmy plate method and Falling ball method. The results were compared with synthetic and standard mucoadhesive polymers like sodium CMC and HPMC. Our experimental results revealed that the isolated biomaterial exhibited pharmaceutically significant mucoadhesive property in comparison with the standard polymers. The conclusion was drawn that the biomaterial can serve as a novel potential bio-mucoadhesive polymer for formulation of various bioadhesive drug delivery systems

Synthesis and Interaction of Novel Platinum Complexes with DNA *in vitro* Representing New Concepts for Improving Antitumor Activity

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The anticancer drug cisplatin is one of the three most extensively used anticancer drugs. Cisplatin is administered intravenously, but only a minority of the molecules find their way to the cancer cells, penetrate them and react with one or more cellular components. Much of the understanding about the mechanism of action of the drugs is derived from data gathered from aqueous model systems simulating "physiological conditions". Since the first clinical application of the antitumor drug cisplatin in 1979, several thousand analogues have been synthesized aimed at improving efficacy and minimizing adverse side effects.

Pt(IV) complexes are inert octahedral compounds that are often used as prodrugs for the more cytotoxic Pt(II) analogues. Upon reduction, the octahedral Pt(IV) loses both it axial ligands generating the tetracoordinate square planar Pt(II) complex. We began studying the stability of Pt(IV) complexes with axial acetate ligands in extracts of different types of cancer cells. We have monitored them by NMR and seen that the rate of reduction of the Pt(IV) complex depends on the type of the parent cancer cell line.

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A General Strategy to Substituted 3-methylene-2-pyridones and its Synthetic Applications

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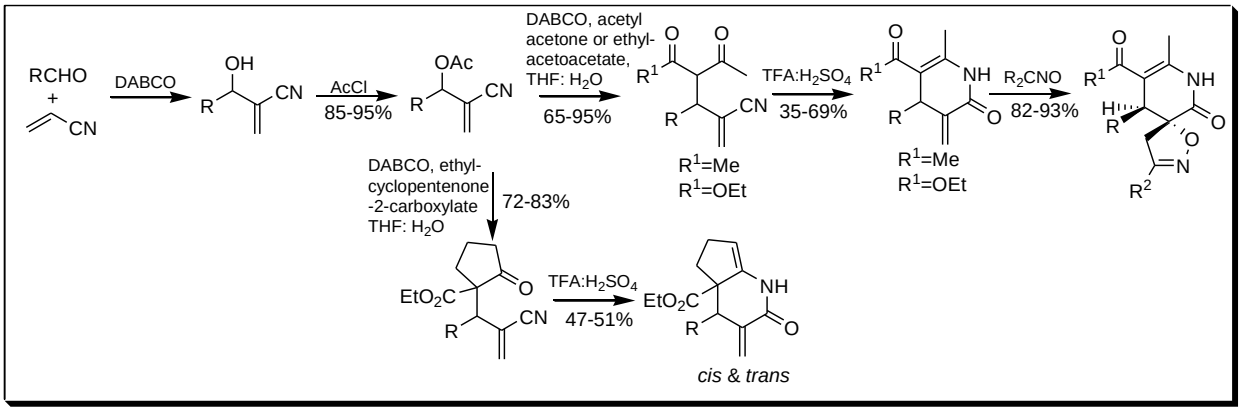
The 2-pyridone core structure is an attractive target for synthetic organic chemists owing to its significance in current medicinal chemistry. In addition, 2-pyridone constitutes a substructural component of several naturally occurring compounds such as nothapodytine-B, akanthomycin, sempervilam and campothecin. Moreover, 2-pyridone derivatives serve as viable synthons to pyridine, piperidine, quinolizidine, and indolizidine alkaloids and pyridone-tethered systems for dyes and pigments.

In recent past the derivatives generated from the Baylis-Hillman chemistry have allowed construction of several cyclic systems including heterocycles, carbocycles, benzannulated systems and natural products. In particular, scaffolds containing exocyclic C-C double bond could be readily synthesized from them. In this context, our group has recently demonstrated practical syntheses of α-methylene-δ-valerolactones, 3-methylene-gluteramides, 3-methylene-2-pyrrolidinones and 3-methylene-[1,5]-benzodiazepin-2-ones.[1a-d] In continuation of our program aimed at construction of heterocyclic scaffolds from derivatives of the Baylis-Hillman reaction, we have now accomplished the synthesis of substituted 3-methylene-2-pyridones and 3-methylene-4a*H*-cyclopenta[b]pyridin-2-one via the S_N2 displacement reaction of the Baylis-Hillman acetate of acrylonitrile with a nucleophile containing a carbonyl moiety to obtain a product which upon acid hydrolysis in the presence of TFA: H_2SO_4 mixture of nitrile group followed by intramolecular cyclization. In our attempts to demonstrate the synthetic utility of these pyridones we have conducted highly regioselective and distereoselective 1,3-dipolar cycloaddition to furnish spiroisoxazolines. The detail results of this study will be presented and discussed.



Scheme 1

References

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The Apicoplast Genome of *Plasmodium vivax*

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Plasmodium vivax accounts for more than half of all malaria infections in Asia and Latin America. Almost one million *P. vivax* malaria cases are reported annually in India. With the recent reports on severe manifestations of *P. vivax* malaria, there arises a need for identification of novel drug targets to combat this disease. Apicoplast, a three – four membrane organelle, carrying various metabolic pathways and a circular DNA is being considered as one such putative drug target. The organelle and its DNA have not been characterized as yet from *P. vivax*. The genome carries various genes of functional importance including *ssu* and *lsu* ribosomal RNA and *tRNA* genes, *sufB, clpC, tufA* genes, *RNA Polymerase B, C* and *D* subunit genes and various ribosomal protein genes. The presence of this organelle and its genome in parasite forms the basis of the present investigation.

Various genes from the Apicoplast genome of *P. vivax* were amplified, sequenced and analyzed. On comparison with the *P. falciparum* sequences variations were observed at both nucleotide and amino acid level. About 8 – 13% differences were observed between *P. vivax* and *P. falciparum* Apicoplast sequences. A comparative analysis of *P. vivax* Apicoplast *tuf A* gene with alleles from other *Plasmodium* species was also done [1]. To colocalize the Apicoplast within *P. vivax* blood stages peptides were designed from the *P. vivax* Apicoplast *tufA* gene and antibodies were raised in swiss albino mice. Apicoplast was colocalized using antibodies raised against Ef – TuA peptides in *P. vivax* infected blood smear slides obtained from the field.

Reference:

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Synthesis, Characterization and Biological Evaluation of Some New Pyrazole Derivatives

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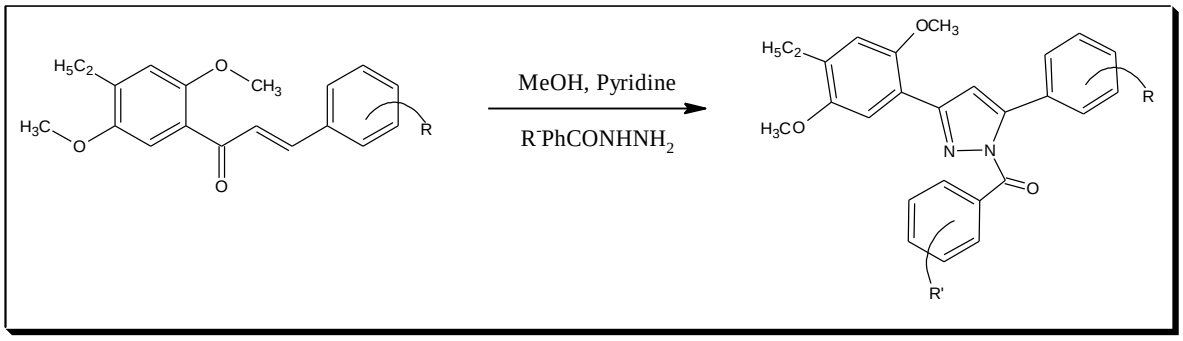
A large number of heterocyclic compounds derived from chalcone group have been reported as active biological entities, Significant biological properties associated with pyrazole derivatives have aroused considerable interest to design the compound with better drug potential and to study their biological profile.

Newly synthesized di-aryl chalcone on condensation with different benzo-hydrazide in presence of pyridine give the corresponding 1-(substituted benzoyl)-5-(substituted phenyl)-3-(4-ethyl-2, 5-dimethoxyphenyl) -1*H*-pyrazole. The structures were supported by IR, ^{1}H-NMR, ^{13}C-NMR and MASS spectroscopy. The compounds were screened for their antimicrobial and anti tubercular activities. The antimicrobial properties of the compound were investigated against various bacterial strains using broth dilution method.



Scheme 1

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Insilico Interaction Studies on DMDP Derivatives as DHFR Inhibitors for Cancer Chemotherapy

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Cancer is a class of diseases or disorders characterized by uncontrolled division of cells and the ability of these cells to spread, either by direct growth into adjacent tissue through invasion, or by implantation into distant sites by metastasis (where cancer cells are transported through the bloodstream or lymphatic system). Cancer may affect people at all ages, but risk tends to increase with age.

Folates play a key role in one-carbon metabolism essential for the biosynthesis of purines, thymidylate and hence DNA replication. Folate metabolism is the target of two major drug groups: dhydrofolate reductases, (e.g., methotrexate) and thymidylate synthase inhibitors (for example, 5-fluorouracil). These agents are widely used in cancer chemotherapy, as treatment for rheumatoid arthritis, and for other conditions.

Nowadays, molecular docking approaches are routinely used in modern drug design to help understand drug–receptor interaction. It has been shown in the literature that these computational techniques can strongly support and help the design of novel, more potent inhibitors by revealing the mechanism of drug–-receptor interaction. However, so far, there has been no report concerning the application of molecular docking methodology methodology for understanding the binding of 2, 4-diamino-5-methyl-5-deazapteridine (DMDP) derivatives.

In this study, we have used docking studies to study the binding orientations and predict binding affinities of 2, 4-diamino-5-methyl-5-deazapteridine (DMDP) derivatives. Such studies have been carried out to understand the forms of interaction of eighty three compounds, sysnthesized by Suling *et al.* for the *human* DHFR. The results obtained from this study would be useful in both understanding the inhibitory mode of the 2, 4-diamino-5-methyl-5-deazapteridine (DMDP) derivatives as well as in rapidly and accurately predicting the activities of newly designed inhibitors on the basis of docking scores. These models also provide some beneficial clues in structural modification for designing new inhibitors for the treatment of cancer with much higher inhibitory activities against DHFR

Statistical Analysis of Amino Acid residues within the Classes of Protein Structure

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Understanding sequence-structure relationship is the key step in protein modeling and de novo protein design. Although almost all protein structures at atomic resolution can be classified into four major classes of fold, elucidating sequence-structure relationship is still a challenging task. A statistical analysis is performed to understand the preference of amino acid residues for the four major classes of protein e.g., α-proteins, β-proteins, α/β proteins and α+β proteins. We use non-homologous proteins from (< 30% identity) April 2007 release Brookhaven Protein Data Bank (PDB) with resolution better than 2.5 Å. It is observed that within α-proteins, other than Gly and Pro, Ile and Val have significantly less helical propensity whereas in β-proteins, Ile and Val have significantly high β-sheet propensity. In case of mixed proteins (α/β proteins and α+β proteins) Val and Ile has significantly high preference for β-sheet region whereas Ala, Glu and Gln have higher preference for helical region. Interestingly, it is observed that the helical propensities of hydrophobic residues are increased significantly in mix proteins than the helical proteins alone. In other hand, the helical propensity of hydrophilic residues are reduced in mixed proteins. This difference in helical propensity of hydrophobic and hydrophilic residues in different fold may be due to differential folding mechanism. The size of protein may play a crucial role.

Ethyl Gallate, an Active Compound, from *Terminalia bellerica* and its Antimicrobial Activity against Human Skin Pathogens

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Plants synthesize a diverse array of secondary metabolites, many of which have antimicrobial activities. Interest in plants as sources of antimicrobial agents is growing. This is because plant-derived medicines have been part of traditional health care in most parts of the world and antimicrobial properties of plant-derived compounds are well documented. The fruits of *Terminalia bellerica* are important herbal raw materials containing polyphenols and form the major constituents of widely used Ayurvedic formulations like Triphala churna The present work shows that a compound identified as ethyl gallate found in *Terminalia bellerica* is specifically inhibitory to Gram-positive bacteria *Staphylococcus aureus* and *Streptococcus pyogenes*; Gram-negative bacteria *Pseudomonas aeruginosa;* and dermatophytes *Trichophyton rubrum, Microsporum canis* and *Epidermophyton floccosum*. The isolation of ethyl gallate from the plant, its highly specific action against skin diseases causing organisms and the demonstration of combination activity of ethyl gallate with ciprofloxacin, is the first published information. The MIC of ethyl gallate was found to be in the range of 32-128 μg/ml and 64-512μg/ml against bacteria and fungi, respectively. The extracts of the fruits were standardized with respect to their total ethyl gallate contents by HPLC method. The present work also describes the potentiating effect of ethyl gallate with ciprofloxacin in *in vitro* combination studies against *Staphylococcus aureus* by broth checkerboard method. The final concentrations ranged from 0.03μg/ml to 64μg/ml for ciprofloxacin and from 0.2 μg/ml to 25 μg/ml for ethyl gallate. This combination of ciprofloxacin with ethyl gallate showed a twofold reduction in the MIC of ciprofloxacin for *S. aureus* when tested in combination with ethyl gallate at 12.5 μg/ml.

Computational Approaches in Drug Development of Novel Anti Cancer Drug Iressa- Selenium metal Complex

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The use of anticancer agents forms an important part for treatment of cancer of various types. The role of selenium in the prevention of cancer has been recently established by laboratory experiments, clinical trials, and epidemiological data. In this paper we are reporting a computational design of novel anti cancer drug Iressa-selenium metal complex. The structure and relative energies of the Iressa- Selenium complex are predicted using Hartree- Fock method. The methods of theoretical chemistry have been used to elucidate the molecular properties of Iressa- Se metal complex. The analysis of molecular descriptors defined by Lipinski has shown that the candidate drug obey 'rule of five'. The solubility of drug in water has been determined as it is of useful importance in the process of drug discovery and development from molecular design to pharmaceutical formulation and biopharmacy. Electrostatic potential map has been constructed and the nature of Electrostatic Potential maps for the predicted bioactive conformations to identify the electrophilic and nucleophilic regions has been discussed. To avoid rejection of drugs, it is becoming more important to determine pKa, absorption, polar surface area and other physiochemical properties associated with a drug, before synthetic work is undertaken

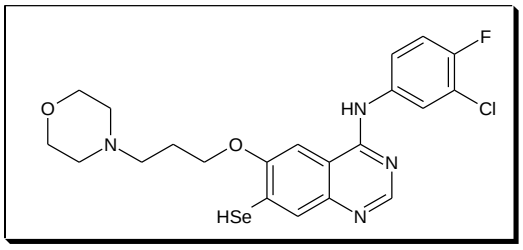

Fig1. Structure of Iressa- Selenium metal Complex

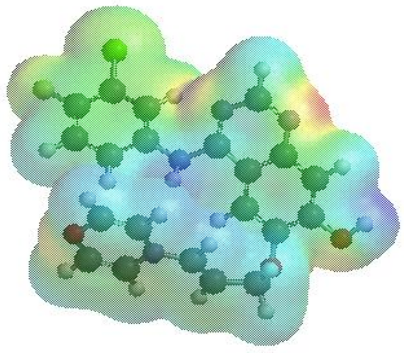

Fig. 2. A 3D-view of LUMO orbitals for Iressa

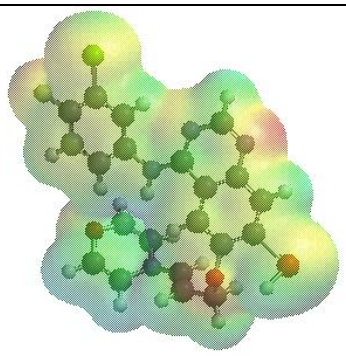

Fig.3. A 3D-view of LUMO orbitals for Iressa-Selenium metal complex

AR Inhibitory Activity of Herb

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Cataract is the leading cause of blindness worldwide. Apart from ageing, diabetes has been considered to be one of the major risk factors of cataract. The high sugar levels in diabetes may cause tissue disruption and intumescences by osmotic changes induced via aldose reductase (AR) mediated polyol pathway. Therefore agents that can inhibit AR and prevent sorbitol accumulation may be helpful to combat sugar-induced cataract. The effect of aqueous extract of herb, an inhibitor of advanced glycation on the development of cataract was studied in lens culture. Aqueous extract of herb (*Tylophora indica*) showed potential inhibitory activity with an IC50 value of 20 µg/ml against rat lens AR. Incubation of goat lens with super-physiological concentrations of glucose (100 mM) for 12 days, led to the loss of lens transparency associated with increased in AR activity, Lipid peroxidation(LPO), protein carbonyls and glycation, while interstingly the activity of Superoxide Dismutase (SOD) and soluble protein fraction in lens proteins found to be significantly decreased.. Addition of *Tylophora indica* aqueous extract to the medium, preserved transparency and ameliorated the decrease in lens soluble protein fraction resulted due to hyperglycemia and also reduced the formation of glycated protein. Interestingly herb inhibited aldose reductase activity in lens, which was incubated with 100 mM glucose (Table No.1.). *Tylophora indica* decreased LPO and protein carbonyls, increased SOD. These results suggest that *Tylophora indica* aqueous extract protect the lens against sugar-induced cataract by multiple mechanisms.

Table No.1.

Sample	Specific activity*
Control	1.493 ± 0.38
Glucose 100mM	2.428 ±0.17
Tin(herb extract)	1.761 ±0.42

Aldose reductase activity in lens culture; n = 6
Analyzed by ANOVA; $p<0.001$
* µmoles NADPH oxidized /h/100mg protein

Molecular Docking Studies for Anti Tuberculosis Activity

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About one third of the world's population has latent tuberculosis, caused by Mycobacterium tuberculosis infection. From this pool, roughly 9 million cases of active tuberculosis emerge annually, resulting in 2-3 million deaths. Most new cases occur in the most populated nations, India and China but the highest rates of disease are seen in sub-Saharan Africa, the Indonesian and Philippine archipelagos, Afghanistan, Bolivia, and Peru. Rifampicin and isoniazid are the main drugs used today as standard anti tuberculosis therapy. Tubercle bacilli undergo random chromosomal mutations that have made them resistant to every drug used to treat tuberculosis. The challenge of managing multidrug resistant tuberculosis is complex and creates the need the new drug candidate to fight the battle against Tubercle bacilli. High-throughput and virtual screening are important components of modern drug discovery research. Computational approaches that 'dock' small molecules into the structures of macromolecular targets and 'score' their potential complementarily to binding sites are widely used in hit identification and lead optimization. We have conducted a virtual screening using a ligand library of synthetic heterocyclic entities (Imidazolines, Azetidinones, Acetamide derivatives etc.). The docking studies were carried out was using successful target (Fatty acid synthase subunit beta, Malonyl-CoA:acyl carrier protein transacylase, Arylamine N-acetyltransferase etc.) and research target (Isocitrate lyase, Nicotinate-nucleotide pyrophosphorylase [carboxylating],DP-diacylglycerol—inositol 3-phosphatidyltransferase, Alkylhydroperoxidase AhpD, Beta-ketoacyl-ACP synthase 3-oxoacyl-[acyl-carrier-protein] synthase II, Thymidine monophosphate kinase etc.)

2,3,16–Trihydroxy-4, 20-hydroxymethylolean–12–en–28-oic acid: A Bioactive Triterpene from the Seeds of *Cassia angustifolia.*

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Cassia angustifolia L. is a short low growing shrub belonging to family- Fabaceae (Sub family- Caesalpiniaceae) and is commonly known as 'Sena' [1]. The plant is reported to have medicinal properties. Leaves and pods are cathartic and chemically contains sennoside A, B, C, D and aloe-amine in free and compound form [2].

The dried and crushed seeds of *Cassia angustifolia* were defatted with petroleum ether. The defatted seeds were further subjected to hot soxhalation with methanol for 14-16 hrs. Vacuum dried methanolic extract was redissolve in water. This aqueous fraction was sequentially partioned with n-hexane, ethylacetate, chloroform and n-butanol to give a total of five fractions. The butanolic fraction exhibiting antimicrobial activity [3-4] was subjected to purification by column chromatography [5]. Silica gel column chromatography of crude compound by gradient elution with $CHCl_3$: MeOH: H_2O from 65:30:5 to 50:45:5 was done. Each fraction was checked by TLC and triterpene rich fractions were pooled together. Partially purified compound was rechromatographed by eluting with $CHCl_3$: MeOH (60:40 to 55:45). Repeated chromatographic separation furnishes a triterpene glycoside. The structure of the aglycone of new triterpene was established as 2, 3, 16 – Trihydroxy - 4, 20 - hydroxymethyl olean–12–en–28-oic acid by analysis of ^{1}H NMR, ^{13}CNMR, UV-VIS, FTIR and FAB-MS spectroscopic data.

The study of sugars is under way which finally gives the complete structure of new triterpene glycoside isolated from the seeds of Cassia *angustifolia.*

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C-3 Branched-2,3-dideoxy Glucopyranosides as Antitubercular Agents

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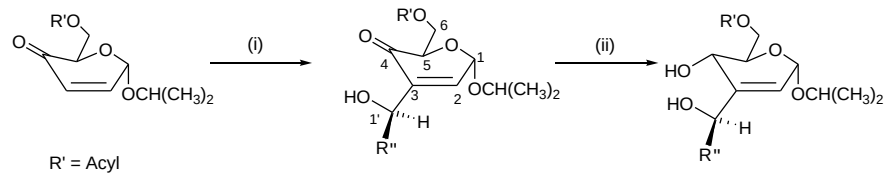
The emergence of MDR-TB and of late XDR-TB along with the problem of co-infection with HIV has made the threat from TB very serious [1]. To effectively combat the menace of T.B. in its present manifestation there is an urgent need for development of new, potent and selective anti TB agents, that have unique mechanisms of action from presently used anti-tubercular drugs. Among the targets for the development of new anti-TB drugs, the mycobacterial cell wall made up of polysaccharides, proteins and lipids is of special interest, since it is responsible for the impermeability of the bacterial cell to numerous drugs [2]. The inhibition of the glycosyltransferases involved in their biosynthesis could result in a disturbance of the cell wall biosynthesis thus making them ideal targets for the development of new anti-mycobacterial agents [3].

Carbohydrates have recently come under scrutiny as offering a source of scaffolds superior in many respects than the scaffolds presently employed in drug discovery and hence much effort is being directed nowadays towards the development of carbohydrate-based therapeutics [4]. Our group has also been focusing on the development of new, potent, carbohydrate based anti-T.B. therapeutics targeting the cell wall biosynthesis. We have reported the synthesis of several novel anti-TB agents during the last few years [5]. In continuation of our endeavor we have recently synthesized a novel series of C-3 branched 2,3- dideoxy hex-2-enopyranosides exhibiting anti-tubercular activity in the range of 50 μg/ml to 1.56 μg/ml [6]. The above findings will be discussed in detail.



Scheme : (i)$TiCl_4$/TBAI, RCHO, DCM, 3-48 h, -78^{0}C- 30^{0}C; (ii) $NaBH_4$, $CeCl_3.7H_2O$, C_2H_5OH, 2-5 h, rt.

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A Study on Microbial Biodiversity of Tobacco Farm Isolates and its Pharmacological Activity

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Nicotine is an alkaloid found in the nightshade family of plants (Solanaceae), predominantly in tobacco, and in lower quantities in tomato, potato, eggplant (aubergine), and green pepper. Nicotine alkaloids are also found in the leaves of the coca plant. Nicotine has been found to constitute approximately 0.6-3% of dry weight of tobacco, with biosynthesis taking place in the roots, and accumulating in the leaves. It functions as an antiherbivore chemical, being a potent neurotoxin with particular specificity to insects; therefore nicotine was widely used as an insecticide in the past, and currently nicotine derivatives such as imidacloprid continue to be widely used. In present work more 18 bacterial strains were isolated from the Tobaco farm soil. The isolates were further examined for the morphological and biochemical heterogeneity. The growth response of all the isolates was studied in variable range of the tobacco extract (0-50%) with the normal bacillus strain. The variable response starting with no activity to growth promotion and growth inhibition was recorded. The strains were examined for presence of intracellular or extra cellular agents reducing the mutagenic effect of nicotine *Salmonella typhimurium* strains with aims test. Besides, the isolates were investigated for the production antimicrobial compound.

Virtual Screening Based on Drug Likeness and anti HIV Activity from Library of Novel Compound Containing Pyrimidines and their Derivatives

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Human immunodeficiency virus (HIV) is a retrovirus that can lead to *acquired immunodeficiency syndrome* (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections. There is currently no vaccine or cure for HIV or AIDS. The only known method of prevention is avoiding exposure to the virus. Current treatment for HIV infection consists of highly active antiretroviral therapy. Pyrimidines and their derivatives are well known heterocyclic units in the realm of natural and synthetic organic chemistry due to their therapeutic and pharmacological properties. They are medicinally important as calcium channel blockers as well as antihypertensive agents [1], anti HIV agents [2] and α-1a-antagonistneuropettide Y (NPY) antagonists [3]. Various fused pyrimidine derivatives and their synthetic approaches have been reported. They possess calcium antagonist, anti-inflammatory, analgesic, antitumor, antidepressant, antibacterial and antifungal effects. In present work an attempt has been carried out to evaluate anti HIV action of the small library of new compound belonging to pyrimidines and their derivatives against success full target (Protease, Integrase and Reverse transcriptase etc.) and research target (C-C chemokine receptor type 5, HIV aspartyl protease, HIV envelope protein gp120, HIV-1 gp160, Nucleocapsid protein, NCP7, NC71 etc.) of HIV. Beside that library compounds were also examined for drug-likeness. Molecular docking studies were carried out with docking programme GOLD Docking results compared with docking score against known ligand followed by visual inspection.

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