Cyanuric Chloride Mediated Mild Protocol for Rapid Access to Biologically Relevant Pyridoimidazole/Imidazobenzothiazole Annulated Polyheterocycles

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Polyheterocycles are invaluable structural motifs, with wide application in pharmaceutical[1] and material sciences.[2] The pyridoimidazole (PI) and imidazobenzothiazole (IBT) substructures are found in several drugs and biologically active molecules.[3] In this perspectives, we developed a general protocol to *N*-fused polyheterocycles *via* Pictet-Spengler type 6-*endo* cyclization catalyzed by cyanuric chloride (CC). The protocol was applicable to a wide range of aryl/heteroaryl aldehydes, ketones, electron rich metallocene aldehyde and indoline-2,3-diones using CC (15-20 mol %) with DMSO at 80-90 °C to afford the desired polycycles in good to excellent yield (66-90%). Some of the synthesized compounds were found to exhibit antiplasmodial activity against chloroquine sensitive (CQ-S) 3D7 and chloroquine resistant (CQ-R) K1 strains of *Plasmodium falciparum*.

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POSTER

Synthesis of Diverse 2,5 Dihydropyrroles via Base Mediated Intramolecular Carbocyclization of Ugi-Propargyl Precursors

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Among the five-membered nitrogen heterocycles, the 2,5-dihydropyrroles are privileged structural core present in vast array of natural products[1] and biologically relevant compounds. These compounds have been shown to exhibit a broad range of biological activities, including anti-tumor,[2] anti-inflammatory,[3] antioxidant,[4] antibiotic activities,[5] thrombineinhibitor,[6] and so forth. In the light of above fact, herein we wish to report a synthetic protocol for the synthesis of highly substituted 2, 5 dihydropyrrole. The protocol involves base mediated carbanion-yne intramolecular cyclization of Ugi-propargyl adduct to afford the 2,5 dihydropyrrole derivatives in good to excellent yield even under air atmosphere.

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POSTER

In-silico Design of Novel HIV-1 Entry Inhibitors Targeting gp41.

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According to the WHO report of 2013, globally around 35.3 million people have been infected with HIV (Human immunodeficiency virus). HIV-1 is the cause of the current worldwide pandemic while HIV-2 is found in West Africa but rarely elsewhere. HIV-1 penetrates cells by membrane fusion leading to the release of the viral genetic material into the cell. The HIV-1 glycoprotein Env on the viral surface, mediates the initial stages of viral entry. This Env consists of two glycoproteins: gp120 and gp41. Triggered by gp120 binding to CD4 and a co receptor, gp41 undergoes a conformation shift from a native prefusogenic state to a fusogenic state, in which the N-terminal heptad repeat (NHR) and C-terminal heptad repeat (CHR) associate to form a six-helix bundle (6HB), representing the fusion-active gp41 core [1,2]. Any compound that disrupts the gp41 sixhelix bundle formation may inhibit the gp41-mediated membrane fusion, thereby blocking HIV-1 entry into target cells. The agent, T-20 (enfuvirtide), which has been approved for HIV inhibition, can restrain Gp41 function in the fusion process but has disadvantages like instability, high cost of production and oral bioavalilabilty. Later, molecules like NB-2 and NB-64 have been discovered which are being used as template compounds to design and develop more effective small molecules functioning as HIV-1 fusion inhibitors targeting Gp41 [3,4]. Till date, no pharmacophore study has been reported for the anti-HIV molecules that target GP-41. So here, we have developed a four point ligand based pharmacohore using SybylX1.3 from the NB-2, NB-64 and few published diverse ligands [5,6]. The pharmacohore was validated by GH scoring method (GH Score: 0.7) and ROC analysis (AUC: 0.8). Pharmacohore based virtual screening was performed using IBS and NCI database. From the resulted hits, those who have high or comparable Q_{fit} values to that of the training set molecules were selected for docking. The hits which have shown promising interactions with the crucial amino acid residues and high docking score were considered as novel *in-silico* leads targeting the GP-41 and inhibit the entry of HIV-1 into the host cells.

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POSTER

Studies on Ecofriendly Microwave Assisted Synthesis of Coumarin and Cyanopyridine Heterocycles and Their Antimicrobial Activity

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Green Chemistry emphasizes the development of environmentally benign chemical processes and technologies. Microwave-assisted organic synthesis is an enabling technology for accelerating drug discovery and its development processes. This technique is also beneficial for synthesizing various complex drug structures in a fraction of time as compared to other techniques. Recently many coumarin based clubbed hybrid moieties have been explored for inhibitory activity against HIV-1 & HIV-2 type viruses. Cyanopyridin based drugs are well known for their antimicrobial, anti-inflammatory and anticancer activities. In continuation to this, we have synthesized 2–((2,5-dimethylfuran-3-yl)methyleneamino)-4-(aryl)-6-(2-oxo-2*H*-chromen-3-yl)nicotinonitriles by using both conventional and microwave methods. Structures of synthesized compounds have been confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectra. Antimicrobial activity of the compounds were studied against several bacteria (*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyogenes*) and fungi (*Candida albicans, Aspergillus niger, Aspergillus clavatus*) by using serial broth dilution method.

POSTER

Synthesis of Five-atom Sugar Modified Mercaptoacetamido-linked Nucleoside Dimers

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Nucleic acid based therapeutics has allured medicinal chemists due to its ease in specific control of gene expression. Persistent efforts have resulted in the FDA approval of nucleic acid based drugs vitravene, macugen and recently of kynamro, leading to a sudden leap in the number of active clinical trials involving the nucleic-acid moieties. Beginning with antigene and antisense technology, nucleic-acid therapeutics have recently accredited with more potent strategies, *e.g.* RNA interference, ribozyme, decoy oligonucleotide and aptamer; involving various chemical modifications to improve their utility. We have designed and synthesized the five-atom sugar modified mercaptoacetamido-linked dimers **I**, **II**, **III** and **IV** (**Figure-1**). The detailed synthetic scheme will be presented during the poster session.

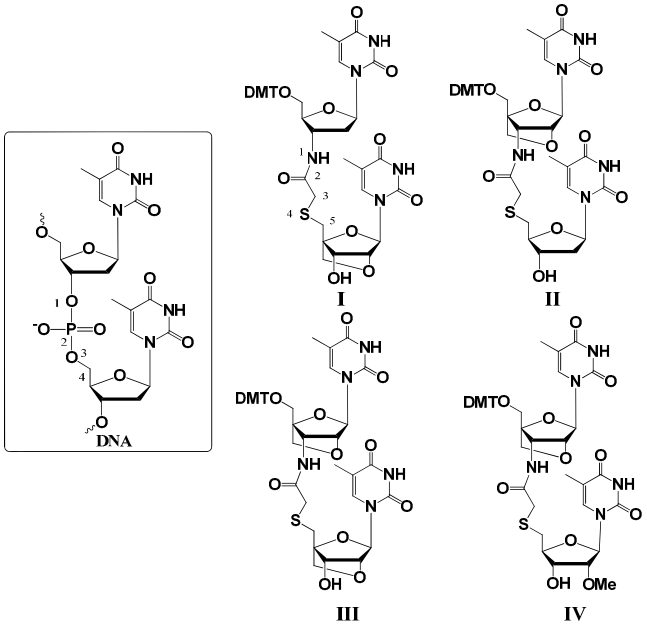

Figure-1

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POSTER

Polyvinyl Alcohol Solutions as Fluorescent Probes

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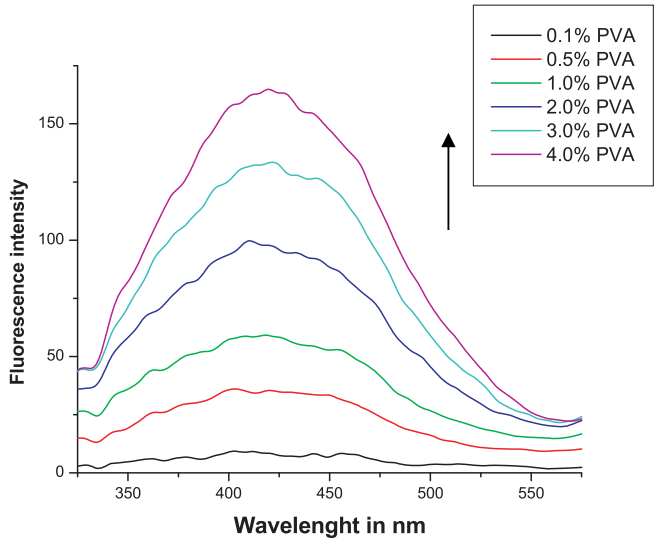
Fluorescent compounds mostly contain π bonds or aromatic systems. Certain polymeric compounds have also been found to be intrinsically fluorescent eg., poly {9,9-di[30-(dimethylethylamonium)propyl]-2,7-fluorenyl-alt-4,7-(2,1,3-benzothiadiazole) dibromide}or BtPFN which has a π-conjugated backbone. Conjugated polymers have been found to be highly efficient at harvesting and emitting light energy, and have been explored as highly sensitive and selective chemical/biological sensors and fluorescence imaging agents [1,2]. In this report for the first time we describe the appearance of fluorescence in polyvinyl alcohol (PVA#89000-98000) solution with increase in concentration in water medium. Fluorescence emission was observed at ~420 nm with an excitation wavelength of 300 nm. As the concentration of PVA solution increases from 0.1%-4%, there is a slow increase in the emission. At a concentration of 4% there is a sharp increase and thereafter the solution becomes highly viscous. Since PVAs have a multitude of applications in the biomedical field, the nature of fluorescence emission spectrum may contribute to explain several interaction studies. In this work we have studied the interaction of different species of iron (Fe^{3+}/Fe^{2+}), chromium (Cr^{3+}/Cr^{6+}) and manganese (Mn^{2+} and Mn^{7+}) with PVA solution fluorimetrically. The results are highly species dependent and are suggestive of further analytical applications. There may be other functional applications of this property of PVA solutions as fluorescence is a leading signal transduction method for the formation of chemosensory devices and polymerbased fluorescent chemosensors are gaining immense attention.



Fluorescence emission in PVA with its increasing concentrations

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POSTER

Silver-Morin Nanocomposites in their Antimicrobial Action

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Morin (2',3,4',5,7-pentahydroxyflavone) is a flavonoid which consists of a yellowish pigment found in almond (*Prunus dulcis*), fig (*Chlorophora tinctoria*) and other moraceae used in food and herbal medicines. Morin has been reported to possess a variety of biological properties against oxidative stress-induced damage. The antibacterial actions of morin and its metal complexes (Mg^{2+} and Ca^{2+}) are established in the literature [1]. Metallation increases the antimicrobial activity by chelate formation. In this light we have investigated the complexation of Ag^{+} with morin. Silver was chosen as it has proven medical applications. The silver ion (Ag^{+}) is bioactive and readily kills bacteria *in vitro* at sufficient concentrations. A synergistic enhancement of the overall antibacterial property is expected in the nanocomposite formed due to complexation of Ag with morin.

In methanol medium Ag reacts with morin to give a brown colored solid product insoluble in almost all solvents. Upon addition of silver, the solution turns brown and the color slowly deepens with subsequent precipitation of the compound after 24 hours standing. The product may be solubilized with a protecting agent, 4-hydroxy cumarin. The same reaction occurs in a surfactant, Triton X-100 medium however the product remains encapsulated in the micelles of the surfactant and does not precipitate out.

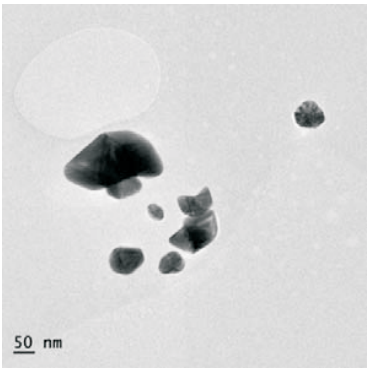

Fig 1: Silver-morin complex in methanolic medium with 4 hydroxy cumarin as the stbilizer

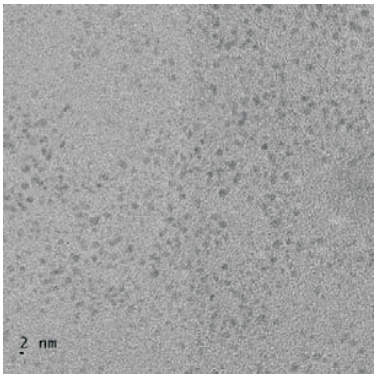

Fig 2: Silver-morin complex in Triton X-100 medium

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POSTER

On Water: Silver-Catalyzed Domino Approach for the Synthesis of Benzoxazine/Oxazine-Fused Isoquinolines and Naphthyridines from *o* - Alkynyl Aldehydes

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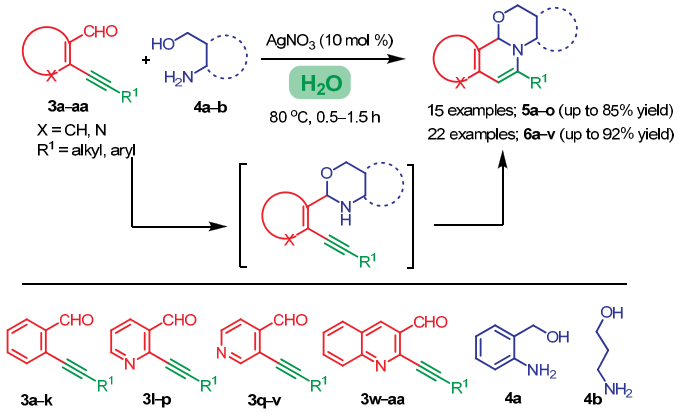
In continuation of our ongoing work on the synthesis of heterocyclic scaffold using *o*-alkynylaldehyde.[1,2] We have synthesized an operationally simple domino approach for the silver-catalyzed synthesis of oxazine/benzoxazine-fused isoquinolines **5a–q** and naphthyridines **6a–v** by the reaction of o-alkynyl aldehydes **3a–aa** with amines having embedded nucleophiles **4a–d** under mild reaction condition in water is described. The reaction shows selective C–N bond formation on the more electrophilic alkynyl carbon resulting in the formation of 6-endo-dig cyclized product. The competitive experiments show the viability of an intramolecular nucleophilic attack over an intermolecular attack of the external nucleophile.[3] This methodology accommodates wide functional group variation, which proves to be useful for structural and biological assessment.



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POSTER

Synthesis, Characterization and Antimicrobial Activity of Some Novel S-Triazine Containing Benzenesulfonamide and Isonicotinohydrazide Derivatives

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In the present work we have synthesized novel 4-(4-(2-(2-phenylacetyl)hydrazinyl)-6-(arylamino)-1,3,5-triazin-2-ylamino)-*N*-(pyrimidin-2-yl)benzenesulfonamides and *N'*-(4-(2-(2-phenylacetyl)hydrazinyl)-6-(arylamino)-1,3,5-triazin-2-yl) isonicotinohydrazide derivatives and evaluated for their *in vitro* antibacterial activity against Gram-positive bacteria [*Staphylococcus aureus* (MTCC 96), *Streptococcus pyogenes* (MTCC 442)], Gram-negative bacteria [*Escherichia coli* (MTCC 443),*Pseudomonas aeruginosa* (MTCC 1688)] and antifungal activity against [*Candida albicans* (MTCC 227), *Aspergillus niger* (MTCC 282), *Aspergillus clavatus* (MTCC 1323)]. Some of the synthesized compounds have exhibited significant antimicrobial activity on several strains of microbes. The structures of newly synthesized compounds were elucidated by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectra.

POSTER

Solid support mediated chemo and regioselective synthesis of 3*H*-1,5-benzodiazepines from diversely substituted α-oxo ketene dithioacetals

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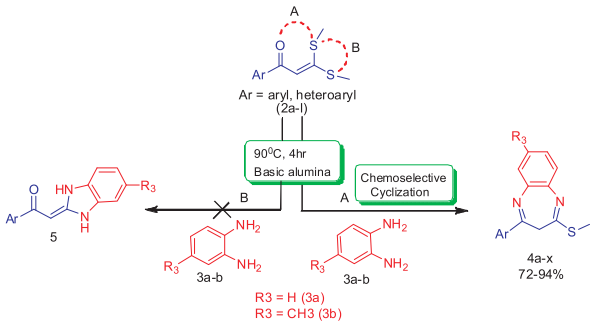
Benzodiazepines have been the target of intense investigation in medicinal chemistry and 1,5-benzodiazepine core is indeed a ''privileged scaffold'' found in compounds active against a variety of target types [1]. Thus, to develop the synthetic strategy for this heterocyclic nucleus is of current importance.

In view of the reported limitations such as impure desired products, high thermal conditions and prolonged reaction time of previous methods [2, 3], we describe herein a solid state approach for the rapid synthesis of 4-aryl-2-methylhio-3*H*-1,5-benzodiazepines by chemo and regioselective cyclization of α-oxo ketene dithioacetals with o-phenylenediamines 3a/3b (Scheme 1) by varying different parameters which include various solid supports such as (i) acidic, basic or neutral aluminas, (ii) strongly acidic montmorillonite KSF, (iii) silica gel.



Scheme : 1

This methodology having advantages such as (i) no need of additional reagent/catalyst, (ii) nontoxic reaction medium, (iii) no waste generation, and (iv) ease of product isolation, fulfils the triple bottom line philosophy of green chemistry.

Synthetic strategy, experimental details and characterization of new molecules will be presented in the symposium.

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POSTER

Mn(III) Based Binaphthyl Schiff Base Complex Heterogenized Over Organo-Modified Sba-15

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A heterogenized organocatalyst was synthesized by the covalent anchoring of the complex chloro (S,S)(−)[N-3-tert-butyl-5-chloromethylsalicylidene]-N'-[3',5'-di-tert-butyl salicylidene] 1,1'-binapthyl- 2,2'-diamine manganese(III) over modified mesoporous surface of SBA-15 [1] through the reactive 3-aminopropyl trimethoxysilane (3-APTMS) group. The surface properties of the functionalized catalyst were analyzed by a series of characterization techniques such as elemental analysis, XRD, N_2 sorption measurement isotherm, FT-IR, TGA–DTA, XPS, and solid state ^{13}C NMR. The XRD and N_2 sorption measurement, UV reflectance and CP MAS NMR spectroscopy (^{13}C and ^{29}Si) of the catalyst confirmed the structural integrity of the mesoporous hosts and the spectroscopic characterization technique proved the successful anchoring of the metal complex over the modified mesoporous support. The screening of the catalyst Mn(III)-L-SBA-15 and neat Mn(III)-L complexes was done in the oxidation reaction of thioanisole (methyl phenyl sulfide) by using TBHP as an oxidant. Mn(III)-L-SBA-15 catalyst shows higher activities and turnover number (TON) and exhibit enhanced enantiomeric excess comparable to homogeneous catalyst [Mn(III)-L]. [Mn(III)-L-SBA-15] catalyst was found more active than homogeneous catalyst [Mn(III)-L]; Moreover bulkier alkene like 1,2-dihydronapthalene was also efficiently epoxidised with the synthesized supported catalyst.

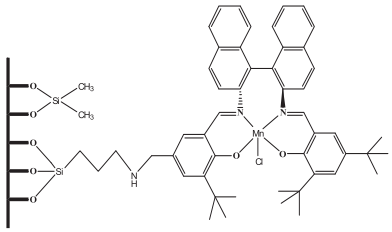

Figure 1. Mn(III)-L-SBA-15

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POSTER

Synthesis and Spectroscopic Properties of *B*-Triazole Linked Porphyrin-Xanthone Conjugates

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Porphyrins are an important class of π-conjugated macrocycles, which demonstrate great applications in various scientific fields such as biomimetic models for photosynthesis,[1] catalysis,[2] molecular sensing,[3] supramolecular chemistry[4] and photosensitizers in photodynamic therapy.[5] Similarly, xanthone-based fluorophores have also been found very useful for bioconjugation and bioimaging purposes[6] and display great fluorescence and various biological properties.[7] By considering the unique photochemical and biological utility of these two classes of heterocycles, a series of *β*-triazole linked porphyrin-xanthone conjugates have been synthesized by combining the porphyrin, [1,2,3]-triazole and xanthone moieties in a single molecular frame work *via* copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of *β*-azidoporphyrins with various xanthone attached alkynes. These hybrid molecules may prove useful as new molecular materials with enhanced electrochemical and luminescence properties. Synthesis, characterization and photophysical properties of these compounds will be presented.

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POSTER

Synthesis and Antimicrobial Activity of Some Novel Thiazole Clubbed 1,3,4-Oxadiazoles

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A series of novel thiazole clubbed 1,3,4-oxadiazole derivatives bearing a range of electron withdrawing (-F and $-NO_2$) and electron releasing ($-CH_3$,$-OCH_3$) substituents at ortho, meta and para position have been efficiently synthesized and characterized by IR, ^1H NMR, ^{13}C NMR spectroscopy and mass spectrometry. The newly synthesized compounds **5a-l** were evaluated for their in vitro antibacterial activity against four bacterial and three fungal human pathogenic strains using conventional broth microdilution method. The results of antimicrobial study revealed that compounds 5c and 5i displayed the most potent antibacterial activity, while compound 5f emerged as the most potent antifungal agent compared to standard drugs chloramphenicol and ketoconazole, respectively. From the standpoint of SAR studies, it was observed that the presence of electron withdrawing groups at para position of phenyl ring remarkably enhanced the antibacterial activity of newly synthesized compounds.

POSTER

Synthesis, Characterization and DNA Binding Studies of Copper(II) Complexes Containing Polypyridyl Ligand Systems

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Considering the importance of the phenantholine complexes in nucleic acid chemistry, we have probed the role of the extended aromatic ring of the heterocyclic base on the DNA binding and cleavage activity by choosing the dimethyl derivative of dipyridophenazine (Me_2dppz). The copper(II) complexes $[Cu(N^N)](NO_3)_2$ and $[Cu(N^N)_2](NO_3)_2$ (N^N= 1, 10 phenanthroline (*phen*), 2, 2' bipyridyl (*bpy*) and dimethyl dipyrido[3,2-a:2',3'-c] phenazine (*me_2dppz*) have been synthesized and characterized using spectroscopic and magnetic studies. Moreover a single crystal of one of the complexes, $[Cu(bpy)_2](NO_3)_2$. H_2O has been isolated and structurally characterized by single crystal X-ray studies. The interaction of the synthesized complexes with calf thymus-DNA was investigated by absorption and emission spectroscopic titrations and viscosity studies [1]. The binding constant values revealed that the copper complexes of me_2dppz are having higher binding affinity towards Calf-Thymus DNA. Viscosity studies revealed that $Cu(bpy)(NO_3)_2$ & $Cu(phen)(NO_3)_2$ are exclusively bind in the DNA grooves by partial and/or non classical intercalation. Other four Complexes binding through Intercalation mode, among which, the extend of intercalation is greater in case of Copper Me_2dppz Complexes. Gel electrophoretic studies were done using pBR 322 plasmid DNA. Since the complexes have redox active Cu(II) centers, the chemical nuclease activity was studied with H_2O_2 oxidizing agent in TAE buffer [2]. Among the six complexes $Cu(Me_2dppz)_2(NO_3)_2$ is having highest DNA cleavage ability, it shows a smearing pattern even in the absence of H_2O_2. The chemical nuclease activity in the presence of H_2O_2 confirms the DNA cleavage through a hydroxyl radical pathway.

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POSTER

Synthesis of Isoindolo Quinoline Derivatives *via* Imino Diels-Alder Reaction of *N*-acyliminium Intermediates with Viny Acetate

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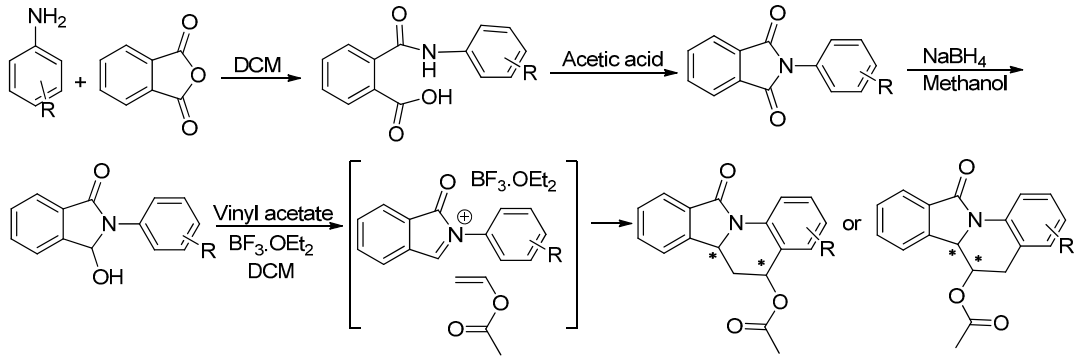
Isoindolo [2,1-a]quinolinones represent a class of molecules which are equiped with large number of biological activities, e.g. inhibitory activities against bacterial DNA gyrase & human topoisomerase and against N_2-induced hypoxia. *N*-Acyliminium ions are important reactive species for the construction of carbon-carbon bond. Numerous *N*-acyliminium ion-based intramolecular cyclizations has been utilised for the synthesis of alkaloids. It has been observed that the *N*-acyliminium ions could be reacted easily with alkenes activated by electron-donating groups. In contrast, deactivated olefins usually do not participate with ease in reactions of *N*-acyliminium ions. We herein report the synthesis of isoindolo quinoline derivatives starting from substituted anilines and phthalic anhydride *via* [4 + 2] cycloaddition of *N*-acyliminium ion intermediate with vinyl acetate as dienophile in presence of $BF_3.OEt_2$ (**Scheme 1**). The detailed synthetic scheme will be presented during the poster session.



Scheme 1.

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POSTER

Plasmodium Falciparum Purine Nucleoside Phosphorylase (PfPNP): A Potent Drug Target

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The malaria parasite obtains preformed purines by the salvage pathway. The purine salvage pathway in *Plasmodium* is streamlined with adenosine deaminase (ADA), purine nucleoside phosphorylase (PNP) and hypoxanthine-xanthine-guanine-phosphoribosyltransferase (HGPRT) representing the major pathway for purine acquisition. The enzyme purine nucleoside phosphorylase (PNP) catalyzes the phosphorolysis of inosine to ribose-1-phosphate and hypoxanthine, which is the primary purine precursor for the salvage pathway.

Plasmodium falciparum Purine nucleoside phosphorylase (PfPNP) was successfully cloned and expressed in BL21 (DE3) E.Coli host cell. Protein was purified by affinity chromatography. PfPNP a homohexamer contained single tryptophan residue per subunit, the role of this tryptophan residue in catalysis was studied that accepts inosine and guanosine but not adenosine for its activity. The enzyme shows disorder to order transition during catalysis.Modification of tryptophan residue by N-bromosuccinamide resulted in complete loss of activity showing its importance in catalysis. Inosine was not able to protect enzyme against N-bromosuccinamide modification. Extrinsic fluorescence studies revealed that tryptophan might not be involved in substrate binding.Results of studies indicated that tryptophan residue is essential for catalysis and not required for substrate binding.

Biochemical and biophysical properties of PfPNP enzymes were studied in dilute buffer system, which are far from the crowded physiological condition of cell. The enzyme kinetics and refolding of (PfPNP) under crowded conditions showed that enzyme catalytic efficiency was inversely affected in the presence of polyethylene glycols and Dextran whereas it was increased in the presence of osmolytes.The knowledge about modulation of inherent properties of this enzyme in crowded environment will be helpful in better understanding of this drug-target enzyme and in further inhibitor design.

POSTER

Oxazolo[4,5-b]pyridine-2-one - 1,2,3-triazole Conjugates as Novel GSK-3 Inhibitors

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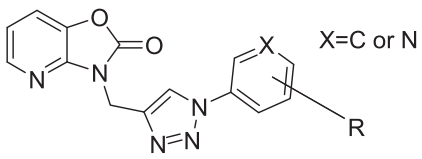
Glycogen synthase kinase (GSK-3), a multifunctional serine/threonine kinase has attracted much drug discovery attention in the recent past. It is a key regulator of various signaling pathways involved in diverse physiological processes. In many of these pathways, GSK-3, when dysregulated, has been implicated in the development of human diseases such as diabetes, Alzheimer's, cancer, bipolar disorder, etc, making it a tempting therapeutic target [1]. Thus its inhibition may represent a viable strategy to develop novel medicinal entities for treatment of such diseases.

Recently, oxazolo-pyridines have been reported as potent GSK-3 inhibitors and have drawn more attention [2]. So far not much work has been done on this scaffold and there is a scope for the development of more potent inhibitors from this ligand. Therefore we focused our attention on the development of novel oxazolo[4,5-b]pyridine-2-one based GSK-3 inhibitors by combining 1,2,3-triazoles to oxazolo[4,5-b]pyridine-2-one through a click chemistry approach. A library of 21 compounds encompassing oxazolo[4,5-b]pyridine-2-one and 1,2,3-triazoles under one construct has been synthesized by conjugating them through a methylene bridge. The synthesized compounds are being screened for their GSK-3β inhibitory activity. The potent compounds obtained from the screening results would be evaluated for their *in-vitro* anti-cancer activity against human cancer cell lines.



Key words: serine/threonine kinase , signaling pathways, click-chemistry
Acknowledgement: The author acknowledges HNF for financial support.

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POSTER

Novel 3,5-bis(arylidiene)-4-piperidone Based Monocarbonyl Analogues of Curcumin: Anticancer Activity Evaluation and Mode of Action Study

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Curcumin, a well-known yellow crystalline natural product isolated from the rizhomes of Curcuma longa L exhibits various pharmacological activities including anti-inflammatory, antioxidant, antibacterial, anti-HIV and anticancer [1]. Inspite of its safe toxicological profiles, curcumin itself is not a good candidate for further clinical development because of its poor solubility, low systemic bioavailability, undesirable absorption and rapid metabolism when tested *in vivo*. Detailed pharmacological studies confirmed that the central β-diketone functionality of curcumin is a substrate for liver aldoketo reductases which lead to rapid metabolism of curcumin [2]. In order to improve bioavailability of curcumin, several types of analogues have been prepared and among them diarylidenyl-piperidone (DAP) based curcumin derivatives are known to exhibit potent anticancer activity and metabolic stability [3]. In recent years, the concept of molecular hybrids has gained attraction, in which two or more pharmacophores are covalently attached to each other in anticipation of improved activity. Sulphonamide moiety connected to aromatic/hetrocyclic/aliphatic ring is an important pharmacophore for the generation of new drugs. Therefore keeping in mind the concept of hybrid molecules and in continuation of our on-going efforts in this area [4-7], we decided to make molecular hybrids consisting of 3,5-bis(arylidene)-4-piperidone and aryl sulphonamide moiety. Representative analogues were tested on NCI 60 cancer cell line panel and showed cytostatic potential at sub-micromolar concentrations against several cell lines specially against leukemia (upto 34 nM) and colon cancer. These results motivated us for mode of action studies which point towards apoptotic cell death via DNA fragmentation and caspase activation.

Mechanism of action studies of piperidone-sulphonamide curcumin conjugates

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POSTER

Involvement of Contact Ion Pair Formation for the Heterolysis of C-O Bond During Copper(I)-Promoted ATRC in Unusual Benzannulation Reactions

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Copper(I)-mediated halogen atom transfer radical cyclization (HATRC) reactions of allylaryl trichloroacetates produced benzannulated chloroarenes, symmetrical biaryls along with reductive dechlorination products. Mechanism via 8-*endo-trig* radical cyclization of the allylaryl trichloroacetates was proposed. The formation of the final products chloroarenes and biaryls were explained by the loss of the ester group as carbon dioxide through the intermediate formation of contact ion pair (CIP). Thus, the mechanism extended from simple radical to radical ionic.

***Keywords*:** CIP, Decarboxylation, HATRC, CuCl/bpy, Benzannulation.

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POSTER

Ethyl 2-(*tert*-Butoxycarbonyloxyimino)-2-Cyanoacetate (Boc-Oxyma) as Coupling Reagent for Racemization free Peptide Synthesis

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Amides are one of the versatile functional groups in realm of organic synthesis and biomolecules [1]. Amides derived from the reaction of amino acids are important as they constitute a significant part of the chemical space of biologically active compounds [2]. To date, voluminous coupling reagents have been developed for peptide synthesis. The most of the effective coupling agents are those that not only afford fast reaction rates and high yields, but also the suppression of any undesired racemization. We developed Boc-Oxyma [3]. as an efficient new coupling reagent for racemization free amidation and peptide synthesis that uses equimolar amounts of acids and, amines or amino acids respectively by solution phase as well as solid phase peptide synthesis. We synthesized the Hexapeptide sequence NFGAIL, known to be the core sequence responsible for the initiation of aggregation of the Amylin peptide that leads to type 2 diabetes using Boc-Oxyma as coupling reagent by SPPS. Which is similar to the well known coupling agent COMU, HATU and HBTU in terms of its high reactivity and mechanism of action However, it is much easier to not only prepare, but also to recover and reuse, thereby generating far less chemical waste.

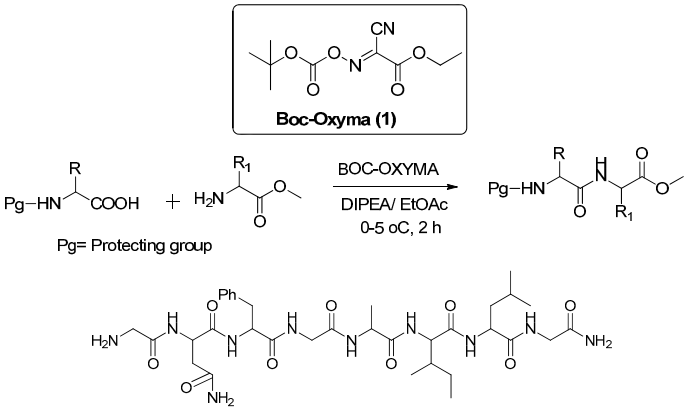

Figure 1.Synthesis of GNFGAIL-NH_2 Peptide by solidphase by using Boc-Oxyma (1)

Table 1. Comparison of % yield and % racemization of a tripeptide (Z-Gly-Phe-Val-OMe) synthesized using various coupling reagents and with Boc-Oxyma

Entry	Peptide	Coupiling Reagent	yield (%)	Racemization (%)
1	Z-Gly-Phe-Val-OMe	HATU	90	1.56
2		HDMA	90	0.65
3		HBTU	89	5.90
4		HDMB	90	2.90
5		**Boc-Oxyma**	90	0

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POSTER

Synthesis, Crystal Structure and Antimicrobial Study of Cu(II) Complexes of Schiff Base Ligands Derived From 4-Formylpyrazolone

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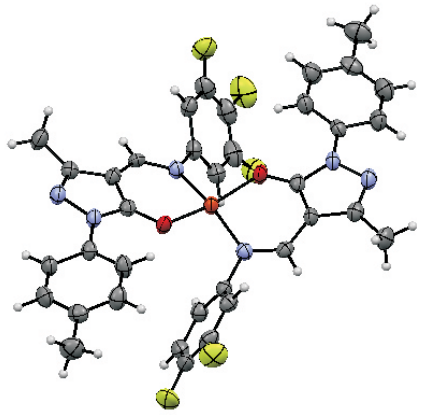
Schiff base ligands of 4-formylpyrazolone were synthesized and characterized by ^{1}H NMR, elemental analyses, Mass spectrometry and IR spectroscopy. The geometry of one of the Schiff base was also determined by single-crystal XRD technique. Copper(II) complexes of these Schiff bases were synthesized and characterized by molar conductivity, IR, UV–Visible, ESI Mass, magnetic measurement, TG-DTA studies and single-crystal XRD. Single-crystal XRD of complexes reveals that the two *O,N*-chelating Schiff base ligands occupy the equatorial plane of the Cu(II) complex, creating a square planer geometry. Thus, the two ligands form two six-membered chelating rings with the metal center. The Schiff base ligands and their metal complexes have been tested for antimicrobial activity against Gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis* and Gram-negative bacteria; *Escherichia coli* and *Pseudomonas aeruginosa*.



Crystal structure of Cu(II) complex of Schiff base ligand.

POSTER

In-Vitro Antioxidant Activities of Three Genders of Minor Millets

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We evaluated the *in-vitro* antioxidant properties and phytochemical constituents of the crude extracts of 1% acidified methanolic, 95% ethanolic, and water for three genders of Minor millets *viz*. *Echinochloa crus-galli*, (Bhagirath [1], Husrve et al. [2]) *Panicum sumatrense*, (Kim et al. [3], Aruachalam et al. [5]) *Panicum miliaceum L* (Reddy et al. [4], Barik [6]).

The antioxidant activity of the extracts was measured using scavenging of 2, 2'-Diphenyl-1-picrylhydrazyl hydrate (DPPH), bleaching of b-carotene and % inhibition of H_2O_2. The contents of flavonoids and total phenolic compounds could be correlated with the antioxidant activities observed for minor millets. Our finding suggests that crude extracts of three millets contains potential antioxidants, which could be isolated in pure from to use as natural antioxidants having no side effects and could be tested as drug candidate against oxidative damaged by free radicals.

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POSTER

Activity Guided Isolation and Characterization of Antihyperglycemic Agents from Oplismenus *burmannii* and their In-vitro and Docking Studies

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Bioactivity guided separation of combined *n*-hexane and chloroform extracts of *Oplismenus burmannii* resulted in the isolation and characterization of five new glycoglycerolipids, (2S)-1,2,6'-tri-*O*-hexadecanoyl-3-*O*-β-D-galactopyranosyl glycerol (**1a**), (2S)-1,2,6'-tri-*O*-[(9Z,12Z)-octadeca-9,12-dienoyl]-3-*O*-β-D-galactopyranosyl glycerol (**1b**), (2S)-1,6'-di-*O*-[(9Z,12Z)-octadeca-9,12-dienoyl]-3-*O*-β-D-galactopyranosyl glycerol (**2b**), (2S)-1,6'-di-*O*-[(9Z,12Z,15Z)-octadeca-9,12,15-trienoyl]-3-*O*-β-D-galactopyranosyl glycerol (**2c**), and (2*S*)-1,2-di-*O*-[(9Z,12Z)-octadeca-9,12-dienoyl]-3-*O*-(6-sulpho-α-D)-quinovopyranosyl glycerol (**3b**) along with five known glycoglycerolipids (**1c**, **2a**, **3a**, **3c** and **4**), a cerebroside (**5**) and three monoacylglycerols (**6a-c**). The isolated compounds, **1-5** were *in-vitro* tested for their antihyperglycemic potential in terms of increase in 2-deoxyglucose uptake in L6-GLUT4*myc* myotube cells. The results showed that compounds, **1-5** were showing percentage increase in the glucose uptake by 52.39 ($P<0.05$), 49.76 ($P<0.05$), 27.65, 49.33 ($P<0.05$), 49.81 ($P< 0.05$) at concentration of 10 µg/mL and 71.28 ($P<0.001$), 74.27 ($P<0.001$), 49.81 ($P<0.05$), 76.16 ($P<0.001$), 74.27 ($P<0.001$) at concentration of 25 µg/mL concentrations respectively. The percentage increase in the glucose uptake by the standard antidiabetic drug Rosiglitazone was 58.8% at the concentration of 10µM. Further, docking studies of compounds, **1a-6c** on peroxisome proliferator activator receptor (PPAR) γ showed binding affinities of compounds **1a-c**, **4** and **5** between (-4.9) to (-5.6) kcal mol^{-1}, which were almost equal to that of the standard antidiabetic drug Rosiglitazone (-5.6 kcal mol^{-1}). Further work on optimization of the anti-diabetic lead is under progress.

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POSTER

Combined Use of Pharmacophore Mapping, Homology Modeling Together With Virtual Screening and Docking Study for Identification of Sirt1 Activators

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Metabolic impairment is one of the possible reasons for pathogenesis of growing number of diseases including type-2 diabetes. Illustration of sirtuins1 (SIRT1) as new regulators of many metabolic aspects makes SIRT1 as fascinating drug targets for the treatment of type-2 diabetes. Herein, we described pharmacophore-based virtual screening, homology modeling combined with docking study as a rational strategy for identification of novel hits or leads as SIRT1 activators. Pharmacophore models of SIRT1 activators were established using the DISCOtech and refined with GASP module. The best pharmacophore model consisted of one hydrogen bond acceptor (HBA), one hydrogen bond donor (HBD) site and three hydrophobic (HY) features. The pharmacophore models were validated through receiver operating characteristic (ROC) and Güner-Henry (GH) scoring methods, which indicated that the model-2 was statistically valuable and reliable in identifying SIRT1 activators. Pharmacophore model as a 3D search query was searched against Zinc database. Several compounds with different structures (scaffolds) were retrieved as hits. The X-ray crystal structure of SIRT1 is yet not available; thus homology model of *Human* SIRT1 was constructed, followed by identification and characterization of binding sites, there by assessing druggability of the proteins. Molecules with a Q_{fit} value of more than 82 and two other known SIRT1 activators were docked in the SIRT1 modeled protein to further explore the binding mode of these molecules. The hits reported here showed good potential to be SIRT1 activators.

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POSTER

Coal Depolymerising Activity and Haloperoxidase Activity of Manganeseperoxidase

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Mn peroxidase has been purified to homogeneity from the culture filtrate of a new fungal strain *Fomes durissimus* MTCC-1173 using concentration by ultrafiltration and anion exchange chromatography on diethylaminoethyl (DEAE) cellulose. The molecular mass of the purified enzyme has been found to be 42.0 kDa using SDS-PAGE analysis. The *Km* values using $MnSO_4$ andH_2O_2 as the variable substrates in 50mM lactic acid-sodium lactate buffer pH 4.5 at 30 C were 59μM and 32μM, respectively. The catalytic rate constants using $MnSO_4$ and H_2O_2 were 22.4 s^{-1} and 14.0 s^{-1}, respectively, giving the values of *k*cat*/Km* 0.38 $\mu M^{-1}s^{-1}$ and 44 $\mu M^{-1}s^{-1}$, respectively. The pH and temperature optima of the Mn peroxidase were 4 and 26 C, respectively. The purified MnP depolymerises humic acid in presence of H_2O_2. The purified Mn peroxidase exhibits haloperoxidase activity at low pH.

POSTER

Ascorbate Peroxidase of Musa Paradisiaca Stem Juice: A Convenient Enzyme for Sulfoxidation of Methyl Phenyl Sulphide

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Enantiometrically pure sulphoxides are important synthons in asymmetric synthesis .The sulphoxide functional group is involved in different biological activities and optically pure sulphoxides are of great importance[1]. Several heme peroxidases[2,3] catalyse the enantioselective sulphoxidation of alkyl aryl sulphoxides. So for only pure heme peroxidases have been used for this transformation. This communicatin reports a crude preparation of Ascorbate peroxidase from Musa paradisiacal stem which can be conveniently prepared and used for the transformation of methyl phenyl sulphide to its sulphoxide in 96% yield.

The method for the preparation of ascorbate peroxidase from the stem of Musa paradisiaca has been developed. The enzymatic characteristics like Km for the substrates ascorbate and H_2O_2, pH and temperature optima of the enzyme have been determined. The enzymatic transformation of methyl phenyl sulphoxide has been demonstrated. The result of the above studies will be presented.

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POSTER

3D-QSAR Studies of Dipeptidyl Peptidase-4 Inhibitors Using Various Alignment Methods

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Dipeptidyl peptidase-4 (DPP-4) is one of the most attractive and novel target in the treatment of type 2 diabetes [1]. In view of this development, a critical analysis of structural requirements of the DPP-4 inhibitors was performed to identify the significant features toward design of selective inhibitors. Three-dimensional quantitative structure–activity relationship (3D-QSAR) analyses were carried out on 36 reported quinoline and isoquinoline derivatives as DPP-4 inhibitors [2,3]. The studies include Comparative Molecular Field Analysis (CoMFA) and Comparative Molecular Similarity Indices Analysis (CoMSIA) using different alignment methods using SybylX1.3 [4]. The significant CoMFA and CoMSIA models were obtained by means of Distill rigid body alignment of 27 training set molecules, with cross-validated coefficients (q^2) of 0.812 and 0.793, respectively, and conventional coefficients (r^2) of 0.998 and 0.988, respectively. Validation by test set of 9 molecules gave satisfactory predicted correlation coefficients (r^2_{pred}) of 0.772 and 0.701 for CoMFA and CoMSIA models, respectively. Analysis of CoMFA and CoMSIA contour maps helped to identify the structural requirements of inhibitors, with implications for the design of the next generation quinoline & isoquinoline derivatives as DPP-4 inhibitors for the treatment of type-2 diabetes.

Acknowledgment: Authors would like to thank GUJCOST, Gandhinagar for providing financial support to carry out this research work.

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POSTER

The Structure and Stability of Insulin in Ammonium and Imidazolium-Based Ionic Liquids

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The self-aggregation and thermal instability of insulin (*In*) was considerably controlled in the presence of ammonium-based protic ionic liquids (PILs). The thermal stability of *In* in PILs was observed using fluorescence and absorption spectroscopy of the Tyr environment of the biomolecule. Additionally, from circular dichroism (CD) measurements, we observed the shift in the wavelength towards lower values in the presence of PILs, which indicates the formation of monomers of *In*, further evidently supported by dynamic light scattering (DLS) measurements. Surprisingly, it is the monomeric form of the *In* that exists in the active form. For the first time, ammonium-based PILs have been shown to be novel solvents for *In*, which prevent it from associating into an inactive form and also stabilizes *In* against thermal influence. On the other hand, imidazolium-based ionic liquids enhanced the β-sheet structure in *In*.

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POSTER

Development of Anticancer Polymeric Nano-Colloids Using Traditional Ayurvedic Component "Trikatu" With Curcumin as Natural Bioenhancer

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Curcumin, a major active constituent isolated from curcuma longa, has a wide range of biological activities like antioxidant, anti-inflammatory, ant proliferative, anticancer. Even though being such a potential molecule its use is restricted because of its poor aqueous solubility and poor systemic bioavailability. Present study was emphasized on the development of polymeric nanoparticles of pure curcumin (CMN) with trikatu (a major component of traditional ayurvedic formulations containing natural bioenhancers) using poycaprolactone (PCL) by nanoprecipitation method. Curcumin incorporated in PCL nanospheres using stabilizer tween 80 and pluronic F-68 was found to have comparatively high encapsulation (70%) with particle size 203.2±2.9 nm and 215.12 nm with zeta potential of -26.2±2.6 mv and -22.4±1.9 mv. The developed formulations had incredible antioxidant potential and also capable of lowering the viability in PC3 cell line and 8 times increased response of CMN was observed in Curcumin-trikatu-PCL formulations than CMN alone against prostate cancer and also enhance the stability of the curcumin formulation. The curcumin-trikatu-PCL formulations showed a strong antioxidant activity by inhibiting reactive oxygen species (ROS) 4 times more effectively than CMN, thus protect from ROS (associated with various carcinomas and inflammation during disease). The formulation was found stabile for 12 weeks in respect to particle size and size distribution.

POSTER

Chemoselective Multicomponent Novel Route to Coumarinyl Dihydropyrimidine and 3-Amino-1, 3-Thiazine

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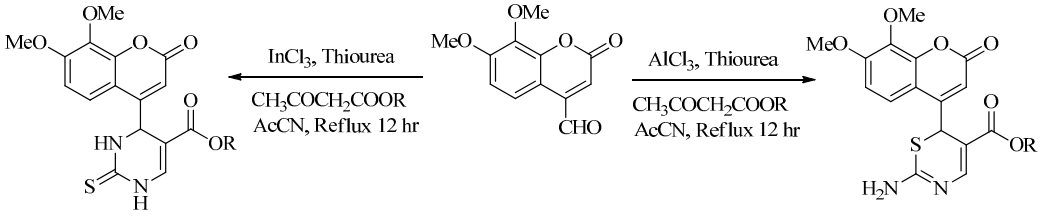
Multicomponent reactions (MCRs) represent a powerful strategy in diversity-oriented synthesis of heterocycles, like 1,3-thiazines and DHPM(S) which are compounds of outstanding importance for pharmaceutical industries. Coumarin is starting material for these heterocyclic compounds which possess pharmacological and therapeutic properties depending upon its pattern of substitution. 1,3-Thiazines and their derivatives possess very good biological activities, including antibacterial, antitumor, insecticidal and fungicidal activity. The alkyl 2-amino-6-aryl-1,3-thiazin-5-carboxylate scaffold has received a rare attention despite its close structural similarity to the alkyl 4-aryldihydropyrimidin-2-thione-5-carboxylate [DHPM(S)] which has well documented pharmacological properties.

Here we are presenting the synthesis of some novel coumarin-based thiazines(I) and DHPM(S)(II) analogs using $AlCl_3$ and $InCl_3$ respectively as lewis acid by multicomponent reaction of coumarin aldehyde, thiourea and different alkyl carboxylates in acetonitrile.



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POSTER

Physico-Chemical Characterization of *Acacia Nilotica* Gum Exudates Collected From Different Agro-Climatic Zones

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Physico-chemical properties are the measurable physical and chemical characteristics by which the interaction with other systems takes place and they also collectively determine the quality, suitability, applicability and their end-uses. In gums, these properties are directly influenced by the botanical type, age, location, nature of the soil and the climatic conditions around the resource gum tree. Gums from different species exhibit characteristics that are intrinsically different. Even within the same species, different varieties produce gums with different characteristics. Besides botanical source, the season of collection, harvesting and post-harvest handling also affect the quality. Therefore, physico-chemical characterization of gums is an essential step towards establishing their suitability for industrial applications. Twenty *Acacia nilotica* gum exudates were collected from ten Indian States covering five agro-climatic zones. The gum exudates were characterized by determining their solubility, pH, moisture %, total color difference (ΔE), ash %, swelling index (%, v/v), elemental (CHNS) analyses, specific rotation [a], heavy metals, tannin content and viscosity. The highest moisture % (6.33) was found in the exudates collected from Amritsar (Punjab) falling in the Trans Gangetic plain region and the lowest (2.21 %) in the exudates collected from Sitapur (Uttar Pradesh) in Upper Gangetic plain region. The highest ΔE (29.36) was found in the exudates of IINRG Farm, Ranchi, falling in the Eastern plateau and hills region and the lowest (4.99) in the case of collection from Amritsar (Punjab). None of the gum exudates showed any swelling property even after 48 hrs. The highest ash % (1.91) was found in the gum exudates collected from Amritsar (Punjab) and the lowest (0.68 %) from Gondia (Maharashtra). The quantitative elemental analysis showed that the gum contained low percentage of nitrogen indicating amino acid cross linkage as also the ratio of carbon to hydrogen, which was over 8:1 showing polysaccharide composition. All the gum exudates were found to be dextrorotary ranging from +44.57 to +86.28. Amongst heavy metals, Ni was found to be nil in all the gum exudates, whereas other metals viz. Fe, Cd and Pb were found to be within limit. The highest tannin content (12.25 mg/g) was found in the gum exudates collected from Balaghat (M.P.) and the lowest (0.125 mg/g) in the gum exudates collected from Jodhpur (Raj.). Twenty percent solution of exudates from Jabalpur (M.P.) at 100 RPM, showed highest viscosity (77.1cP) in comparison to other gum exudates.

POSTER

Evaluation of *Annona Squamosa* Extracts for Anti-Inflammatory Activity and Wound Healing Potential

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Ethnopharmacological relevance: *Annona squamosa* L. is extensively used in Indian systems of medicine for its medicinal properties. The aim of this study was to evaluate the antioxidant activities and the potential anti-inflammatory activity of *A. squamosa.*

Material and methods: Various extracts of *A. squamosa* were prepared and screened for their 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging capacity and antioxidant activity using the NO inhibition assay and inhibition of erythrocytes haemolysis. These extract were subjected to antibacterial assay and NO inhibition on macrophages J774. Pure extracts were used for in vivo wound healing experiment. Identification and quantification of marker compounds in extracts were done after fractionation through Flash chromatography by Camag HPTLC.

Results: The present study has demonstrated that the extracts have properties to render them capable of promoting accelerated wound healing activity compared with placebo control, which was evidenced by decrease in period of epithelization, increase in rate of wound contraction. There was no significant hemolytic activity against rat erythrocytes. The antibacterial activity for gram positive bacteria was observed in all extracts (hydro alcohol, ethanol with pronounced effect in 50% hydroalcoholic extract of *A. squamosa* followed by ethanol extract of *A. squamosa*. The extracts of *A. squamosa* (2mg/ kg body weight) were given to individual groups were screened for its effect on bleeding time (BT), clotting time (CT), prothrombin time (PT), platelet count and platelet adhesion in albino rats after 1-day, 7-day , 14 day and 21-day treatment. The *A. squamosa* showed period of epithelisation of 21day while comparison to this the control had the wound area mm^2 (% of wound contraction) 175 ± 2.86 (67.71) on 21st day. The HPTLC profiling indicate the reasonable content of all three ursolic acid, lupeol and beta sitosterol markers in blood coagulation profile of the plant.

Conclusion: Thus results shown by *A. squamosa* explain that the sitosterol, lupeol and urosolic acid present in *A. squamosa* extract synergize its antioxidant, anti- inflammatory and wound healing potential of *A. squamosa*.

POSTER

1,3-Dipolar Cycloaddition Based Multicomponent Reactions for the Green and Efficient Synthesis Of 1,2,3-Triazoles and Spirooxindoles based Molecular Hybrids

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1,3-Diploar cycloaddition based multicomponent reactions (MCR) which involve click chemistry when combined with some condensation reactions generate highly diverse five-membered heterocyclic compounds conjugated to other heterocyclic units from readily available starting molecules. Oxindoles structural units form the core of many alkaloids and natural products which exhibit important biological activities. They display a fascinating array of biological applications such as antidiabetic, antimycobacterial, antimicrobial, anticholinesterase, and anticancer etc. Five-membered [1,2,3]-triazoles display biological activities such as neuroprotective agents, anticancer, antitubercular, and antimicrobial.

Two novel series of spirocyclic pyrrolidine and/or oxindole linked 1,2,3-triazole derivatives have been synthesized using multicomponent environmentally benign protocols coupled with click chemistry. Spirocyclic pyrrolidine linked 1,2,3-triazoles were synthesized by one pot four-component reaction of 5-arylidene-3-(prop-2-ynyl)thiazolidine-2,4-dione, isatin, sarcosine and substituted azides. While spirocyclic oxindole linked 1,2,3-triazoles derivatives were synthesized by one pot four-component reaction of propargylated isatin, arylaldehydes, 1,3-dicarbonyl and substituted azides using green protocols. Anti-microbial, anti-fungal and photophysical studies of these compounds were also carried out.

POSTER

Syntheses, Pharmacokinetic and Biological Evaluation of Borrelidin Analogues for Inflammation

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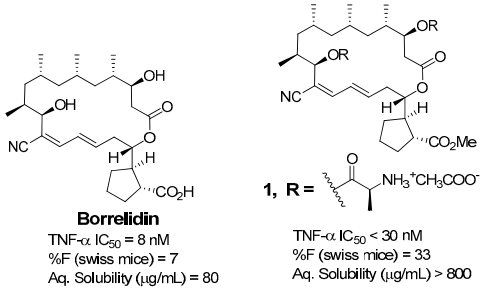
Borrelidin, a structurally unique 18-membered macrolide, isolated from a cultured broth of *Streptomyces rochei* in 1949 [1] is a very potent TNF-α inhibitor, with IC_{50} value of 7 nM in freshly isolated synovial and human peripheral blood mononuclear cells [2]. TNF-α inhibitors are currently in use for autoimmune disorders and the major obstacle to Borrelidin's clinical development is its poor bioavailability (%F = 7 in swiss mice) and dose-limiting toxicity (p.o. route LD_{50} in mice = 16.4 mg/kg, MTD in nude mice 5-15 mg/Kg, i.v.) [3]. Chemical syntheses of analogues, harnessing the carboxylic acid at C22 and the hydroxyl groups at C3 and C11 were carried out and bis-alaninate ester **1** was found to have an improved bioavailability of 33% in swiss mice, while still being a potent TNF-inhibitor (IC_{50} <30 nM) and a ten-fold better aqueous solubility as compared to Borrelidin.



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POSTER

Synthesis, Design and Evaluation of ^{99m}Tc-G(KDP)$_2$ as Neuroimaging Biomarker

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Aim: The shortest peptide domain of γ1 laminin that promotes neurite outgrowth of human embryonic neurons is a tripeptide KDI. The rationale of this study was to obtain novel modified KDI analogue for neuroreceptor imaging by convenient solid phase synthesis. The laminin has an important role in the neuronal development and treatment of neurodegenerative disorders. We have modified the KDI tripeptide by replacing the terminal amino acid with proline (P). It would prove to be an attractive strategy to take advantage of laminin activity for regeneration in the central nervous system for diagnostic purposes.

Methods: We have designed and synthesized novel glutamic acid-bis(KDP) peptide analogue and introduced N_2S_2 system for radiocomplexation with ^{99m}Tc. The designed KDP tripeptide was synthesized by Fmoc solid phase strategy using rink amide resin on solid phase. This tripeptide was further bisfunctionalised with α and γ carboxylic acid ends of glutamic acid. The primary amine end of glutamic acid was functionalised with cysteine-glycine-cysteine based tripeptide in order to suitably radiolabel the resulting peptide with ^{99m} Tc in aqueous solution at pH 7-8.

Results: The cys-gly-cys based G(KDP)$_2$ was prepared with more than 90% yield by solid phase synthesis. The peptide was characterized by mass spectroscopy and confirmed by the molecular ion peak at 1089.25g/mole. The compound has been purified by HPLC. G(KDP)$_2$ binds with ^{99m}Tc with high specific activity and the radiolabeling efficiency was found to be >95% and the stability in serum indicated that ^{99m}Tc remained bound to the drug upto 24h.

Conclusions: We have successfully optimized, synthesized and characterized the bis peptide G(KDP)$_2$ on solid phase. After its biological evaluation, the synthesized peptide scaffold can prove to be an excellent diagnostic agent.

POSTER

Novel Seco-artemisinin Analogues: Design, Synthesis and *In Vivo* Antimalarial Assessment in Search for Putative Antimalarial Structural Motif via Pruning of Artemisinin Framework

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The discovery of artemisinin **1**, as the active principle of the Chinese traditional drug *Artemisia Annua*, is a major milestone in malaria chemotherapy.[1] Artemisinin and its derivatives e.g, dihydroartemisinin **2**, artemether **3**, arteether **4** and artesunic acid **5**, owe their activity to peroxy group present as 1, 2, 4-trioxane in their molecular structures (Fig. 1).[2,3]

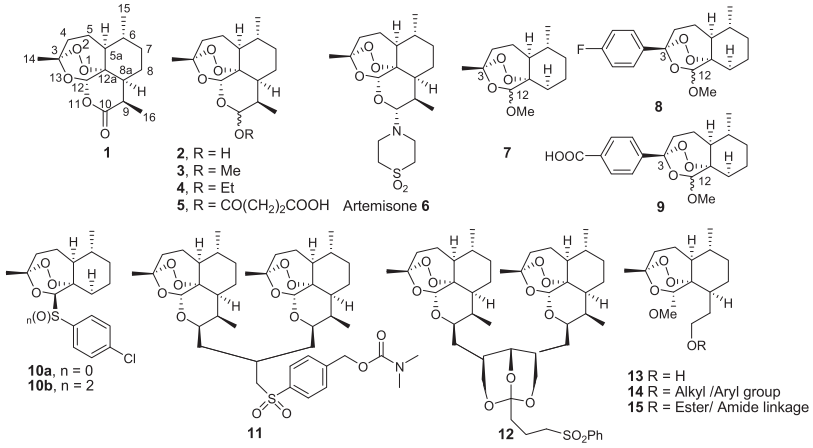

Figure 1. Artemisinin **1** and its clinically useful derivatives **2-5** and other promising analogs **6-15**.

Since its discovery, several highly potent artemisinin analogues **6-15** have been prepared, by different group,[4] including our group,[5] by either incorporating biologically privileged substructure at various positions, especially at C-3, C-9 and C-10 or by making artemisinin dimer (Fig. 1). It is interesting to know that excellent antimalarial activity have been shown by only those derivatives in which the tetracyclic core of artemisinin is almost wholly preserved. So far, few reports are available for the synthesis and structure-activity relationship studies of seco-artemisinin analogues. There had been no study done by any group directly on artemisinin.

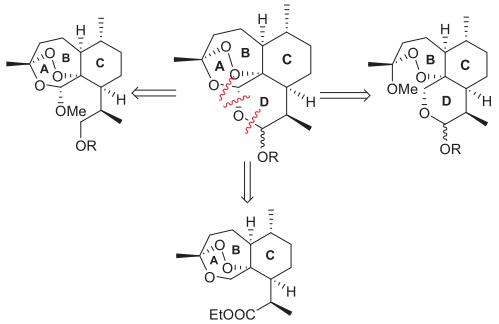

Figure 2. Prototypes of seco-artemisinin analogs.

POSTER

Therefore, in order to better understand the putative antimalarial structural motif in artemisinin and to examine the cause for showing intrinsic antimalarial property in artemisinin, for the first time, we have synthesized several seco-artemisinin analogues which were prepared by pruning of tetracyclic A, B and D rings of artemisinin (Figure 2). All these seco-analogues were assessed for their *in vivo* antimalarial efficacy against multi-drug resistant *P. Yoelii nigeriensis* in Swiss mice via i.m and oral routes. The details of the study will be presented.

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POSTER

Polyglycerol Based Dendritic Amphiphiles For Gene And Drug Delivery

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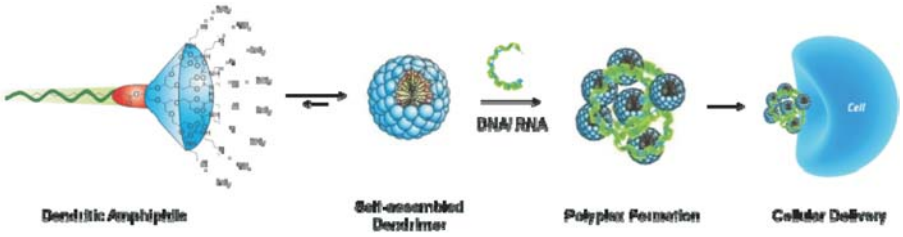
Development of non-viral vectors for the successful siRNA/DNA transfection of cells is still a great challenge in current research.[1] A number of effective gene vectors that can condense and protect oligonucleotides for gene transfection are currently being developed: free oligonucleotides and DNA are rapidly degraded by serum nucleases in the blood and also could not easily pass through the negatively charged cell surface barrier.[2] We have developed amine terminated multivalent polyglycerol dendron based amphiphiles with well-defined molecular structures.[3-6] The dendritic amphiphiles self assembles in aqueous solutions to form micellar aggragates which enhances the biological activity of the system. The structure–activity relationships with respect to the siRNA complexation, toxicity and transfection profiles were studied. Our findings revealed that a second generation amphiphilic dendrimer having eight amine groups on its surface and a hydrophobic C_{18} alkyl chain at the core of the dendron, acts as an efficient vector to deliver siRNA and achieve potent gene silencing by investigating the knockdown of luciferase and GAPDH gene activity in HeLa cells.[4] Our modular approach is highly flexible and shows successful in vitro siRNA transfection using dendritic amphiphiles.



Besides siRNA delivery applications of the dendritic amphphiles, we also have successfully used these types of nanocarriers for drug and dye delivery.[7]

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POSTER

Structural Characterization and Kinetic Regulation of Guanylate Kinase, a Nucleoside Monophoshate Kinase of Filarial Parasite *Brugia Malayi*

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Nucleotide metabolism is a key pathway in life cycle of any organism and Nucleoside monophosphate kinases (NMPKs) play an important role in supplying DNA and RNA precursors, hence considered important target protein. Guanylate kinase (ATP: GMP phosphotransferase, guanosine monophosphate kinase, EC 2.7.4.8) belongs to NMPK superfamily and is critical for the synthesis of GTP/dGTP since it catalyses reversible phosphorylation of GMP/ dGMP to its diphosphate form GDP/dGDP. It's inhibition will modulate the synthesis of nucleotides, which are indispensable for any organism. In addition to being a critical enzyme in the biosynthesis of GTP and dGTP, Guanylate kinase functions in the recovery of cGMP and is, therefore, thought to regulate the supply of guanine nucleotides to signal transduction pathway components.

In the present study *Brugia malayi* Guanylate kinase (BmGK) was characterized. BmGK differs from its host enzyme in its kinetic parameters and showed specificity for ATP as a phosphate donor and GMP as phosphate acceptor. Mg^{+2} is essentially required for enzyme activity in form of Mg-ATP and in addition to this free Mg^{+2} unbound to ATP was found to activate the enzyme while GTP at high concentration showed end product inhibition. Thus, Mg^{+2} and GTP play a regulatory role in catalysis of BmGK. Since understanding the folding and assembly of the parasite enzyme may be of importance in designing molecules that can impede association of the subunits, unfolding study of BmGK was done. Effect of denaturant was tested and it was found that BmGK was denatured at 4M Urea and 2M GdnCl while complete loss of activity was seen at 1.5M Urea and 80mM GdnCl suggesting that inactivation of BmGK is prior to its structural denaturation.. Molecular modelling study revealed that BmGK consist of three domains: the core, the lid and the NMP-binding domain like most NMP kinases. The core domain consists of a four-stranded β sheet flanked by α helices and also contains the P-loop which binds the ATP phosphate.

POSTER

Anomalous Chronoamperometric Response of Ferrocene in 1-Butyl-3-methylimidazolium hexafluorophosphate [BMIM][PF6] at Glassy Carbon Electrode: Theory and Experiment

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Electrochemical measurements were made on morphologically characterized glassy carbon rough electrode for ferrocene in 1-Butyl-3-methylimidazolium hexafluorophosphate[$BMIm^+$][PF_6^-]. Experimental validation of Kant's equation for chronoamperometric response of a rough electrode is performed in an ionic liquid medium. Equation includes the influence of electrode roughness through the power spectrum (PS) of surface. Ferrocene in [$BMIm^+$][PF_6^-] at the glassy carbon electrode shows reversible charge transfer. The influence of uncompensated solution resistance on chronoamperogram is also accounted in our theory. The PS obtained from SEM image shows a finite fractal nature of roughness. It provides the knowledge of electrode surface morphology through a fractal dimension (D_H), lower cutoff length scale (ℓ), upper cutoff length scale (L) and topothesy length (ℓ_T). Microscopic area (A) and Roughness factor (R*) are also extracted from chronoamperometric measurements on glassy carbon rough electrode.

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POSTER

DFT Study on the Thermal Decomposition of Protonated Formyl Azide and Diazoethanone

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The Schmidt and Wolff rearrangements are 1,2-rearrangement reactions where the substituent in azides and diazo compounds, respectively, migrates from one atom to another at the site of nitrogen expulsion. These rearrangement reactions are regularly used in organic chemistry for the synthesis of new organic compounds. In this work, the thermal Schmidt and Wolff rearrangement of protonated formyl azide (I) and diazoethanone (II), respectively, are studied in the gas-phase. The DFT approach has been used to examine the possible alternative mechanisms of the monomolecular conversions of I and II. 1,3-dipolar molecules like azides and diazo compounds generally exist in two conformations, s-cis and s-trans. It is believed that the former undergoes product formation via a concerted mechanism and the latter through a stepwise mechanistic pathway. On exploring the potential energy profile, we propose that these reactions should take place via the concerted mechanism only, since the potential energy surface of the non-concerted pathway is almost flat at the product side. This conclusion holds for the thermal decomposition of both I and II, and suggests that both proceed in a similar manner by the splitting off of nitrogen, followed by anion migration.

POSTER

Synthesis and Antioxidant Activity Evaluation of Chromenones

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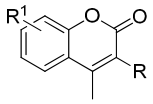
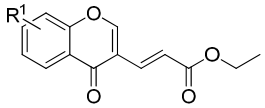
In vivo, lipid oxidation may play a role in coronary heart disease, atherosclerosis, cancer, and the aging process. Lipid oxidation occurs when reactive oxygen species (ROS) reacts with lipids in a series of free radical chain reactions that lead to complex chemical changes. Antioxidants, the compounds that can delay or inhibit lipid oxidation, when added to foods can minimize rancidity, and retard the formation of toxic oxidation products. [1,2]

Our group has been involved in the synthesis and antioxidant study of a wide variety of compounds.[3,4,5] Herein, the antioxidant activity (AOA) of two different classes of phenolic compounds *viz* chromen-2-ones and chromen-4-ones was systematically studied using DPPH, ABTS, FRAP, and *in vitro* lipid peroxidation inhibition assays. Among all the compounds studied for their anti-oxidant potential, some showed very good activity, even higher than the Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), a well-known antioxidant, which is used as standard in most of the testing methods. We have studied the effect of incorporation of phenolic and hydrophobic group on AOA. The synthesis and antioxidant activity results will be presented during poster presentation.





$R = H, C_2H_5, C_6H_{13}$
$R^1 = OH / (OH)_n$

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POSTER

Strong Visible Light Absorption Ability and Bio-imaging Applications of *fac*-Re(CO)$_3$ Based Dinuclear Metal Complexes

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Recently, *fac*-Re(CO)$_3$-based metal complexes have also been applied as fluorochromes for cell-imaging applications.[1] These complexes exhibit advantageous properties such as room temperature luminescence, photo-stability, large Stock's shift, high cellular uptake and low cell-toxicity. Hence the *fac*-Re(CO)$_3$-core containing transition metal based luminophores have emerged as better cell-imaging agents as compared with lanthanides or organic based bio-imaging agents. Herein, we present a series of amino-quinonoid containing *fac*-Re(CO)$_3$ based luminescent, dinuclear metal complexes that show strong ability towards visible light absorption and are capable of selectively staining the lysosomes in HeLa cells without being toxic towards the cells.

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POSTER

Design, Synthesis and Characterization of Fluroine-18 labelled MPP Derivative as Novel D_3 Receptor Ligand for PET Imaging

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Aim: D_3 receptors a subtype of dopamine receptor play major role in cognitive emotional functioning and behavioral action. However, conclusive behavioral studies have been hampered by the lack of highly selective D_3 agonists and antagonists. Methoxyphenylpipearazine (MPP) derivative possess high affinity and good selectivity for the human D_3 receptor. In an attempt to develop a novel PET radio ligand we have synthesized 1-(3-(4-(3-^{18}Fluoroprpyl)-1H-1,2,3-Triazol-1-yl)propyl)-4-(2-methoxyphenyl)piperazine.

Methods: The secondary nitrogen of (MPP) was functionalized using 1-Bromo-3-chloroprpane to give 1-(3-chloroprpyl)-4-(2-methoxyphenyl)piperazine with the yield of 65%, which was further converted into its corresponding azide (98%).The 4-pentyn-1-ol was tosylated to give pent-4-ynyl-4-methylbenzenesulfonate with the yield of 97%. The tosylated alkyne and MPP azide were conjugated via a triazol ring by click chemistry to give 3-(1-(3-(4-(2-methoxyphenyl)piperazin-1-yl)propyl)-1H-1,2,3-triazol-4-yl)propyl 4-methylbenzene sulphonate with the yield of 72%..

Radiolabelling: The tosylated click analogue was radio fluorinated with $K^{18}F$/Kryptofix at 110°C in FX-N GE Module to yield fluorinated ligand. The radiolabelling efficiency was found to be >98%.

Results: The synthesized ligand has been characterized by different spectroscopic technique (NMR and Mass). Radiolabeling efficiency was achieved more than 98% and the radio conjugate was found stable under physiological condition. Further biological evaluation is under progress.

Conclusion: We have developed short-lived ^{18}F ($t_{1/2}$=110min) in inhouse cyclotron and labelled MPP based derivative to yield 1-(3-(4-(3-^{18}Fluoroprpyl)-1H-1,2,3-Triazol-1-yl)propyl)-4-(2-methoxyphenyl)piperazine and fully characterized the ligand. This class of imaging agent holds promising future in imaging D_3 receptor for the treatment of neuropathological disorders.

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POSTER

Biocatalytic Route to the Synthesis of 3'-Amino-3'-deoxy-3'-*O*,4'-*C*-methylene-5-methyluridine

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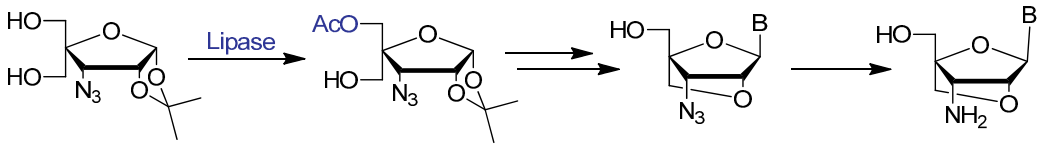
The synthesis of nucleoside analogues is of great interest because of their application as antiviral and antitumor agents. Further oligonucleotides involving modified nucleotides find their application as antisense and / or antigene agent to regulate targeted gene expression. 3'-Amino-3'-deoxynucleosides are component of oligonucleotide with N3'→P5' phosphoramidate linkage that are well known to have high binding affinity with ssRNA, ssDNA and dsDNA.

Herein, we report an efficient chemoenzymatic synthesis of 3'-amino-3'-deoxynucleosides a building block for the synthesis of N3'→P5' phosphoramidate oligonucleotides. The details of the synthesis will be presented in the poster.



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POSTER

Evaluation of Radioprotective Efficacy of DMA, a Bisbenzimidazole against Ionizing Radiation in Balb/c mice

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Radiotherapy is commonly being used in the treatment of cancer. For selective protection of normal tissues over tumor tissues, an effective and safe radioprotector is required. In our laboratory, Bisbenzimidazole (DMA), [5-(4-methylpiperazin-1-yl)-2-[2'-(3,4-dimethoxyphenyl)-5' benzimidazolyl]benzimidazole] has been evaluated for its *in vitro* radioprotection in mammalian cell lines. In the present study, we explored DMA for its *in vivo* antioxidant potential and radioprotective efficacy against whole body exposure in Balb/c mice to ionizing radiation. To evaluate the radioprotective efficacy, dose reduction factor (DRF) and endogenous spleen colony forming assay were performed. Optimum dose of DMA was selected as 300mg/kg body weight that showed maximum radioprotection. DMA oral administration at its optimum dose prior to whole body irradiation in mice, at a dose rate of 1.836 Gy/min reduced the radiation induced mortality and increased the survival. DRF was calculated by using the graded radiation dose (5, 6, 8, 9 and 10 Gy). DMA elevated radiation LD50/30 from 5.21 to 7.06 Gy, indicating the DRF of 1.35. DMA pretreatment also maintained the spleen index (spleen weight/body weight×100) and stimulates the endogenous spleen colony forming units (CFU) thus protects hematopoietic system. Radiation induced fall in endogenous antioxidant enzymes in liver tissue homogenates was prevented by DMA pretreatment and significant elevation of the endogenous antioxidant enzymes (GR, GST and SOD) and reduced glutathione in mice liver homogenates at 24h post irradiation was observed. DMA also protected the mice against radiation damage by significantly reducing the lipid peroxidation. In the above study, we have proved the in vivo radioprotective potential of DMA against ionizing radiation.

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POSTER

Quest for Novel Radioprotectors: A Boon to Medical Sciences

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Radiotherapy is one of the commonest regimens for cancer. However, effective use of ionizing radiation is compromised by the side effects of radiation induced damage to normal tissue. This necessitates the protection of normal cells surrounding the tumor, leading to the cognizance of agents that can protect against radiation induced damage termed *Radioprotectors.* Till date, amifostine is the only known clinically potent radioprotector that necessitates the search of novel safe and effective radioprotectors**.** A bisbenzimidazole analogue of Hoechst 33342 was synthesized and screened in our laboratory for its radioprotective efficacy in mammalian cell lines (BMG-1, U-87 and HEK cell lines). *In vitro* results revealed that it is less cytotoxic and better radioprotector as compared to parent analogue. Based on the above findings, a series of bisbenzimidazoles was synthesized and evaluated for their cytotoxicity in A549 (epithelial lung carcinoma) cell lines in search of novel potent radioprotector. Out of the 25 molecules screened, **NNVF** was found to be less cytotoxic and showed better radioprotection. This might be due to the presence of *N,N*-dimethylaminoethyl side chain which increases the charge on piperazine nitrogen and involved in its protonation thus enhances the interaction with DNA effectively.

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POSTER

Synthesis of Bengamide Analogues towards Anticancer Drug Discovery

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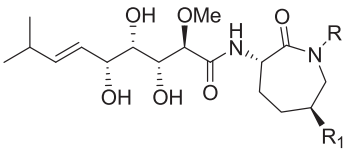
Bengamides are sponge-derived natural products of mixed biosynthesis (polyketides and amino acids); the first two members, isolated from Jaspidae sponges in coral surrounding Fiji island.[1] To this date, 19 members of these natural products have been identified; they share a common *syn*,*syn*,*anti*-polyol-containing C10 side chain and structural variation is found on the 3-aminocaprolactam moiety (Figure 1). Beyond the synthetic challenge, some of them (Bengamide A, B) have a great intrinsic value as they are endowed with nanomolar level of antiproliferative activity against various cancer cell lines, with striking differential cytotoxicity.[2] These interesting biological features, together with their limited supply from natural sources, have made bengamides popular targets for synthetic chemists.[3]

We have developed a modular synthesis of bengamide analogues from a common chiral pool. The key step in this approach is a cross-metathesis coupling of various terminal olefins and a common alkene bearing the required stereogenic centers of bengamides lateral chain, which was easily derived from α-D-glucoheptonic-γ-lactone. Structural variation of C10 side chain was also attempted by replacing the triol part with 1,2,3-triazole moiety and various substituted 3-aminocaprolactums were prepared.[4] The new bengamide analogues showed good bioactivity.



Bengamide A, R = H, R_1 = $OCO(CH_2)_{12}Me$
Bengamide B, R = Me, R_1 = $OCO(CH_2)_{12}Me$
Bengamide E, R = R_1 = H

Figure 1. Three natural bengamides

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POSTER

Development of Potent Antibacterial Agent targeting Topoisomerase IA

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Most bacterial pathogens are developing antibiotic resistance which is a major clinical problem these days. Novel bisbenzimidazole inhibitors of bacterial type IA topoisomerase are of interest for the development of new antibacterial agents that are impacted by target-mediated cross resistance with fluoroquinolones. In the present study we tried to develop antibacterial agent that targets Topoisomerase IA. PPEF (bisbenzimidazole) had most significant effect among the series of compounds synthesized against *E. coli* topoisomerase IA showing IC_{50} = 2± 0.005 μM. Interestingly these compounds did not show inhibition of *E. coli* DNA gyrase and human topoisomerase IB even upto 100 μM. In addition, PPEF has shown lowest MIC against most of the clinical, pathogenic, and resistant to commonly used antibiotics *E. coli* strains among 24 compounds evaluated. Docking studies have shown that the binding free energy of PPEF to *E. coli* topoisomerase IA-dsDNA complex was observed to be - 8.57 *Kcal* mol^{-1}. *In vivo* mouse systemic infection and neutropenic thigh model experimental results confirmed the therapeutic efficacy of PPEF, suggesting further development of this class of compounds as antibacterial agents. In continuation to our study we also tried to track the occurrence of Topoisomerase IA mutant genes. As per database Topoisomerase IA mutants against drug are not known till date. Thus we have done sequencing of Topoisomerase IA gene from the strains which have shown resistance against bisbenzimidazoles and/or those which were resistant to most of the standard antibiotics. As per our results there were no mutant found in these strains either. As per our query, how frequent the target can be affected with long term exposure to this class of compounds, we exposed DH5alpha (standard *E. coli* strain) to it continuously for one week. According to our study though these bacteria could develop resistance against bisbenzimidazole when exposed for long time but, the cause was not Topoisomerase IA mutations. This study illuminates new properties of bisbenzimidazole, which may be further modified to develop an efficient anti-bacterial agent targeting a stable gene Topoisomerase IA.

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POSTER

Biological Evaluation of HIV-1 Integrase Strand Transfer Inhibitors and Identification of Integrase Interaction with the Host Protein

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HIV-1 is responsible for millions of deaths every year by causing acquired immunodeficiency syndrome (AIDS). HIV requires the support of its host for the survival and propagation like any other parasite. The HIV-1 genome encodes nine open reading frames .Three of these encode the Gag, Pol, and Env poly proteins, which are subsequently proteolyzed into individual proteins common to all retroviruses. The three Pol proteins, PR (protease), RT (reverse transcriptase), and IN (integrase), provide essential enzymatic *f*unctions. Integrase(IN) performs different tasks that include cooperation in reverse transcription, nuclear import of preintegration complex, and integration of viral DNA into the host genome. IN is an attractive and validated target for anti-HIV drug design because of its crucial role in the viral life cycle and also because of the fact that, it has no cellular homologue in human. Several potent HIV-1 IN inhibitors have been identified based on β-diketo acid (DKAs). DKAs selectively inhibit the Strand Transfer reaction of IN and exhibit antiviral activity against HIV-1 infected cells in a manner consistent with the inhibition of integration. But only DKA moiety is not sufficient for the inhibitory action, an aromatic or heteroaromatic portion and carboxylic functionality also contribute to the definition of pharmacophore for HIV-1 IN inhibition because they allow the correct orientation of the molecule within the active site of IN through a series of interactions with the protein chain. The synthesized dihydroisoquinoline analogues were initially screened by (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTT) assay for cytotoxicity in the TZM-BL cell line and the anti-integrase activity was determined through direct biochemical assays(strand transfer assay and 3'processing assay), aiming to find potent and selective HIV-1 strand transfer INIs. In this series of compounds more than ten showed 70-91% inhibition at a concentration of 10μM with IC_{50} (600 nM to 11.82 μM) for strand transfer process of integration. In our study we have also identified a new host cell interacting factor for HIV-1 IN, SFPQ- a RNA splicing factor by cross linking, pull down and mass spectrometry. A better appreciation for the role of the host proteins should lead to better intervention for AIDS.

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