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Natural Product scaffolds in Drug Discovery – A case study

Structurally diverse & medicinally active natural products have proven to be effective drugs since many years. We'll use few intellectually analyzed online Chemistry/BioChemistry databases of drug patents and articles. These databases are created after decoding techno-legal descriptions of molecules, peptides, drug targets etc. Scientists involved in creation of these intellectually analyzed databases spend considerable amount of time to identify each disclosed molecule and its structure, enter them systematically in database(s) (which currently holds more than 77 million molecules) and assign their reported & published biological activity. Without whose aid, it's an impossible task to search and analyse published due to in-consistent nomenclatures, ambiguous ways of claim structure in patents & public literature.

These databases allow scientists to scan public literature by drawing skeleton structure of scaffold or upload a bio-sequence code and analyse it from various aspects such as properties, derivatives reported and create a matrix of relationships between searched molecules and reported therapeutic activities.

In order to demonstrate the same - we'll first zero-in on a few naturally occuring scaffolds, locate published literature around them and then further analyse and correlate scaffolds vis-à-vis it's therapeutic area & biological targets. We'll then focus on one of the scaffolds of interest and present a research landscape.

Take Home Message – A discussion on how intellectually analyzed online Chemistry/BioChemistry database of drug patents and articles can help research scientists to generate ideas, screen them, validate them, and plan the future research pathway

SHORT LECTURE

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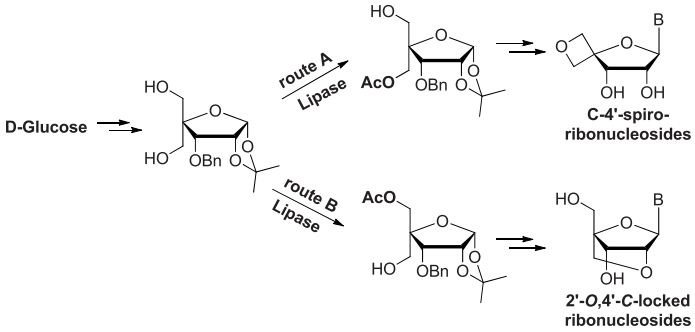
Chemo-enzymatic Access to Sugar Modified Nucleosides of Biological Importance

Nucleosides are among the most widely studied fundamental building blocks of biological system that are used as therapeutic agents to treat cancer, fungal, bacterial and viral infections. The ribose ring in the natural nucleosides experience rapid flipping between the two preferential conformations, *viz.* $C_{2'}$-*endo* (*S*-type) and $C_{3'}$-*endo* (*N*-type) due to the low energy barriers. The conformational behaviour of natural or modified nucleosides has demonstrated great importance in terms of their metabolic pathways and interactions with the biological targets. This has resulted in the synthesis of chemically modified nucleoside analogues having conformationally restricted pentofuranose ring. Prominent among these are the locked nucleic acid and spironucleosides. Since, the synthesis of clinically useful modified nucleosides is an arduous task and requires selective manipulation of multiple functionalities present in sugars or nucleosides, the use of biocatalysts in the synthesis of nucleoside analogues has become an attractive alternative over conventional chemical methods due to their selectivity and high efficiency. We have successfully used lipases for the synthesis of locked nucleic acid and C-4′-spironucleosides (Scheme 1).



Scheme 1. Chemo-enzymatic Synthesis of *C*-4′-Spiro- & Locked-ribonucleosides; B = nucleobase.

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SHORT LECTURE

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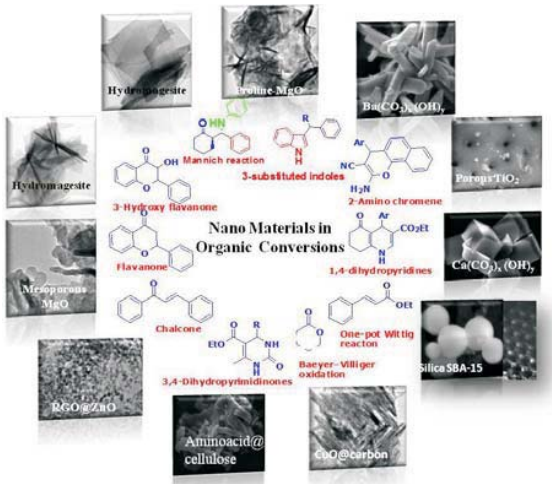
SHORT LECTURE

Development of Nano Materials as Recyclable Heterogeneous Catalysts in Organic Conversions

The development of nano structured materials as recyclable heterogeneous catalysts for the synthesis of organic intermediates or fine chemical is an important research topic for green and sustainable society.[1] Eventhough such heterogeneous catalysts unveiled lower activity as compared to homogeneous system, it avoids the difficulty of catalyst separation from f nal product and improves the economic and environmental benefits in industrial scale synthesis.[2] Thus, there is a need to develop efficient nano structured materials to explore applications in heterogeneous catalysis. Recently, we have reported the synthesis of flower like thin sheet morphology of hydromagnesite with surface area 45.5 m^2/g and used as a novel solid base catalyst in synthesis of flavanones, flavanols and 1,4-dihydropyridines in aqueous medium.[3] This opens up a new direction for further design of more efficient hydromagnesite material with high surface area 110 m^2/g. We presented here the synthesis and catalytic potential of various recyclable nano materials such as hydromagnesite, mesoporous MgO, aminoacid grafted on cellulose, barium/calcium carbonate hydroxides, mesoporous silica and TiO_2 based material, CuO/carbon sheet and RGO/ZnO composite[4] etc. in various organic reactions.



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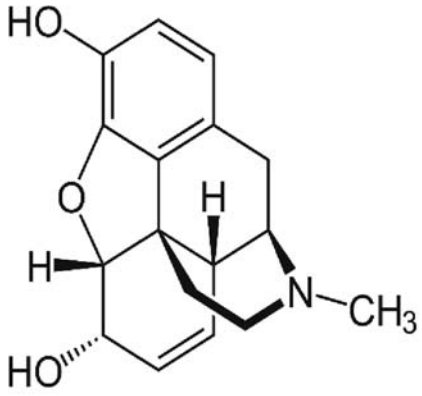
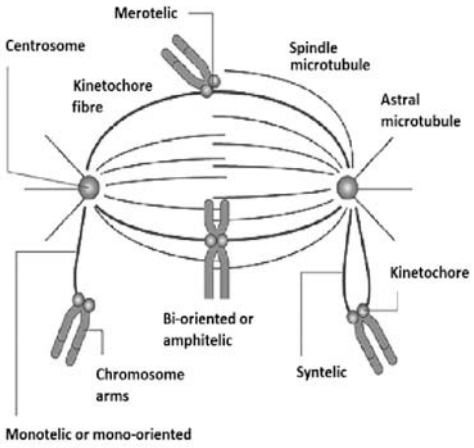
Poster





20th ISCB International Conference

Positively Charged PNA Analogue: A Novel Ethano Locked PNA (ethano-PNA)

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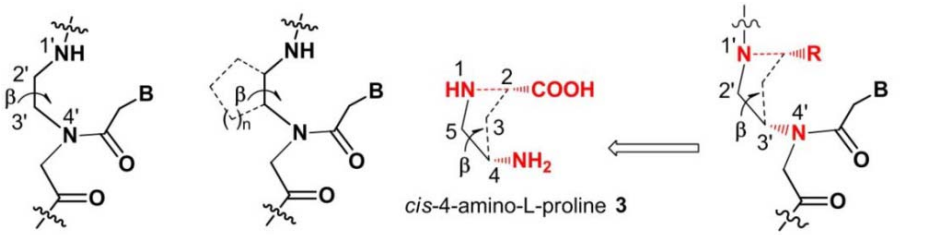
Peptide nucleic acid (PNA) [1] is one of the successfully designed oligonucleotide mimics, which act as excellent structural mimics of DNA/RNA and exhibit strong sequence specific binding with complementary oligonucleotide. PNA binds to ssDNA and ssRNA without any discrimination to form structurally diverse PNA: DNA and PNA: RNA duplexes due to acyclic flexible backbone. The major difference is in the preferred dihedral angle *θ* in the ethylene diamine segment (N1'-C2'-C3'-N4') of PNA units, which is 60°-70° in PNA: RNA and ~140° in PNA: DNA duplexes [2, 3]. The gauche interactions of the substituent amino group in 4-amino-L-proline and the vicinal ring nitrogen allow either C4-*endo*/*exo* conformations, depending upon the *R/S* stereochemistry at C4 centre, restricting the N1-C5-C4-N4 dihedral angle in the pyrrolidine ring around 60º-80º [4]. In the present PNA design, this N1-C5-C4-N4 segment of the pyrrolidine ring coincides with the aminoethyl segment (*i.e.* N1'-C2'-C3'-N4', Figure 1) of aegPNA and the gauche geometry of the vicinal substituent would coincide with the preferred dihedral angle *θ*, in *aeg*PNA: RNA duplexes. The conformational restriction was introduced in the form of an ethylene bridge between aminoethyl linker of *aeg*PNA, hence, called as ethano-PNA [5].



*aeg*PNA **1**

trans-cyclopentyl PNA **2a**, n=1
cis-cyclopentyl PNA **2b**, n=1
cis-cyclohexyl PNA **2c**, n=2

ethano-PNA **4**
H-ethano-PNA R=H
Am-ethano-PNA R= Aminomethyl
Gu-ethano-PNA R=Guanidinomethyl

Figure 1 Structure of *aeg*PNA monomer along with proposed ethano-PNA monomer and related PNA analogues

Result and Conclusion

A novel PNA analogue has been synthesized with a constraint in the aminoethyl segment of the aegPNA backbone so that the dihedral angle *θ* is restricted within 60º-80º. The oligomers discriminate between RNA and DNA and showed better binding affinity towards RNA than DNA. The oligomers were further functionalized to amino and guanidino group for better aqueous solubility and cellular uptake.

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POSTER

Synthesis of Novel Sulfonamide Based [1,2,3]-Triazoles via Click Chemistry and their Evaluation for Antibacterial Activity

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Sulfonamides, are known to be the first clinically available antibacterial agents [1] that became associated with miracle treatments for the variable bacterial infections. In addition, these molecules have demonstrated various pharmacological properties like antitumor, anticarbonic anhydrase, diuretic, hypoglycaemic, antithyroid, anticysteine protease and anti HIV protease [2] activities. On the other hand, [1,2,3]-triazoles have demonstrated diverse biological profiles such as antibacterial, antifungal, anticancer, antileishmanial, antituberculosis, anti-HIV, antimalarial, antiepileptic and antiallergic. [3] agrnts. By considering the biological significance of these two classes of compounds, it was contemplated to attach the triazole moiety with sulfonamides via click chemistry.On antibacterial evaluation, some of the newly prepared compounds have shown moderate efficacy against different strains of Gram negative and Gram positive bacteria.

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POSTER

Discovery of Novel Anti-Cancer Agents: Pharmacophore Mapping, Database Searching, Molecular Docking, Synthesis, *In Silico* Admet and Anti-Cancer Activity

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Cancer is a disease characterized by uncontrolled growth and spread of abnormal cells. The primary function of chemotherapeutic agents is to inhibit the cancer cells without affecting the normal cells. The discovery of novel anticancer agents will hopefully provide the desired degree of selectivity for cancer cells. One of the most important therapeutic targets for cancer is Topoisomerase-I, a essential enzyme for DNA replication, and chromosome segregation. Here, we used CADD approaches using Sybyl X1.2 software [1] followed by synthetic approaches to design novel quinoline carboxamide derivatives. Twelve molecules were selected to generate ten (10) pharmacophore models using DISCOtech and refined generated model from Genetic Algorithm Similarity Program (GASP). The best model contained six features viz. 2 donor sites, 2 acceptor atoms and 2 hydrophobic regions. Best model generated was used as query for virtual screening from NCI and Maybridge database. A total number of 5216 molecules were obtained after Lipinski filtering. From this results, various molecules bearing quinoline-carboxamide core structure were designed by knowledge based structure activity relationship study and were docked on hTopo-I enzyme [PDB: 1SC7] [2] to predict the binding orientation of drug candidates. From these, ten 7-chloro-6-fluoro-*N*-substituted-2-phenylquinoline-4-carboxamide derivatives showing comparative score to topotecan and doxorubicin were synthesized [3,4] and characterized by FTIR, ^{1}H NMR and Mass. *In silico* pharmacokinetic and toxicity studies were predicted using OSIRIS property explorer [5]. Anticancer activity was evaluated on three different cell lines; MCF-7, A-375 and HCT-15 by MTT assay [6]. Few compounds showed good activity on cell lines as compared to standard leading to potential development of novel series of anti-cancer agents.

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POSTER

Synthesis of Benzimidazolyl Pyrazolines Derived From Paracetamol Hydrazide and Isoniazide as Potential Antimicrobial Agents

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During the course of our systematic studies on pyrazoles, paracetamol hydrazide and isoniazide were attached to benzimidazolyl chalcones to get desired compounds *N*-(4-(2-(3-(1*H*-benzo[*d*]imidazol-2-yl)-5-(aryl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-oxoethoxy)phenyl)- acetamide **6a-p** and (3-(1*H*-benzo[*d*]imidazol-2-yl)-5-(aryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(pyridin-4-yl)methanone **8a-p** respectively. Benzimidazolyl chalcones were synthesized by Claisen-Schmidt condensation. The structures of newly synthesized compounds were elucidated by IR, ^{1}H NMR, ^{13}C NMR, and mass spectral analysis. All bio-active molecules were tested for their *in vitro* antibacterial activity against the representative panel of Gram-positive (*Staphylococcus aureus*, *Streptococcus pyogenes*) and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*) bacteria by serial broth dilution method. All the newly synthesized compounds were also tested for their inhibitory action against three strains of fungi (*Candida albicans*, *Aspergillus niger*, *Aspergillus clavatus*) and have exhibited moderate to excellent growth inhibition against bacteria and fungi. On the basis of statistical analysis, it was observed that these compounds showed significant co-relation.

POSTER

Studies on Synthesis, Characterization and Biological Evaluation of Novel Heterocyclic Compounds by Utilizing Facile Catalysts

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Heterocyclic motif is an important scaffold which has several pharmaceutical applications. These motifs can be prepared using wide variety of reaction conditions such as the use of catalysts, toxic solvent, harsh reaction conditions like the use of base, high temperature, and multistep reaction. Although various methods are involved, the chemistry arena is now shifted towards the greener way of synthesis. In continuation to this, Nano-catalyst plays an important role in the green synthesis. In the present paper we have synthesized 2-{5-[3-(4-methoxyphenyl)-1-phenylpyrazol-4-yl]-3-(aryl)-2-pyrazolinyl}-1,3-thiazolin-4-ones through a comparative study of utilized catalyst. Also we have characterized the compounds through various spectroscopic techniques and these compounds were screened against different species of microbes.

POSTER

Synthesis, Bio-aatalytic Anomeric Separation and Fluorescent Study of Coumarin-4-Yl-Triazolyl-2-Deoxy-*Ribo*furanosides

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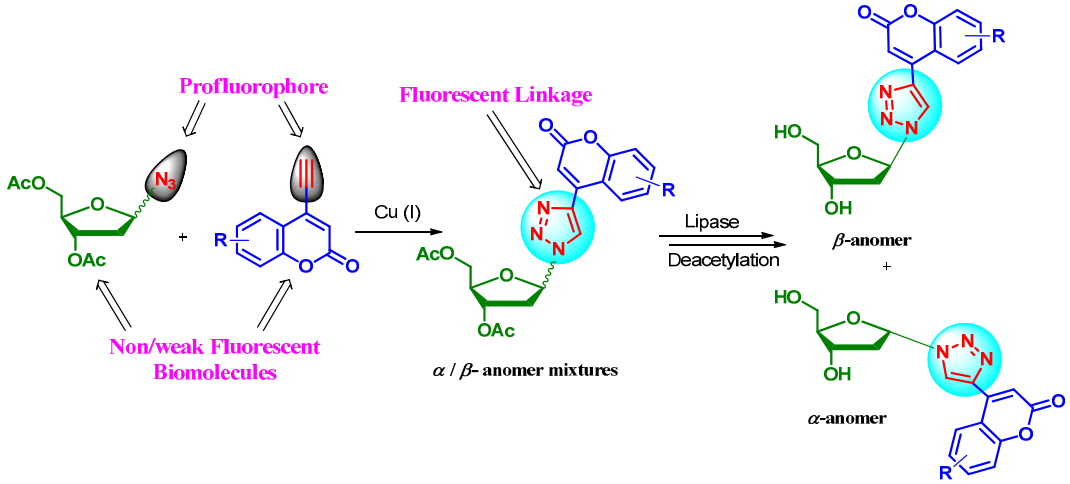
Fluorescent unnatural nucleosides are widely used in fluorescent labelling of DNA/RNA in bioorganic and medicinal chemistry. Over the last few years, different research groups have reported the synthesis of fluorescent coumarin triazolylglycosides using copper (I)-catalyzed azide-alkyne cycloadditon (CuAAC) reaction, which have shown fluorescence in the 400-550 nm region and are compatible with many applications such as surface imaging, bio-labelling, bio-conjugation and drug discovery.[1]

The separation of *α*- and *β*- anomers of nucleosides has always been a challenging task for synthetic chemists.[2-4] Our attempt to separate *α*- and *β*- anomers from anomeric mixtures of coumarin-4-yl-triazolyl-2-deoxy-*ribo*furanosides by column chromatography also failed. Herein, we report successful separation of both *α*- and *β*- anomers of 1-(3,5-di- *O*-acetyl-1,2-dideoxy- *α,β*-D-*ribo*furanos-1-yl)-4-(coumarin-4-yl)-1,2,3-triazole derivatives using Novozyme®-435 catalyzed deacetylation reaction (**Scheme 1**). All synthesized compounds have shown fluorescense in blue or green region with moderate quantum yields (ϕ = 0.1-0.3).



Scheme 1

Acknowledgement: We are grateful to the Indo-German Science & Technology Centre (IGSTC) for financial support. Kapil Bohra and Smriti Srivastava thanks CSIR, New Delhi, India, for the award of SRF and JRF.

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POSTER

Direct Synthesis of N3-Alkylated/Arylated Uracil and Thiouracil Derivatives Using Microwave-Assisted Reaction

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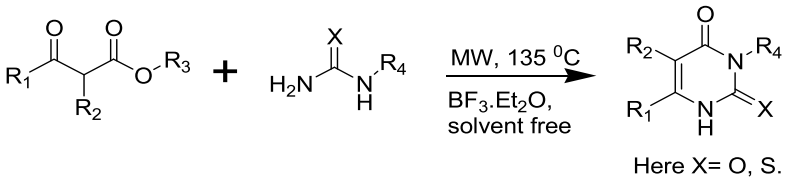
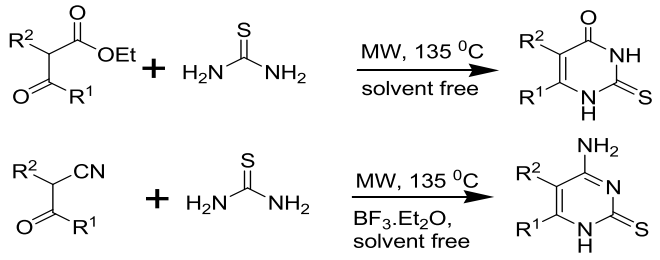
Modified nucleobases, their N-3 derivatives and nucleic acids are important molecules that have been utilized for alternate base-pairing as well as molecular probes for efficient detection of point-mutations in DNA. Many of the derivatives of uracil and thiouracil nucleobases have been applied as potential pharmaceutical drugs. Here we report a microwave-directed synthesis of a variety of modified thiouracil, thiocytosine nucleobases and their alkylated, benzylated/ arylated derivatives at N-3 position, in high yields under solvent-free conditions. The reaction yields were further improved by addition of Lewis acid.

Scheme 1



Scheme 2



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POSTER

L-Proline Based Aqueous Biphasic System: Role of Sodium Alginate to Isolate the Alkaline Earths

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An aqueous biphasic system (ABS) was obtained after mixing an amino acid (L-proline) solution (5 M) with a 90% v/v solution of nonionic surfactant (Triton X-100). The phase diagram of the system was constructed at 23 °C (figure 1) [1]. The system was found to work in a more efficient and economic way when the surfactant is enriched with a cosolute, isoamyl alcohol in a ratio of 2:1. The addition of isoamyl alcohol results in a decrease in density of the surfactant phase, much below the density of a dilute solution of proline (0.1 M). This results in very low consumption of the amino acid for design of the ABS. The tolerance of the ABS towards changes in pH and concentrations have been found to improve drastically in presence of the cosolute. When sodium alginate is used as a complexing agent, the developed system shows a pH dependent separation for the alkaline earth metal ions Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+} from one another. Detection of these metal ions after their separations have been achieved with EBT (for Mg^{2+} at pH 9.5) and arsenazo III (for Ca^{2+}, Sr^{2+} and Ba^{2+} at pH 7.2) using absorption spectrometry. As different pHs are suitable for the complexation and extraction of different alkaline earths, it is possible to have a sequential separation of the individual elements from one another from a mixture as and when required.

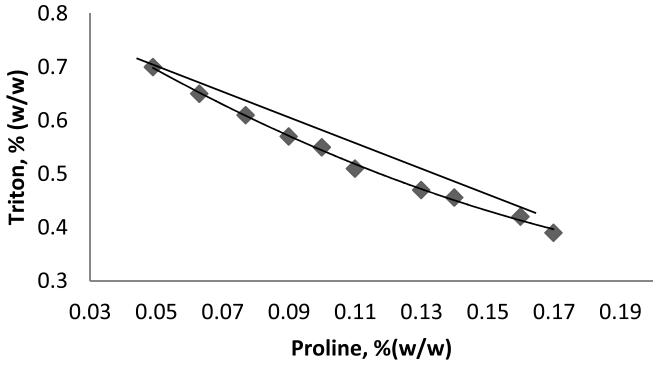

Figure 1: Phase diagram of L-proline-TX aqueous two phase drawn at 23°C

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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] 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 has been observed that excellent antimalarial activity have been shown by only those derivatives in which the tetracyclic core of artemisinin is almost wholly preserved.

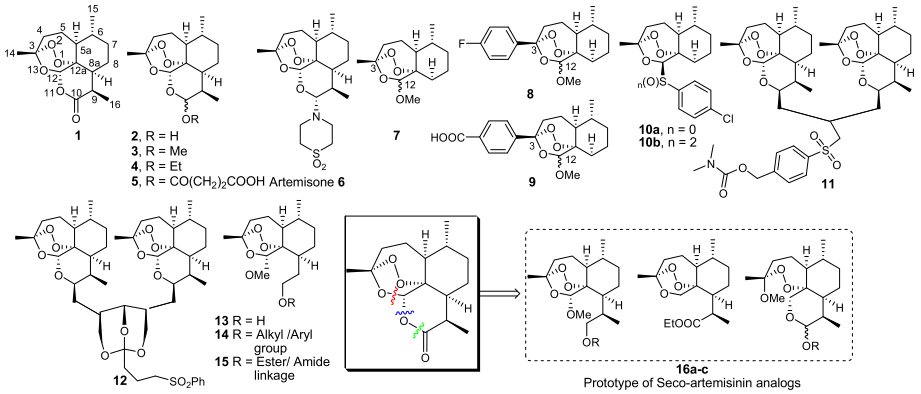

Figure 1. Artemisinin **1** and its clinically useful derivatives **2-5** and other promising analogs **6**-**16**.

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 **1**. 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 of prototype **16a-c** which were prepared by pruning of tetracyclic A, B and D rings of **1** (Figure 1). 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

Synthesis and Characterisation of Ionic Liquid with Prolinol as Recyclable Catalyst for Asymmetric Reduction of Ketones

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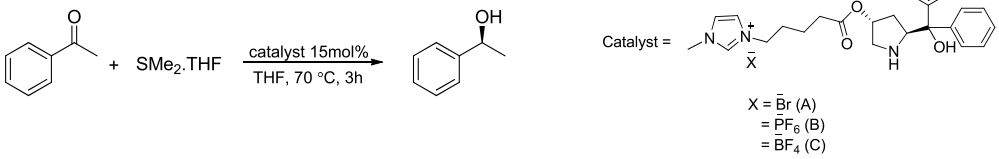
The first enantioselective borane reduction of ketones catalyzed by chiral oxazaborolidines reported by corey *et.al*.[1] we would like to use prolinol catalyst anchored on ionic liquid for its recyclability and reusability. Some attempts were made for immobilization of Prolinol on polymer support,[2,3]for this reaction. However, only few catalysts show high reactivity and high enantioselectivity for the reduction for ketone.

We synthesized chiral ionic liquid with prolinol with different counter anions like Br, BF_4, and PF_6 and applied for reduction of ketone. The synthesis of prolinol based ionic liquid start from hydroxy proline, after 5 steps we got ionic liquid with good yield. The reduction of acetophenone with borane–THF in the presence of chiral ionic liquid oxazaborolidine catalysts (1-3), we got excellent yield (93%) and enantioselectivity (91%) of phenyl ethanol and it's derivative. In addition the effect of solvent and effect of counter ion of ionic liquid also investigated.



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POSTER

Effect of Rottlerin on Calcium Oxalate Induced Nephrocalcinosis in Rats

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Hyperoxaluria is a primary risk factor in calcium oxalate stone formation.CaOx crystals can injure the renal cells and induce oxidative stress by increasing free radical generation, lipid peroxidation and decreasing cellular antioxidant status. Membranes and lipids of cellular degradation products are excellent nucleators of CaOx crystals at physiological supersaturaton of renal tubular fluids. Rottlerin is present in the gland hair covering the fruit of *M. philippinensis* (Kamala Tree). It has antitumor,antioxidant,antiamyloid and anti-inflammatory activities and also is a selective PKC-δ inhibitor. PKC- δ phosphorylates and activates NADPH oxidase which is a major source of ROS in renal cells in addition to mitochondria. Owing to its PKC- δ inhibition and antioxidant properties, Rottlerin can prevent ROS generation as well as maintain pro-oxidant/anti-oxidant status of renal cells, respectively.The present study was designed to study Rottlerin for its ability to reduce hyperoxaluria induced oxidant damage and its manifestations leading to pathogenesis of kidney stone formation. 0.4% Ethylene Glycol + 1% Ammonium Chloride, developed hyperoxaluria,renal injury and crystal deposition in male wistar rats. Rottlerin treatment at two doses (1 mg/kg and 2 mg/kg body weight) maintained antioxidant levels, decreased lipid peroxidation , increased reduced glutathione content and improved renal functionality of hyperoxaluric animals in a dose dependent manner.Thus, Rottlerin can provide crucial insights into pathophysiology of kidney stone formation to help in better understanding and treatment of the disease.

POSTER

Enhanced Antihypertensive Activity of Felodipine Nanosuspension: Formulation, Characterization and Pharmacodynamics Study

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The objective of the present investigation was to enhance the oral bioavailability of poorly soluble antihypertensive drug felodipine by preparing nanosuspension. The nanosuspension was prepared by bottom-up nanoprecipitation technique with ultrasonication and converted to solid state by lyophilization. Polymeric nonionic stabilizer HPMC and PVA were used for the steric stability of the felodipine nanosuspensions. The prepared nanosuspensions were characterized for particle size, zeta potential, polydispersity index, entrapment efficiency, saturation solubility, redispersibility, SEM and TEM. In vitro dissolution and in vivo pharmacokinetic study in rats was performed on the lyophilized nanoparticles and pure drug filled in gelatin capsules. Pharmacodynamics study was performed by NIBP method in DOCA salt treated hypertensive rats. The stable, homogenous and spherical nanoparticles were obtained in the size range of 60 to 410 nm. The saturation solubility of the drug increased 36 folds resulting in higher dissolution of up to 93 % in 2 hours. The pharmacokinetic studies with lyophilized felodipine nanoparticles resulted in 3.8 fold increases in C_{max} and 2.4 fold increases in t_{max} compared to that of pure drug. DOCA hypertensive rats after two weeks treatment showed 24.59±0.03 % decrease in mean blood pressure by nanosuspensions compared to 15.16±0.02 % decrease by pure drug suspensions. Thus, the results conclusively demonstrated a significant enhancement in antihypertensive activity of felodipine when formulated as nanosuspension.

POSTER

Synthesis and Characterization of Metal Complexes of Nalidixic Acid with Ni (II) in Presence of Heterocyclic Compounds

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Quinolones exhibit excellent antimocrobial results to both gram-negative and gram-positive microbe [1]. In clinical practice, the introduction of nalidixic acid (nal), the first member of quinolone group, causes ease for the treatment of various infections Wagman et al. [2, 3]. Nal selectively inhibits the DNA replication in microbes due to the presence of 4-oxo and 3-carboxyl group (Fig. 1). These two groups interact with guanine of susceptible microbial DNA in gyrase-DNA complex. Then the resulting quinolone-enzyme-DNA complex stops the progress of the normal replication fork and finally microbial cell death takes place Uivarosi, Marlans et al. [4, 5].

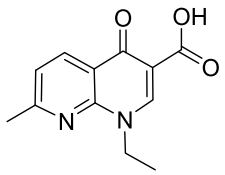

Fig.1 Nalidixic acid

The close proximity of the carboxyl and keto group on the quinolone molecule would account for its good chelating properties. Several quinolone metal chelates are known to possess antibacterial, antifungal, antiviral and anticancer activity and that's why the study of interaction between quinolone and metals is an active area of research in bioinorganic chemistry Akinvemi et al., Singh et al. [6-7].

It has been observed that metal complexes with appropriate ligands are biologically more significant and specific than the metal ions and the ligand itself Skyrianou et al. [8-10].

To enhance the knowledge of the behaviour of nalidixic acid as complexing agent in biological point of view we have synthesised mixed ligand complexes of Ni(II) in presence of another biologically active N-containing heterocyclic compound 1,10-phenanthroline (phen), 2,2'-bipyridyl (bipy). The prepared complexes were characterized and studied with FT-IR, UV-Visible, TGA-DTA and elemental analysis. Spectroscopic studies suggest that the nal acts as bidentate ligand in the complexes and bind with the metal ion through the pyridine and one carboxylic oxygen atom.

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POSTER

Effect of *Eclipta Alba* on *Leishmania Donovani* the Causal Agent of Kala-Azar and *Mycobacterium Tuberculosis*

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The emergence of increasingly drug resistant strains of diseases in the society poses a serious global threat to mankind. The development of newer drug candidates to combat the neglected diseases like leishmaniasis and tuberculosis is needed. People in 98 countries are affected by tuberculosis and leishmaniasis of which 72 are developing countries. In India the incidence of Kala-azar has attained critical level and has been affecting people belonging to low socio-economic strata. Coinfection with other infectious agents, such as HIV and Tuberculosis is also a big concern. Current drugs have many drawbacks which include difficult and lengthy administration, toxicity, high costs which makes them unaffordable and development of resistance. There is an urgent need to develop new potent drugs for effective treatment of Leishmaniasis as well as Multi-drug resistant TB. *Eclipta alba* is a medicinally important plant and has been reported by Akendengue et al., [1] for its anti-microbial activity.

In the present study we have tried to establish the medicinal efficacy of *Eclipta alba* as an anti-leishmanial and anti-tubercular agent. We have tried to assess the effect of crude soluble antigen (CSA) of *Eclipta alba* as an anti- leishmanial agent and compared it with leishmanicidal effect of well known anti-leishmanial drugs Amphotericin- B. *Eclipta alba* showed 100% inhibition of *Leishmania* promastigote proliferation in 24 hours. We have also tried to study the anti-tubercular effect of *Eclipta alba.* The *in vitro* anti-mycobacterial activity of CSA of *Eclipta alba* was determined against the standard *M. tuberculosis* H37Rv strain and MDR clinical isolate 591. Further experiments to establish its i*n-vitro* and *in vivo* efficacy as a therapeutic potential are underway.

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POSTER

Protective Effects of N- Acetyl Cysteine on Ethylene Glycol Induced Nephrolithiasis

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Renal injury and inflammation caused by Reactive Oxygen intermediates under hyperoxaluric conditions play a major role in stone formation. Oxidative stress results in mitochondrial dysfunction and release of pro-apoptotic factors from depolarized mitochondria that result in apoptosis, leads to renal injury. N-acetylcysteine (NAC) is a precursor of the amino acid L-cysteine and helps glutathione synthesis also has reducing and antioxidant properties. The present study was designed to evaluate and compare the protective effect of N-acetyl-L-cysteine (NAC) and Vitamin E supplementation in Ethylene glycol + NH_4Cl induced hyperoxaluria model of Nephrolithiasis. 0.4% Ethylene Glycol + 1% Ammonium Chloride, developed hyperoxaluria in male wistar rats, resulted in renal injury and stone deposition. Oxidative stress was assessed based on the decreased activities of antioxidant enzymes, increased lipid peroxidation and decreased reduced glutathione. Mitochondrial dysfunction has been shown by decreased activities of respiratory complex enzyme, antioxidant enzyme activity along with protein and non-protein thiols in hyperoxaluric animals. NAC treatment (50mg/kg, i.p.) potently prevented the structural and functional alterations in renal tissue while Vitamin E (200mg/kg, i.p.) had only a slight mitigating effect. The results from the study point towards the clinical potential of NAC as an adjuvant therapy to conventional anti-nephrolithiasis regimens for the prevention and/or delaying the progression of renal stone complications.

POSTER

Pyrazole Bearing Pyridyl Oxadiazole Scaffolds as Potential Antimicrobial Agents

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A novel approach was adopted for the synthesis of novel series 1-(2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)-3-(aryl)prop-2-en-1-ones **5a-l** starting from the condensation of 3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **1** and isoniazide **2**. Entitle compounds were tested for their *in vitro* antimicrobial activity against Gram-positive, Gram-negative strains of bacteria as well as fungal strains. Among the screened compounds, **5e**, **5f** and **5j**-**5l** showed most potent antimicrobial activity. Among them, compound **5l** emerged as the most effective antibacterial and antifungal activity with 4-fold higher MIC (12.5 µg/mL) as compared to standard chloramphenicol and griseofulvin respectively. The structure activity relationship revealed that the presence of electron donating groups remarkably enhanced the antimicrobial activity of newly synthesized compounds.

POSTER

Microwave Assisted Synthesis Characterization and Antimicrobial Activity of Nd (III) and Tb (III) Amide Complexes Derived from Heterocyclic Amines

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The amide group containing ligand acts as potential model for naturally occurring and biologically important complexes such as metal carrier proteins, metalloenzymes or antibiotic peptides and as an angiotensin I/II receptor antagonists. The constructions and characterizations of lanthanide complexes are currently of great interest because of their unique physico-chemical properties and various applications in medical field. The present work describes the synthesis, spectral and biological investigations on the complexes of amides derived from heterocyclic amines with Nd (III) and Tb (III) lanthanide ions. A method for the synthesis of complexes has been developed by the use of microwave irradiation which is in agreement to Green chemistry approach. All complexes have been characterized by various physico-chemical techniques. Mass spectrum explains the successive degradation of the molecular species in solution and justifies ML complexes. Vibrational spectra indicate coordination of amide and carboxylate oxygen of the ligand along with nitrate ions. The magnetic moment of Nd(III) and Tb(III) complexes showed slightly higher-values which originated due to low J-J separation leading to thermal population of next higher energy J levels and susceptibility due to first order Zeeman effect. Various energy and intensity parameters such as Racah (E^K), Slater-Condon (F_K), Lande' (z_{4f}), Oscillator strength (P) and Judd-Ofelt parameter (T_I) etc. have been computed using partial and multiple regression methods. The strong luminescence emitting peaks at 543 nm for Tb(III) can be observed, which could be attributed to the ligand have an enhanced effect to the luminescence intensity of Tb(III). Antimicrobial activities of compounds were also carried out against bacteria, fungi and yeast and minimal inhibitory concentration (MIC) have also been also determined.

POSTER

Ring-opening of Epoxides with Alcohols Using $Fe(Cp)_2BF_4$ as Catalyst

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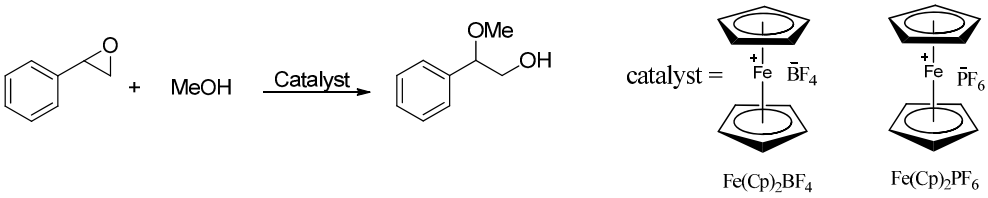
$Fe(Cp)_2BF_4$ is an efficient catalyst for the alcoholysis of aromatic, aliphatic and cyclic epoxides, gave excellent yield of corresponding β-hydroxy ether under ambient conditions. The methanolysis of styrene oxide using **$Fe(Cp)_2BF_4$** (2-5 mol %) as catalyst gave excellent yield and regioselectivity. The ring opening of cyclic epoxides gave 78-81% yield of *trans* β-hydroxy methyl ether, in 4-6 h. The first order rate of reaction with respect to catalyst was observed for the kinetic of ring opening of 1,2-epoxy hexane with methanol.



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POSTER

In-vivo Toxicity Study of Potent Estrogen Receptor Modulator and Anti-Tubercular Sterylchromenone Derivatives

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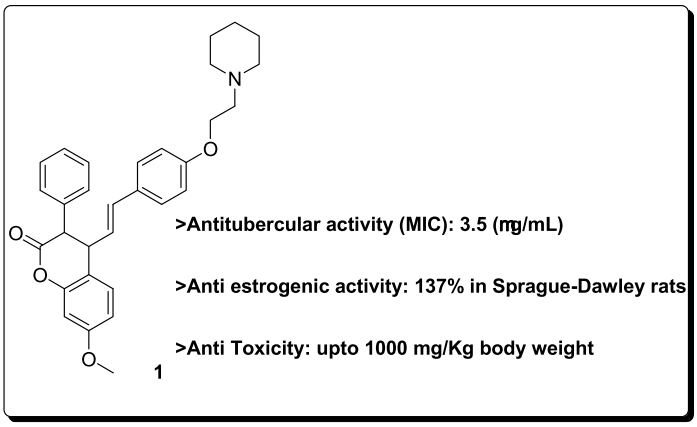
Various substituted chalcones and sterylchromenones, synthesized as estrogen receptor modulator and anti-tubercular agent, exhibited significant *in vitro* anti-tubercular activity (upto 3.5 µg/mL) against *M.tuberculosis* $H_{37}R_v$ strain and *in vivo* estrogen agonist activity (upto 48%) at 10mg/Kg in rat model. Keeping their biological potential in view, further investigation of these compounds have been focused to study their *in vivo* toxicity risk in swiss albino rat model. Compound **1** was well tolerated up to 1000 mg/Kg body weight as a single acute oral dose.



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POSTER

Self Organizing Molecular Field Analysis Assisted Design, Synthesis and Evaluation of Novel Human ptp-1b Inhibitors: 2, 4-Thiazolidinediones

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Diabetes mellitus is considered to be one of the main threats to human health in the 21st century. The prevalence and rising incidence of diabetes emphasized the need to explore the new molecular targets and strategies to develop novel antihyperglycemic agents. Protein tyrosine phosphatase 1B (*h*-PTP 1B) emerged as a molecular level legitimate therapeutic target for the effective management of Type 2 diabetes mellitus (T2DM) due to negative regulation of insulin as well as leptin signal transduction. Therefore, *h*-PTP 1B inhibitors could increase insulin sensitivity by blocking the PTP 1B mediated negative insulin signaling pathway and might be an attractive target for T2DM and obesity [1]. In the present studies, initially self-organizing molecular field analysis (SOMFA) was performed on the reported series of 2, 4-TZD scaffolds having significant inhibitory activity against *h*-PTP 1B enzymes for optimizing the lead. SOMFA models were developed using electrostatic and shape master grids and various compounds containing wide variety of substituent were designed [2]. The above designed and synthesized compounds were evaluated for their *h*-PTP 1B inhibitory along with antihyperglycemic activity using streptozotocin-nicotinamide induced diabetic mice model. Among the series, compounds **ST-06** bearing phosphotyrosine mimic domain as predicted by docking studies emerged as the most potent having activity in the low micromolar range. The outcome of the study is in correspondence to result obtained from our QSAR study which could be used as a new guideline for further development of selective and more potent *h*-PTP 1B inhibitors.

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POSTER

Effects of Ortho Substituent Groups of Protocatechualdehyde Derivatives on Binding to the C1 Domain of Novel Protein Kinase C

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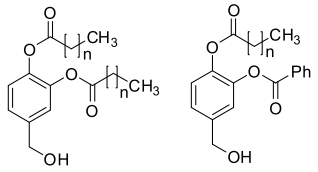
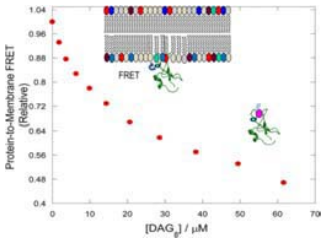
Diacylglycerol (DAG) regulates a broad range of cellular functions, including tumor promotion, apoptosis, differentiation and growth. Therefore, DAG-responsive C1 domains of protein kinase C (PKC) *isoenzymes* are considered as an attractive drug target for the treatment of cancer and other diseases. In order to develop effective PKC regulators, we designed and synthesized hydroxymethyl-phenyl ester analogs targeted to the DAG binding site in the C1 domain. Protein binding affinities and molecular docking analysis showed that hydroxymethyl group, hydrophobic side chains and ester group at the *ortho* position are essential for their interactions with the C1 domain. Modifications of these groups showed diminished binding to the C1 domain. The active hydroxymethyl-phenyl diesters **5** and **8** showed more than 5 fold stronger binding affinity for C1 domain than DAG. Therefore, our findings reveal that hydroxymethyl-phenyl ester analogs represent an attractive group of C1 domain ligands that can be further structurally modified to improve its binding and activity.



5 **5a**, **8a** (n = 14) **8**
5b, **8b** (n = 6)



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POSTER

Chemical Constituents of *Aconogonon Molle a*nd their Antioxidant Properties

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Aconogonon molle (D. Don) H. Hara (syn. *Polygonum molle* D. Don) (Polygonaceae) is subshrub, distributed throughout Nepal, India, Indonesia, Myanmar, Thailand, South and South East Asia. It is locally called as "Thotne" in Nepal. The tender shoots are used in diarrhea and young shoots are eaten as vegetable and pickle. The whole plant is astringent [1]. There are no previous reports on the chemical isolation of *A. molle,* thus the present work was aimed at chemical analysis and biological activities of this plant.

The shade dried leaves and flowers of *A. molle* were separately extracted successively with 70% MeOH and MeOH. The extracts were separately subjected to repeated column chromatography on MCI gel, ODS, Sephadex LH20 and silica gel to isolate compounds **1**-**22**.

Three new glycosides: thotneosides A (**1**), B (**2**) and C (**3**) along with thirteen known compounds (**4**-**16**) were isolated from the leaves of *A. molle*. Similarly, eleven known compounds (**4**-**6**, **10**, **11**, **16**-**21**) were isolated from the flowers. All these compounds were isolated for the first time from *A. molle.* The structures were elucidated on the basis of chemical and spectroscopic methods. *In vitro* antioxidant activity of the isolated compounds was evaluated by DPPH free radical scavenging assay.

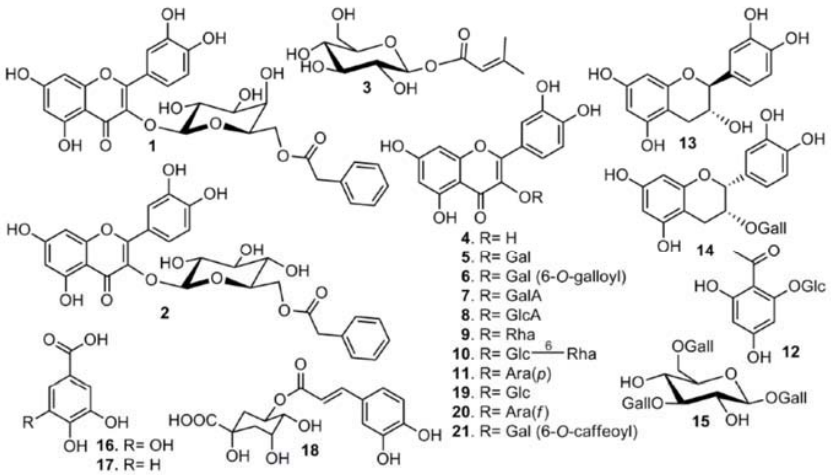

Fig. Structures of compounds **1**–**21**.

Reference:

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POSTER

An Eco-Friendly Synthetic Approach to Pyrrolo[1,2-A]Quinoxalines

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Pyrrolo[1,2-a]quinoxaline scaffold can be found as an integral part of many biodynamic heterocyclic molecules, possessing a wide range of pharmacological properties. A large number of pyrrolo[1,2-a]quinoxaline derivatives are known to exhibit potent anti-HIV [1], antimalarial [2] and anticancer [3] activities. They are also found to be an important intermediate for the construction of 5-HT_3 receptor antagonist [4]. Thorough literature survey revealed that the strategies available for the preparation of these compounds are limited. Moreover, some of these methods suffer from many disadvantages such as longer reaction times, harsh reaction conditions and poor yields of the products. Therefore, the development of an efficient, simple and eco-friendly methodology for the construction of these heterocycles is highly desired.

In continuation of our on-going work to develop convenient methods [5-8] for the synthesis of diverse biologically relevant molecules, we wish to report herein an efficient and eco-friendly synthetic protocol for the preparation of various pyrrolo[1,2-a]quinoxaline analogues.

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POSTER

One-Pot Synthesis of Octahydroquinazolinone Derivatives Using Environmentally Benign Conditions

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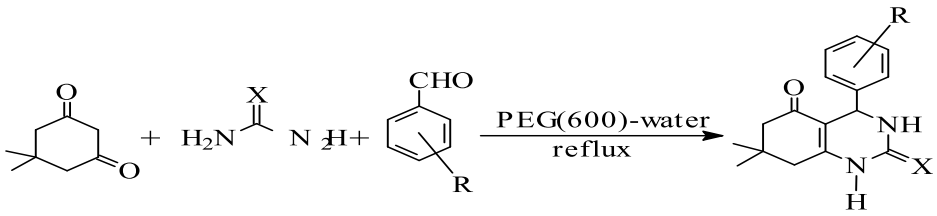
Octahydroquinazolinones is an important class of nitrogen heterocycles that have attracted significant attention because of their potent antibacterial activity against *Staphylococcus aureus, Escherichia Coli, Pseudomonas aeruginosa* Kidwai et al [1] and calcium antagonist activity Yarim et al [2]. Literature survey reveals several methods have been developed for the synthesis of quinazolinone derivatives. However, in general, the reported methods for the synthesis of these derivatives involve hazardous and expensive reagents or solvents and display moderate to low yields with low atom efficiency.

Organic solvents are high on the list of toxic chemicals. There are many potential advantages to replacing volatile organic compounds (VOCs) into with water or polyethylene glycols (PEGs) Chan et al [3]. The most obvious are low cost, low flammability and reduced toxicity. In continuation of our ongoing program on the development of novel synthetic methods in organic synthesis under mild conditions Bandgar and More et al [4,5], we now wish to report a simple and efficient, one-pot, three-component version of the Biginelli reaction for the synthesis of octahydroquinazolinone derivatives in PEG (600)-water without any added acid or base catalyst.



Scheme

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POSTER

Convergent Synthesis of Carbohydrate-based Novel Macrocyclic Compounds

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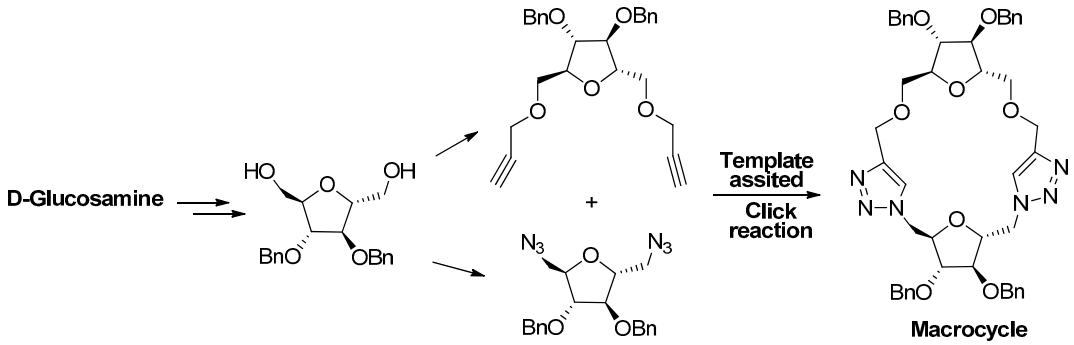
In the quest of greener and cheaper approaches, the ongoing synthetic methodologies are now utilising natural resources as the starting materials. Macromolecules are important building blocks and have diverse applications as molecular pores, artificial receptors, complex supramolecular architectures and chiral recognition agents. Like naturally occurring macromolecules, synthetic ones also represent a class of large-sized compounds designed with a degree of preorganization and, which are capable of binding to target sites with least entropy loss. In conformationally restricted manner, these can show favourable drug like properties, *e.g.* good solubility, high lipophilicity, improved membrane penetration, enhanced metabolic stability and oral bioavailability with desirable pharmacokinetic and pharmacodynamic properties.

The synthesis of macrocycles is considered as crucial and challenging task. We herein report the convergent synthesis of triazole linked sugar-based macrocycles starting from D-glucosamine. The detailed synthetic scheme will be presented during the poster session.



Acknowledgement: We are thankful to the Indo-German Science & Technology Centre (IGSTC) for financial support. Ankita Singh thanks DRDO for Junior Research Fellowship.

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POSTER

Simultaneous HPLC Estimation Method for Mefloquine and Clarithromycin

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Clarithromycin, a semi-synthetic macrolide anti-biotic exhibiting good antimicrobial activity over erythromycin. Mefloquine is an anti-malarial agent (falciparum malaria). Clarithromycin, a cytochrome P450 inhibitor, can cause reversal of mefloquine resistance in Plasmodium strains. Hence a simple, sensitive, selective and reproducible HPLC method was developed for their determination in dug solution and human plasma. HPLC resolution of mefloquine and clarithromycin was achieved on a RP-18e Lichrosphere® column (250 X 4 mm, 5µm) at 25ê3^0 C utilizing mobile phase consisting of methanol: 0.05M monobasic sodium phosphate buffer (pH adjusted to 4.0 with ortho-phosphoric acid) (65:35 v/v); flow rate being 1.0 mL/min and injection volume-20 µL. Column effluent was monitored at 205 and 220 nm (PDA detection) which afforded both mefloquine and clarithromycin at 10.5 and 12.10 min respectively. The LOD and (LOQ were 0.2 µg ml^{-1}; 0.05 µg ml^{-1} and 1 µg ml^{-1}; 0.01 µg ml^{-1} and standard calibration curve for clarithromycin was linear (r^2 = 0.9991; 0.9973) over the concentration range of 2–200 µg ml^{-1} and 2-800 µg ml^{-1} for human plasma and drug solution respectively.

The standard calibration curve for mefloquine was linear (r^2 = 0.9961; 0.9942) over the concentration range of 2–100 µg ml^{-1} and the LOD and LOQ were 0.02 µg ml^{-1}; 0.03 µg ml^{-1} and 0.04 µg ml^{-1}; 0.05 µg ml^{-1} in both human plasma and drug solution respectively. The present method was successfully applied for estimation of the said drugs in biological samples containing the same.

POSTER

Synthesis, Characterization and Reactivity Studies of a Highly Reactive Mono-Radical Co(III) Complex

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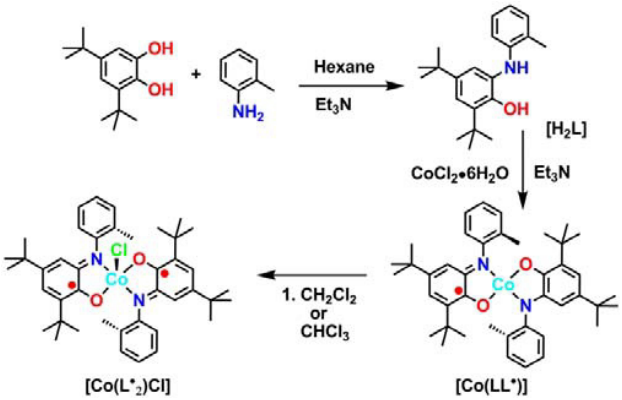
Square planar cobalt complex of redox active amidophenolate ligand (fully reduced form) is highly reactive and undergoes to the redox reaction through electron transfer bond formation at cobalt(III) centre.[1] Thus, it's important to synthesize and stabilize the square planar cobalt complexes as the general trend of the cobalt ion to form more stable square pyramidal, or octahedral complexes. Herein, we synthesized and structurally characterized the square planar cobalt(III) complex [Co(LL^{ñ})] which upon crystallization from dichloromethane formed square pyramidal cobalt(III) complex [Co(L$^{ñ}_2$)Cl] (Scheme 1).



Scheme 1

Complex was well characterized by mass spectrometer, single crystal X-ray diffractometer, ESR-technique as well as by SQUID magnetometer.

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POSTER

Gallic Acid Based 2-Benzyloxy Analogues of 2-Methoxyestradiol as Anticancer Agents

B. Sathish Kumar[a], Amit Kumar[b], Jyotsna Singh[b], Mohammad Hasnain[b], Arjun Singh[a], Kaneez Fatima[a], Dharmendra K. Yadav[a], Vinay Shukla[b], Suaib Luqman[a], Feroz Khan[a], Debabrata Chanda[a], Jayanta Sarkar[b], Rituraj Konwar[b], Anila Dwivedi[b] and Arvind S. Negi[a*]

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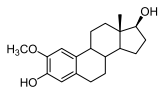
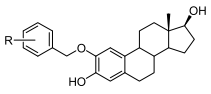
Estrogens are key hormones responsible for the development and maintenance of female reproductive physiology and secondary sexual characteristics.. However, over-expression of these hormones may lead to various types of cancers like breast, uterine, ovarian, prostate and endometrial [1]. 2-Methoxyestradiol a metabolite of endogenous estrogen 17β-estradiol has emerged as a potent anticancer investigational drug. It inhibits microtubule assembly after binding to tubulin near the colchicine binding site [2]. It has completed phase II clinical trials against ovarian cancer and prostate cancer. There is an increasing interest on synthesis of 2ME2 analogues for better activity and bioavailability.

In the present study, we have synthesized gallic acid based 2-benzyloxy analogues of 2-methoxyestradiol. The best analogue showed stabilization of tubule polymerisation process after binding to the 'paclitaxel binding pocket'. In acute oral toxicity it was found to be non-toxic and well tolerated up to 1000mg/kg dose in Swiss-albino mice. The chemistry and biological evaluation of the best analogue will be discussed at length.



2-Methoxyestradiol



Synthesized analogues

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POSTER

Synthesis of Pyrimidone Based 1,2,3-triazoles as GSK-3 Inhibitors

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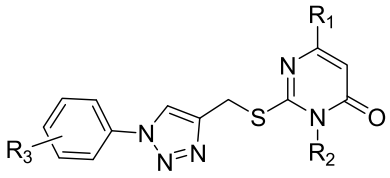
Protein kinases are important therapeutic targets for diabetes, cancer, inflammation, and neurodegenerative disorders, because aberrant protein kinase signaling is implicated in these human diseases. Glycogen synthase kinase 3 (GSK-3) acts as a downstream regulatory switch that determines the output of numerous signaling pathways initiated by diverse stimuli [1,2] GSK-3 specific inhibitors might be promising effective drugs for the treatment of devastating pathologies such as neurodegenerative diseases, stroke, and mood disorders [3]. Diverse chemotypes such as indirubins, paullones, aminopyrimidines, pyridine, pyimidine, pyrimidone, bis-indolylmaleimides, triazole etc have been reported as GSK-3 inhibitors. Among the many nitrogen-containing heterocycles, the pyrimidone nucleus represents a very interesting and versatile scaffold for the synthesis of potential drug candidates acting on a wide range of biological targets[4].The pyrimidones have shown potential inhibitory activity against GSK-3β, TNF-α, IL-1β, LDL PLA-2 etc. we have synthesized a library of pyrimidone based 1,2,3- triazoles using click-chemistry approach. The synthesized compounds are being screened for their GSK-3β inhibitory activity.



Key words: Protein kinases, neurodegenerative diseases, click-chemistry
Acknowledgement: The author Imran Khan acknowledges DST funded project for financial support.

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POSTER

Comparative Antioxidant Activity, FT-IR Spectra and Mineral Element Analyses of Different Taxa of *Lantana Camara*

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The present study investigates the FT-IR spectra, mineral elements and antioxidant activity of four taxa of *Lantana camara* L. (Verbenaceae) leaves by using different *in vitro* antioxidant models. The phenolic content [1] was highest in the Chandigarh yellow taxa (CYt) followed by Palampur red taxa (PRt), Chandigarh yellow turning pink taxa (YTPt) and Chandigarh purple taxa (CPt). The flavonoid content [2] are in the order of YTPt, PRt, CPt and CYt.. The qualitative DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging test were carried on TLC plates (F_{254}) initially and then IC_{50} values were estimated quantitatively [3] which are in the order of Vitamin C < CYt < PRt < YTPt < CPt. The highest total antioxidant capacity [4] was observed in CYt followed by PRt, YTPt and CPt. The ferric ion reducing antioxidant potential (FRAP) [5] was in the order of butylated hydroxytoluene (BHT) > CYt > PRt > YTPt > CPt. The IC_{50} values for the 2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulfonate) (ABTS) cation radical scavenging assay [6] were in the order of BHT < PRt < CYt < YTPt < CPt. The extracts showed the inhibition of *in vitro* lipid peroxidation [7] with PRt showing the maximum inhibitory effect followed by standard rutin, CYt, YTPt and CPt. Fourier transform-infrared spectroscopy (FT-IR) show more peaks in CYt than in PRt, YTPt and CPt which may be attributed to their radical scavenging activity in the same order. The concentration of various mineral elements were determined using Wavelength Dispersive X-ray fluorescence spectroscopy (WD-XRF) and a difference in the levels is observed among them. Hence, out of the four taxa investigated, CYt and PRt are good source of nutrients and antioxidants.

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POSTER

Studies on Substituted Benzo[*H*]Quinazolines, Benzo[*G*]Indazoles, Congested Pyrazoles, 2,6-Diarylpyridines as Antioxidant Agents

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Various 4-(substituted)-5,6-dihydro-8-methoxybenzo[*h*]quinazolin-2-amine and 1-(substituted)-4,5-dihydro-7-methoxybenzo[*g*]indazol-2-yl)ethanone and congested pyrazole derivatives have been synthesized by an efficient methodology from the precursor (*E*)-2-(4-hydroxybenzylidene)-6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one and other suitable precursors . The synthesized compounds were evaluated for their *in vitro* antioxidant activity in ascorbate assay. Compound **1-4** have shown a significant in vitro antioxidant activity.

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POSTER

Synthesis of Naphthofurans v*ia* Iodine Mediated Oxidative Cyclization of 1-(1-arylvinyl)naphthalen-2-ol

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Naphthofuran and benzofuran ring system is ubiquitous structural motif present in natural products such as Malibatol-A, Hopeafuran and Iantheran-A.[1,2] These motifs have been reported to have several biological and pharmacological properties such as adenosine antagonist XH-14 inhibition, 5-lipoxygenase inhibition, mutagenesis, antitumor, anticancer, cytotoxic activity on sarcoma ascites, anti-HIV and $P2Y_{11}$ receptor in immune system.[3-5] Numerous synthetic methods have been developed for 2-arylbnezofurans, however, methods for the synthesis of 3-arylnaphthofurans are limited. There are few reports for the synthesis of 3-arylnaphthofurans by cyclodehydration of aryloxyketones.[6] Palladium catalyzed Sonogashira of terminal alkynes with 2-iodo/1-iodonapthols followed by cyclization has become popular strategy for the synthesis of naphthofurans. Recently, naphthofurans were also synthesized from 2-hyroxy-α-arylstyrene derivatives using copper acetate in presence of atmosphere oxygen, 8-OQ and base.[7] We developed a novel synthetic methodology for the synthesis of 3-arylnaphtho[2,1-*b*]furans by oxidative cyclization of 1-(1-arylvinyl) naphthalen-2-ol using molecular iodine as catalyst. The method is one-pot and gives excellent yields of 3-arylnaphtho[2,1-*b*]furans under milder reaction conditions. The detailed experimental procedure will be shown in poster presentation.

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POSTER

In Silico and Admet Studies of Some Newly Synthesized Malonamic Acid Hydrazones as Anti-Tubercular Agents

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Organic compounds containing reactive methylene group provide excellent intermediates in synthetic organic chemistry. Such substances have been found to be useful as synthon for various anti-tubercular, anti-viral, anti-diabetic, anti-fertility, anti-bacterial and anti-fungal agents. The problem of tuberculosis (TB) drug resistance and the continuing rise in the disease incidence has prompted the research on new drug development as well as on increasing the understanding of the mechanisms of drug resistance. The full therapeutic possibilities of hydrazides were realized after the discovery of isonicotinic acid hydrazide (INH). Hydrazide-hydrazones have been reported to possess a wide variety of pharmacological activities such as anti-bacterial, anti-convulsant, anti-inflammatory, antitubercular, intestinal antiseptic, anti-depressant, or anti-platelet activity. Due to their excellent hole-transporting properties and relatively simple synthesis, hydrazones are often mentioned among the most effective charge transporting low molecular weight materials used in electrophotography.

The present work includes synthesis, characterization, molecular docking and ADMET studies of substituted malonamic acid hydrazones. Computation studies were undertaken to test the inhibitory affect of the synthesized molecules on protein kinase PKnB from *Mycobacterium tuberculosis.*

Details of experimental procedure, purification, spectroscopic characterization, molecular docking and virtual screening methods will be presented during the meeting.

POSTER

Synthesis and Characterization of Self Assembled Chitosan-Pluronic F68 Copolymer Based Miceller Nano-Templates Comprising Amphotericin B

Vivek Kumar, Pramod K. Gupta, Vivek K. Pawar, Ashwni Verma, Renuka Khatik and Anil K. Dwivedi*

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In an attempt to develop an alternative more safe and effective Amphotericin B (AmB) parenteral drug deliviery system for antileishmanial chemotherapy, Chitosan-g-Pluronic F68 self-assembled nanoaggregates (CPNs) were developed. Chitosan-g-Pluronic F68 copolymer (CPF) was synthesized by activating pluronic F68 (PF-68) with succinic anhydride and then coupling it with chitosan using 1-Ethyl-3-(3-dimethyllaminopropyl) carbodiimide hydrochloride/N-Hydroxysulfosuccinimide sodium (EDC/NHS) at RT. This was further characterized by IR spectroscopy. The obatained co-polymer has ability to self assembled under aqueous phase at constant stirring. The different formulations were optimized for particle size, zeta potential and drug loading efficiency by varying copolymer concentration and copolymer to AmB ratio. The optimized CPNs has mean hydrodynamic diameter, zeta-potential and drug loading as 130.4±27 nm, (+)22.3±1.4 mV and 14.3%, respectively which suggested its suitability for parenteral administration. Further, optimized formulation was evaluated on the basis of drug release pattern, haemolytic activity and *in-vitro* antileishmanial activity. *In-vitro* drug release study showed that initially, AmB was released from the CPNs in a burst manner followed by time-dependent release. Optimized formulation showed 13.47±3.74% haemolysis with respect to free AmB (100 %) at 50 µg/mL. These obtained results evoke together that our formulation was potential alternative delivery system for safe and efficient delivery of AmB for chemotherapy of leishmaniasis.

POSTER

Identification of New Anti-TB Agents as Potential Inhibitors of GlmU by I*n silico* Approach

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Mycobacterium tuberculosis (TB) has covered one third of the world population by infection. Control and prevention of tuberculosis is a major challenge along with emergence of 0.63 million cases of multidrug-resistance (MDR) and extensive drug resistant (XDR). A total of 1.4 million people died from TB, while around 70,000 children died in 2011. Currently, many drug targets are being studied by research community. N-Acetylglucosamine-1-phosphate uridyltransferase (GlmU) is one of the attractive targets due it mainly involved in bacterial cell wall synthesis. Thus mycobacterial infection can be obstruct by blocking cell wall synthesis targeting the GlmU. Molecular docking study and virtual screening of FPMD (Facility for Preservation of Molecular Diversity) database having more than 7000 small organic molecules was carried out. Identified potential hits from *in silico* study were studied against GlmU for their uridyltransferase activity. Molecules from the FPMD repository were characterized by various analytic studies using UPLC, MASS, NMR etc. Four candidates were found to be potentially active at 25 µM concentration.

POSTER

Ionic Liquids Grafted on Ferrite (ILS@Fe_3O_4) as Magnetically Recyclable Green Catalyst for One-Pot Multi-Component Reactions

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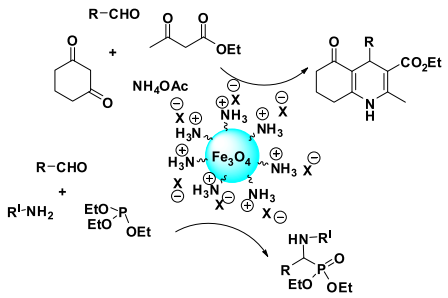
Ionic liquids have attracted strong scientific and technological interest due to their role as green and sustainable solvents/catalysts in organic synthesis, lubricants, plasticizers, electrolyte in batteries etc.[1] Multi-component reactions (MCR) has been considered as a most powerful tool for the construction of medicinally important complex molecules in a single step.[2,3] Recently, nanosized ferrite magnetic materials have attracted increasing interest due to their unique properties to bridge the gap between heterogeneous and homogeneous catalysis for the synthesis of fine chemicals/organic intermediates/drug candidates *via* MCR[4]. Encouraged by these reports and role of grafted materials in the catalysis, we envisioned immobilization/grafting of ionic liquids on ferrite as an useful material for organic conversions due to the advantages such as high surface area resulting in high catalyst loading capacity, inexpensive, non-toxic, chemically stable, simple catalyst recovery by external magnet and easy preparation from low-cost precursors.[5]

To the best of our knowledge, ILs grafted on ferrite based materials has not been much explored as heterogeneous catalysts. In the continuation of our studies on developing novel heterogeneous catalytic systems for multi-component reactions,[6-8] herein we report the synthesis of ILs@Fe_3O_4 material as an efficient recyclable heterogeneous catalyst for the synthesis of biologically important molecules.



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POSTER

A Simple and Efficient Sodium Carbonate-Mediated Regioselective Synthesis of *N*-(Hydroxyalkyl)Cinnamamides Under Mild Conditions

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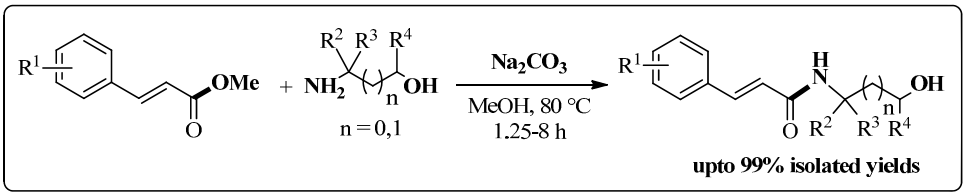
Amides are ubiquitous structural motifs occurring in a variety of natural products, biologically active compounds, pharmaceutical drugs, etc. The amide bonds form an integral part of many organic transformations. Therefore, a number of synthetic procedures have been developed for the formation of amide bond. [1] However, these procedures suffer from one or more limitations such as use of harsh or expensive reagents, harsh reaction conditions such as high reaction temperature or pressure. As a result, realization of such a versatile bond under mild conditions is always of considerable interest.

As part of our ongoing research on the synthesis of biologically active compounds, we were interested in the synthesis of *N*-(hydroxyalkyl)cinnamamides because of their promising anti-convulsant, muscle relaxant and anti-depressant activities. [2] They are also used as precursors for the preparation of other synthetically useful molecules such as oxazolines, oxazolinium salts, benzoxazoles and photoresponsive polymers. [3] The conventional methods of amidation often require use of hazardous chemicals like thionyl chloride or methylchloroformate to generate activated carboxylic acids. [2,4] Thus we became interested in exploring the synthesis of *N*-(hydroxyalkyl)cinnamamides with less hazardous reagents. Herein, we have reported a simple and efficient route to synthesize *N*-(hydroxyalkyl)cinnamamides via 1,2-addition of aminoalcohols to methyl cinnamates in the presence of inexpensive and readily available Na_2CO_3 as the base. [5] A wide variety of *N*-(hydroxyalkyl)cinnamamides with different electronic properties were isolated in upto 99% yields. The results would be discussed in detail during the presentation.



Scheme 1. Synthesis of *N*-(hydroxyalkyl)cinnamamides

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POSTER

Synthesis and Studies of Some Bio-active Thieno[2,3-*D*]Pyrimidine Derivatives

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Some thieno[2,3-*d*]pyrimidine derivatives were synthesized from 2-aminothiophene-3-carboxylic acid ester analogue. The formed compounds have been evaluated by physical methods (melting point & elemental analyses) and upon spectral data (IR and NMR). All newly synthesized compounds have been tested for their antibacterial activity against gram (+)ve and gram (-)ve bacteria and also on different stains of fungi.

Keywords: Azetidinone, Thiazolidinone, Antimicrobial activity.

POSTER

Rapid Profiling and Structural Characterization of Bioactive Compounds in *Berberis petiolaris* Wall. ex G. Don Applying Hyphenated Mass Spectrometric Techniques

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The plants of genus berberis are well known and used extensively as medicinal plants in traditional medicine. Most of the berberis species are evergreen and semi-evergreen shrubs or small trees distributed in the Northern Hemisphere[1]. ***Berberis petiolaris* Wall. ex G. Don** belongs to family Berberidaceae, locally known as Kingora or Kilmora, and is a large deciduous shrub growing upto 20 m high found in Western Himalaya between 8500 and 11500 feet. Genus berberis has many medicinal values attributable to the presence of alkaloids having different pharmacological activities. In genus berberis, protoberberine alkaloids are the characteristic group of compounds in which berberine, jatrorrhizine and palmatine were previously isolated from *Berberis petiolaris*[2-3]. In this study, a method for screening of the phytochemicals of *B. petiolaris* has been developed using HPLC-DAD-ESI-QTOF-MS/MS. A total of 41 compounds were identified and characterised from various parts of *B. petiolaris*. We have also developed UPLC-QTRAP-MRM method for quantification of 5 bioactive compounds. The total contents of five bioactive constituents were abundant in stem followed by root, leaf and fruit. The highest concentrations of individual compounds were chlorogenic acid (19.9 w/w) in leaf, magnoflorine (29.35 w/w) in stem, jatrorrhizine (0.85 w/w), palmatine (0.49 w/w) and berberine (1.99 w/w) in root. Hence, HPLC-QTOF-MS/MS and UPLC-QTRAP-MS/MS possess good potential in simultaneous analysis of secondary metabolites and their quantification in medicinal plants.

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POSTER

Synthesis of Substituted Oxindoles from Isatins by One-Pot Tandem Reduction of Oxo- And Ene-/Yne- Functionalities by Hydrazine

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The structural motif indolin-2-one or oxindole is considered to be an important ring system in heterocyclic chemistry due to its presence in wide variety of natural products and biologically active compounds.[1] Substituted and unsubstiuted oxindoles also serve as a crucial synthetic precursor for the synthesis of highly desirable indole-based heterocycles and alkaloids.[2] In recent past, there have been considerable efforts devoted to develop efficient and general synthesis of substituted oxindoles. In continuation of our interest in developing new reaction methodologies, we have developed a double reduction methodology in which tandem reduction of oxo- and ene-/yen-functionalities of substituted isatins led to the synthesis of oxindole derivatives in excellent yields. The method is an of the Wolff-Kishner procedure. The reaction is simply carried out by the treatment of *N*-alkenyl/alkynylisatins with excess of hydrazine hydrate (25%) under catalyst-free refluxing conditions.

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POSTER

Design, Synthesis of Selective Nsaid: A Structure Based Drug-Designing Approach

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A new generation of NSAID should have the reduce side effect with the precise inhibiton of COX-2 isozymes. Having that in mind, we have designed and characterized novel anti-inflammatory inhibitor by implementing them into the different molecular modeling technique. Selective inhibition were studied with protein-ligand complex simulation, which given the RMSD and RMSF result of the interaction. This simulation study was able to describe the inhibtion effect of design a series of new Arylidine (4a–f) to the COX-2 isozymes. The best compound with the highly specific inhibition to the COX-2 was projected as the novel NSAID. This series of new Arylidine (4a–f) were synthesized by the condensation of 4-(3-methyl-5-oxo-4, 5-dihydro-1-*H*-pyrazol-1-yl) benzenesulphonamide with various substituted aromatic aldehydes in ethanol using catalytic amount of base. The designed compounds were synthesized by the cyclization of 4- hydrazinylbenzene sulfonamide with appropriate keto ester. Synthesized compounds were characterized by IR, NMR, mass spectra and elemental analyzer.

POSTER

Synthesis of Azole-fused-quinazolines *via* One-Pot Sequential Ullmann type C–N bonding and Intramolecular Dehydrogenative C–N Coupling

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Transition metal catalyzed C–H activation/functionalizations are ubiquitous in recent literature owing to their immense advantages such as atom economy, operational simplicity, high functional group tolerance and mainly pre-functionalizations can be obviated for these protocols.[1] By merging C–H activation strategies with an additional multi-bond forming approaches such as multicomponent reactions, tandem reactions, and one-pot sequential procedures will allow access to biologically active complex heterocyclic libraries with simple and readily available precursors.[2] There are several reports found where fused quinazolines have been studies against various biological targets and also found applications in multidisciplinary fields.[3]

In the context of our ongoing efforts to synthesize novel *N*-fused heterocycles,[4] we have attempted the synthesis of 2,3-diaryldiimidazo[1,2-*a*:1',2'-*c*]quinazolines by palladium catalyzed tandem reaction between 2-(2-bromophenyl)-4,5-diaryl-1*H*-imidazole and various azoles such as 1*H*-imidazole and 1*H*-benzimidazole. The expected one-pot sequential reaction proceeds *via* initial copper catalyzed Ullmann-type C–N bonding followed by palladium catalyzed intramolecular dehydrogentive C–N coupling to provide targeted fused-quinazolines. Details of the methodology will be presented in the poster.

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POSTER

Base-Mediated Chemo- and Stereoselective Addition of 5-Aminoindole/Tryptamine and Histamines onto Alkynes

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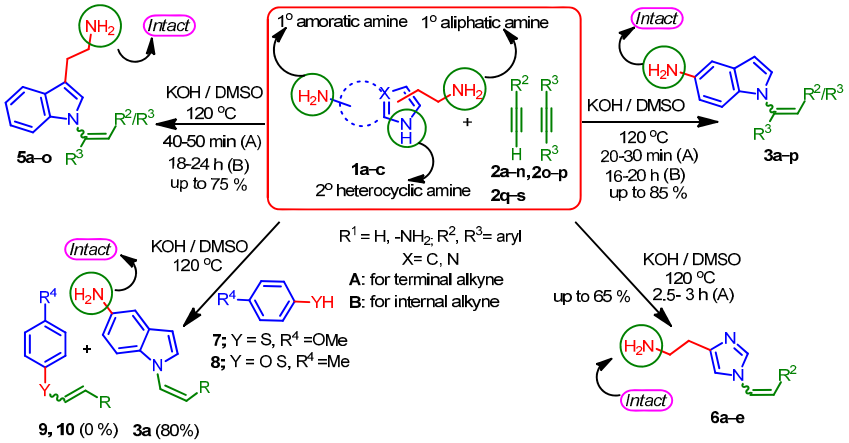
Transition-metal free chemo- and stereoselective addition of *N*-heterocycles **1a–c** onto alkynes **2a–s** to synthesize indolyl/imidazolyl enamines **3a–p**, **5a–o** and **6a–e** in the presence of super basic solution of alkali metal hydroxides in DMSO is described.[1] The addition of *N*-heterocycles onto alkynes takes places chemoselectively without affecting the 1° amino groups (aromatic and aliphatic) of 5-aminoindole, tryptamine and histamine. The products were obtained with *Z* stereochemistry; however increase in reaction time leads to the formation of mixture of E/Z isomers.[2] The chemoselective addition of *N*-heterocycle **1a** onto alkyne over thiophenol **7** and phenol **8** is supported by the control experiment. Present methodology provides an efficient chemoselective method to synthesize a variety of *Z*-enamines of 5-amminoindole, tryptamine and histamine without affecting the 1° amino group. The presence of free amino group in enamines could be further used for the synthetic elaboration, which proves to be highly advantageous for the structural and biological activity assessment.



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POSTER

Synthesis of Aza-heterocycles Using Ionic Liquid-Supported Hypervalent Iodine(III) Reagent through Catch and Release Strategy

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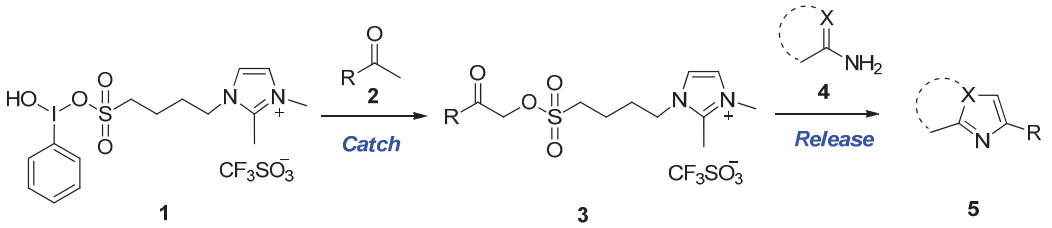
Aza heterocycles are important class of compounds due to their wide range of applications. They are predominant among all types of pharmaceuticals and agrochemicals.[1] In the search for novel methodologies that include the safety, sustainability and wide applicability for the synthesis of aza heterocycles, hypervalent iodine reagents have become an attractive choice for the synthetic chemist's.[2] Polymer-supported hypervalent reagents have been used to overcome some of the disadvantages associated with the corresponding monomeric analogues.[3] Although, polymer-supported hypervalent reagents are very useful for various transformations; they often have lower reactivities than the monomeric analogues. Recently, ionic liquid-supported (diacetoxyiodo)arenes[3] and [hydroxy(tosyloxy)iodo]arenes[4] were prepared and used for oxidation and α-tosylation respectively, but none of them has been used in heterocyclic ring construction so far.

In continuation of our interest towards development of novel ionic liquid-supported reagents and linkers[5] for the applications in library constructions, here in we wish to report synthesis of novel ionic liquid-supported hypervalent iodine reagent **1** and demonstrate its application in "catch and release" strategy for the synthesis of various aza-heterocycles (Scheme 1). The procedure involves no chromatographic separation and gives product in good to excellent yield and high purity.



Scheme 1

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POSTER