21st ISCB INTERNATIONAL CONFERENCE (ISCBC-2015)

CURRENT TRENDS IN DRUG DISCOVERY AND DEVELOPMENTS

25th - 28th February, 2015

At

Central Drug Research Institute

Lucknow

ABSTRACT BOOK

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Indian Society of Chemists & Biologists

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From the desk of
ISCB President and General Secretary

Prof. Anamik Shah

Dr. P.M.S. Chauhan

Indian Society of Chemists and Biologists, Lucknow (ISCB) is celebrating its 20th year of establishment during 25th-28th February, 2015 at modern Campus of 'Central Drug Research Institute', Lucknow encompassing several acres of land and with traditional design architecture of Locknow with world class infrastructure and facility.

It is a matter of great pleasure that the focal theme of the 21st International Conference of ISCB is 'Current Trends in Drug Discovery and Developments'. This conference is going to discuss self reliance, sustainability & affordability of pharmaceutical substances by improving process chemistry through innovation so that India can be more competitive and self reliant on Pharma products, drug intermediates & finished formulations. Scientists across the globe, especially from USA, UK, Germany, France, Belgium, Sweden, Taiwan, Korea, Middle East and many other will participate as keynote/invited speakers to address above mentioned issues. The entire conference will be in parallel sessions and this conference will be addressed by more than 60 senior scientists & professors as key-note/invited speaker while it will also attract more than 400-700 young researchers & post doctoral researchers across the country, who will take part as oral/poster presentations. Young foreign delegates are also encouraged to attend this event.

We are glad that the scientific committee is bringing out an abstract book covering the presentations to be made during ISCBC-2015. Our sincere thanks are due to the members of Organizing Committee. During this conference, a number of eminent scientists and technologists of the country and overseas will be discussing the trends, prospects and future directions of research. We look forward to fruitful deliberations in extremely interesting areas of scientific research. We are happy that an extensive and comprehensive scientific program is arranged. The scientific program beside inaugural function includes plenary lectures, invited lectures by the eminent scientists from India and abroad. Oral presentations by the young researchers are scheduled. The most heartening feature of the conference is that it is being participated with a number of young scientists and Ph. D. students and presentations are schedules in three poster sessions. We are also arranging few exhibitory events which updates researchers in their respective field. We extend our warm welcome to all National and International delegates from pharmaceutical companies, research organization, universities and academic institutes wish them very happy stay at CSIR - CDRI, Lucknow. Now finally we take this opportunity to express our sincere thanks and gratitude to members and office bearers of Organizing Committee of 21st International Conference (ISCBC-2015). We also thank the Director of CDRI for his deep interest for success of the conference. Lastly, we thank all delegates for their overwhelming participation.

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February, 25 -28, 2015

Jointly organized by
Indian Society of Chemists & Biologists, Lucknow, India
&
Central Drug Research Institute, Lucknow, India

SCIENTIFIC PROGRAM

Wednesday, February 25, 2015

9.00 AM - 10.30 AM	**Registration**	
10.30 AM - 12.00 PM	**Inaugural Session**	
	Welcome Address	**Dr. Ram Vishwakarma, Director CSIR-CDRI, Lko**
	Introduction to ISCB	**Dr. P.M.S. Chauhan, Gen. Secretary, ISCB**
	Presidential Address	**Prof. Anamik Shah, President, ISCB**
	ISCB Award Distribution	**Dr. S. K. Puri, Chairman of ISCBC-2015**
	Address by Guest	
	ISCB AWARD Lectures	**ISCB AWARD FOR EXCELLENCE** **ISCB YOUNG SCIENTIST AWARD**
	Vote of Thanks	**Dr. P.M.S. Chauhan, Organising Secretary**
12.00 PM-12.30 PM	**High Tea**	

Session - I

Chairpersons: Prof. Anamik Shah and Dr. Mukund S. Chorghade

PL-1	**Jyoti Chattopadhyaya**
12.30 PM - 1.00 PM	Professor & Chair, Program of Chemical Biology, Dept. of Cell & Molecular Biology, Uppsala University, Sweden **Therapeutic potential of Carba-LNA modified DNA & RNA to control the phosphate degradation of target mRNA by harnessing the relative hydration Diagnostics**

PL-2 1.00 PM - 1.30 PM	**Rui Moreira** iMed.ULisboa, Faculdade de Farmácia da Universidade de Lisboa, Av. Prof. Gama Pinto, Lisboa, Portugal **A ChemogenomicInsight into the Discovery of Single and Dual-Stage Antimalarials**
1.30 PM - 2.00 PM	**Lunch**

Session - II

Chairpersons: Prof .Maurice C.R. Franssen and Prof. Anshu Dandia

IL-1 2.00 PM - 2.20 PM	Ute Schepers KIT, Institut für Toxikologie und Genetik, Germany **Peptoids for organ targeted delivery of bioactive molecules**
IL-2 2.20 PM - 2.40 PM	**Colin Suckling** Glasgow, Scotland **The Antibacterial Drug, MGBBP3, from Discovery to Clinical Trial**
IL-3 2.40 PM - 3.00 PM	**Maria Laura Bolognesi** Bologna, Italy **Designing multitarget drugs for neurodegenerative diseases**
4.20 PM - 4.40 PM	**Tea**

Session - III

Chairpersons: Dr. Ute Schepers and Prof. M.S..Shingare

IL-4 3.00 PM - 3.20 PM	**Christophe LEN** cedex, France **Recent Developments in Aqueous Chemistry** Université de Technologie de Compiègne Centre de Recherches de Royallieu, F-60205 Compiègne
IL-5 3.20 PM - 3.40 PM	**Krishna Nand Singh** Professor of Organic Chemistry, Department of Chemistry, BHU **Development of Some Green Protocols for Organic Synthesis**
IL-6 3.40 PM - 4.00 PM	**Virender S. Parmar** University of Delhi, Delhi **Natural products-inspired anti-microbial, anti-inflammatory and antiplatelet agent.**

IL-7 4.00 PM - 4.20 PM	**Anshu Dandia** University of Rajasthan, Jaipur, **Assessment of catalytic accessibility of nanomaterials towards the synthesis of pharmaceutically imperative heterocycles moieties**
4.20 PM - 4.40 PM	**Tea**
IL-8 4.40 PM - 5.00 PM	**Dalip Kumar** Department of Chemistry, Birla Institute of Technology and Science, Pilani **Synthetic Analogues of Indole Alkaloids as Potent Tubulin Inhibitors**
IL-9 5.00 PM - 5.20 PM	**Amit Kumar** Dept. of Chemistry, Indian Institute of Technology Patna **Some Application of Directing Group in the Synthesis of Functionalize Heterocycles**
5.20 PM - 7.00 PM	**Poster Session -I (Poster Numbers 1-80)**
7.00 PM - 8.30 PM	**Cultural Programme**
8.30 PM	**Dinner**

Thursday, February 26, 2015

Session - IV

Chairpersons: Prof. C. L. Khetrapal and Dr. P. M. S. Chauhan

PL-3 9.00 AM - 9.30 AM	**Branko Stanovnik** University of Ljubljana, Aškereva, Ljubljana, Slovenia **Enaminones in the metal-free synthesis of polysubstituted heterocyclic systems. [2+2] cycloadditions, ring expansion reactions and other transformations**
PL-4 9.30 AM - 10.00 AM	**Tushar Kanti Chakraborty** Ex. Director, CSIR-CDRI, Lucknow, India **Hybrid structures herald new promises**
IL-10 10.00 AM - 10.20 AM	**Om Prakash** Director & Professor, Biomolecular NMR Facility, Kansas State University, Manhattan, USA **Understanding of Molecular Recognition and Function of an Essential Enzyme for Antiviral Drug Developments**

IL -11 10.20 AM - 10.40 AM	**Hussein El-Kashef** Assiut University, Assiut, Egypt. **Towards New Pyrazoles of Potential Biological Activities**
IL -12 10.40 AM - 11.00 AM	**Maurice C.R. Franssen** Wageningen University, Dreijenplein , Wageningen, Netherlands **Chemo-enzymatic synthesis of biobased nitrogen containing bulk chemicals**
IL -13 11.00 AM -11.20 AM	Ashok K. Prasad University of Delhi, Delhi **Chemo-enzymatic Route to Therapeutically Important Sugar Modified Nucleosides**
11.20 AM - 11.40 PM	**Tea**

Session-V

Chairpersons: Prof. Sun Choi and Prof. A. K. Goswami

IL-14 11.40 AM - 12.00 PM	**Athina Geronikaki** Department of Pharmaceutical Chemistry, Aristotle University, Greece **Design and synthesis of novel (4/6-substituted benzo[d] thiazol-2-yl)thiazolidinone-4 ones with antimicrobial activity**
IL-15 12.00 PM - 12.20 PM	**Kartsev Victor** InterBioScreen, PO Box 218, Moscow, 119019 Russia **Targeted Synthesis of Natural Compound Analogs Novel Reactions and Rearrangements**
IL-16 12.20 PM - 12.40 PM	**Diwan S Rawat** Department of Chemistry, University of Delhi, Delhi **Molecular hybridization: a useful tool in the design of new drug prototypes**
IL-17 12.40 PM - 1.00PM	**Sartaj Tabassum** Aligarh Muslim University, Aligarh **Design and Synthesis of Metallic Potential Antitumor Agent, Characterization and in vitro Mechanistic Studies of Cancer Inhibition.**
IL-18 1.00 PM - 1.20 PM	**Farukh Arjmand** Aligarh Muslim University, Aligarh **Molecular drug design , synthesis and a comprehensive biological insight of chiral metal-based antitumor chemotherapeutic drug entities: DNA binding profile, cleavage studies , in vitro cytotoxicity and in vivo systemic toxicity studies.**

1.20 PM - 2.20 PM	**Lunch**

Session-VI

Chairpersons: Prof. Athina Geronikaki and Prof. Rui Moreira

PL-5 2.20 PM - 2.50 PM	**Domenico Spinelli** Department of Chemistry 'G. Ciamician', Alma Mater Studiorum-Università di Bologna, Bologna, Italy **[1,4]Thiazino[3,4-c][1,2,4]oxadiazol-3-ones: an examination of their reactivity and of their biological profile**
IL-19 2.50 PM - 3.10 PM	**N C Desai** Bhavnagar University, Bhavnagar, India **Contemporary Landscaping of 4-thiazodinones: Synthesis and Biological Profile of Small and Hybrid Heterocyclic Molecules**
IL-20 3.10 PM - 3.30 PM	**A. K. Goswami** Department of Chemistry, M.L. Sukhadia University, Udaipur **Metal Based Drugs -An Under Explored Area**
IL-21 3.30 PM -3.50 PM	**R. I. Kureshy** Discipline of Inorganic Materials and Catalysis, Central Salt and Marine Chemicals Research Institute (CSMCRI), Council of Scientific & Industrial Research (CSIR), G. B. Marg, Bhavnagar **Chiral Catalysis an Important Tool for the Synthesis of Pharmaceutically Active Molecules**
IL-22 3.50 PM - 4.10 PM	**Rajnish Prakash** Chairman & Chief Executive, Heavy Water Board, Department of Atomic Energy, Mumbai **Societal Impact of Nuclear Energy and Radiation Technology**
IL-23 4.10 PM - 4.30 PM	**Nicole Jung** KIT, Karshruhe, Germany **Drug Discovery in organic chemistry labs: scope and limitations of academic compound facilities**
4.30 PM - 4.50 PM	**Tea**

Session-VII

Chairpersons: Prof. Krishna Nand Singh and Dr. S. K. Singh

IL-24 4.50 PM - 5.10 PM	**N. H. Khan** Central Salt and Marine Chemicals Research Institute (CSIR-CSMCRI), Bhavnagar, Gujarat, India **Chiral Catalysts for Asymmetric Cyanation Reaction**
O-1 5.10 PM-5.20PM	**Kamal Kumar Chaudhary** Division of Applied Sciences & IRCB,Indian Institute of Information Technology, Allahabad, Deoghat, Jhalwa, U.P. **In-silico screening of chalcone derivatives as potent plasmepsin inhibitors**
O-2 5.30 PM - 5.40 PM	**Sundaram Singh** Deptt Of Chemistry, IIT(BHU), Varanasi **Superoxide Ion Induced One Pot Synthesis of Benzo[c]acridine Derivatives**
O-3 5.50 PM - 6.00 PM	**Kshipra Misra** Defence Institute of Physiology and Allied Sciences Lucknow Road, Timarpur, Delhi **Characterization of Indian Himalayan Medicinal Mushrooms**
O-4 6.00 PM - 6.10 PM	**Pratibha Yadav** Center for Rural Development & Technology, IIT Delhi, Haus Khas, New Delhi, India **Epoxidation of Indene by a Plant Chloroperoxidase**
O-5 6.20 PM - 6.30 PM	**Jyotsana Pandey** CSIR-Central Drug Research Institute,Lucknow **Murrayakoenigii (L.)Spreng. Ameliorates insulin resistance in dexamethasone-treated mice by enhancing peripheral insulin sensitivity**
O-6 6.30 PM - 6.40 PM	**Nayab Ishrat** Division of Biochemistry CSIR- Central Drug Research Institute, Lucknow, India **Aegeline from Aegle marmelos stimulates GLUT4 translocation mediated glucose transport via activation of insulin signaling in the mouse skeletal muscle cells**
O-7 6.40 PM - 6.50 PM	**Ganesh M. Shelke** Department of Chemistry, Birla Institute of Technology & Science, Pilani , India **Facile Access to Substituted Dihydrothiopyrano[2,3-b]indoles via Sequential Rearrangements during S-alkylation and Gold-catalyzed Hydroarylation on Indoline-2-thiones**

6.50 PM - 8.30 PM	**Poster Session -II (Poster Numbers 81-160)**
8.30 PM	**Dinner**

Friday, February 27, 2015

Session -VIII

Chairpersons: Prof. Jyoti Chattopadhyaya and Prof. Victor Kartsev

PL-6 9.00 AM - 9.30 AM	**Anil K. Singh** Ex-Vice Chancellor, University of Allahabad, Allahabad & Professor, Department of Chemistry, IIT Bombay **Photoactivators, Photoswitches and Caged Biomolecules**
IL-25 9.30 AM - 9.50 AM	**Karol Grela** Biological and Chemical Research Centre, Faculty of Chemistry, University of Warsaw, Pasteura 1, 02-093, Warsaw, Poland **Making olefin Metathesis work-recent results in ruthenium catalysts design and applications**
IL-26 9.50 AM - 10.10 AM	**Wafaa Abdou, Reham Barghash** Chemical Industries Division, National Research Elbohouth St., Dokki, Cairo, Egypt **Gem-diphosphonates: the motif of diverse biological and medicinal importance**
IL-27 10.10 AM - 10.30 AM	**Sun Choi** Ewha Womans University, Seoul, Korea **Exploration of GPCR activation via protein dynamics and allostery,and its application to drug discovery**
IL-28 10.30 AM - 10.50 AM	**Prof. H. Illa** Jawaharlal Centre for Advanced Scientific Research, Bangalore, India **From Synthons to Bioactive Molecules: Efficient Stategies for heterocycle Synthesis**
10.50 AM-11.10 AM	**Tea**

Session IX

Chairpersons: Prof. Suryakant Tripathi and Prof. H. Junjuppa

IL-29 11.10 AM - 11.30 AM	**Vishnu K Tandon** Department of Applied Chemistry, Institute of Engineering & Technology, Lucknow, India **Micelles catalyzed chemo- and regio-selective synthesis of 1,4Naphthoquinones in H2O that potently induce apoptosis in cancer cells**
IL-30 11.30 AM - 11.50 AM	**Sunil K. Sharma** Department of Chemistry, University of Delhi, Delhi, India **Chemoenzymatic Synthesis of Amphiphilic Polymeric Architectures for Biomedical Applications**
IL-31 11.50 AM - 12.10 PM	**Anil Kumar** Department of Chemistry, Birla Institute of Technology and Science, Pilani **Synthesis of heterocyclic compounds via transition metal-catalyzed inter- and intramolecular direct arylation**
IL-32 12.10 PM - 12.30 PM	**Ramendra Pratap** Department of Chemistry, University of Delhi, North Campus, New Delhi **Chemistry of 2-Cyanomethylbenzonitrile**
IL-33 12.30 PM - 12.50 PM	**Rajneesh Misra** Department of Chemistry, Indian Institute of Technology, Indore **A smart strategy for tuning the HOMO-LUMO gap**
O-8 12.50 PM - 1.00 PM	**Rashmi Singh** Banaras Hindu University, Varanasi, India **Curcumin ameliorates lipopolysaccharide induced allergic asthma exacerbations and structural changes in murine model**
O-9 1.10 PM - 1.10 PM	**Vipul Gupta** Department of Nanoparticle Translational Research, Tokyo Medical University, Japan **Identification of Ferrochelatase as A Novel Therapeutic Target of Salicylic Acid using Highly Functional Magnetic Beads**
1.10 PM - 2.00 PM	**Lunch**

Session -X

Chairpersons: Prof. Christophe LEN and Dr. K. Deo

IL-34 2.00 PM - 2.20 PM	**Ashok Kumar** President - Centre for Research & Development, Ipica laboratory limited, Mumbai **Yoga of Chemistry and Commonsense: A Short-cut to New Drug Discovery**
O-10 2.20 PM - 2.30 PM	**Sandeep Chaudhary** Malaviya National Institute of Technology, Jawaharlal Nehru Marg, Jaipur, India **An enantioselective synthesis of an anti-hypercholesterolemic drug atorvastatin calcium (Lipitor) via direct catalytic asymmetric aldol reaction of thioamides**
O-11 2.40 PM - 2.50 PM	**Hardik Bhatt** Nirma University, Ahmedabad , India **Design, Synthesis and Anticancer Activity of Novel Pyrimidine Derivatives as CDK2 Inhibitors**
O-12 2.50 PM - 3.00 PM	**Pradeep Kumar Jaiswal** IIT, Indore, Madhya Pradesh, India. **An organocatalytic novel C-C bond forming approach for the direct syntheses of highly substituted tetrahydrocarbazoles and Carbazoles**
O-13 3.00 PM - 3.10 PM	**Poonam Shukla** Department of Chemistry, University of Delhi, New Delhi, India **Chalcones and its complexes in the treatment of diabetes**
O-14 3.10 PM - 3.20 PM	**Sima Kumari** IASST, Guwahati, Assam, India **Comparative analysis of the in vitro antioxidant activities of three medicinal plants of North Eastern region of India**
O-15 3.20 PM - 3.30 PM	**Pramod Kulkarni** Hutatma Rajguru Mahavidyalaya Rajgurunagar Pune **Synthesis of Curcumin Under Grinding Condition**
O-16 3.40 PM - 3.50 PM	**Ram Awatar Maurya** CSIR-Indian ICT, Hyderabad **Reaction of electron deficient olefins with diazo-compounds: metal-free stereoselective synthesis of cyclopropanes & regioselective synthesis of pyrazoles**

O-17 3.50 PM - 4.00 PM	**Siddharth Sharma** Guru Nanak Dev University, Amritsar, India **Homogeneous catalyst recycling: a continuous flow approach for metal catalyzed reaction**
O-18 4.00 PM - 4.10 PM	**Sudeesh Kumar** Research and Development Centre, Bhararthiar University, Coimbatore **Synthesis and cytotoxic evaluation of novel thiazolederivatives bearing quinolone moiety**
O-19 4.10 PM - 4.20 PM	**Sarita Yadav** D.D.U. Gorakhpur University,Gorakhpur, India **An-L- rhamnosiadase from Penicillium greoroseum MTCC-9424**
O-20 4.20 PM - 4.30 PM	**Hena Khanam** Aligarh Muslim University Aligarh, India **Discovery and development of anti-hiv agents**
O-21 4.30 PM - 4.40 PM	**D.N. Singh** Dr. R.M.L. Avadh University Faizabad, India **Identification of Lead Molecule of Biological Significance from Phlebophyllum kunthianum**
4.40 PM - 4.50 PM	**Tea**
4.50 PM - 7.00 PM	**Poster Session -III (Poster Numbers 160 onward)**
7.00 PM - 8.00 PM	**Cultural Programme**
8.00 PM	**Dinner**

Saturday, February 28, 2015

Session -XI

Chairpersons: Prof. Karol Grela and Dr. S. K. Puri

PL-7 9.30 AM - 10.00 AM	**Anamik Shah** Department of Chemistry, Saurashtra University, Rajkot **Collaborative Drug Research in India: The Current Contexts and Future Directions**
PL-8 10.00 AM - 10.30 AM	**Ganesh Pandey** Sanjay Gandhi PGIIMS Campus, Raebareli Road, Lucknow **Complex Natural product Structures a Driving Force for Innovations in Organic Chemistry**

IL-35 10.30 AM - 10.50 AM	**Mukund S. Chorghade** CSO, AGN Biofuels, 14 Carlson Circle, Natick, MA **Biomimiks™ as Chemosynthetic Livers: Predict, Prepare and Prove the Structure, Activity and Toxicity of Drug Metabolites leads**
IL-36 10.50 AM - 11.10 AM	**Indresh Kumar** Department of Chemistry, Birla Institute of Technology and Science, Pilani, Rajasthan, India **Amino-catalyzed transformations of dicarbonyls: Synthesis of medium sized nitrogen heterocycles**
IL-37 11.10 AM - 11.30 AM	**Rachna Sadana** Natural Science Department,University of Houston-Downtown, USA **Using Technology to Improve Student Engagement and Success in a Flipped Classroom**
IL-38 11.30 AM - 11.50 AM	**Mukesh Kumar Madhra** Chemical Research Division, Ranbaxy Research Laboratory, Gurgaon, Haryana, India **Scalable Green Chemistry in Pharmaceutical Applications**
IL-39 11.50 AM - 12.10 PM	**Arun Shukla** Indian Institute of Technology, Kanpur, India **Structural insights in to gpcr signaling: novel avenues for drug discovery**
IL-40 12.10 PM - 12.20 PM	**K.S. Jain** S. F. Jain College of Pharmacy, Telco Road, Chinchwad, Pune, India **Design, synthesis and anti-proliferative activity of condensed 2H-4-heteroarylaminopyrimidines**
12.20 PM - 12.50 PM	**CDRI CHEMTECH PARK IN PUBLIC PRIVATE PARTNERSHIP**
12.50 PM - 1.30 PM	**Valedictory Session**
1.30 PM - 2.00 PM	**Lunch**

PLENARY

PL-1

Therapeutic potential of Carba-LNA modified DNA & RNA to control the phosphate degradation of target mRNA by harnessing the relative hydration

Jyoti Chattopadhyaya

Department of Cell & Molecular Biology, University of Uppsala, Box 581, S-75123 Uppsala, Sweden
Email: jyoti@boc.uu.se

Ideal design of a therapeutic oligonucleotide requires that incorporation of chemical modification will impart correct nucleolytic stability and cell-penetration properties while binding to the target cellular mRNA and degrade it, preferably in a catalytic manner. Current understanding suggests that specific mRNA scaffold formation through its folding with the help of some cofactor, such as metal ion or a ligand, with or without an enzyme, which bring about the specificity of the phosphodiester bond cleavage in the mRNA in the ternary complex. For the degradation of the target mRNA with any of the endonucleases exploited in the antisense (ASO) or siRNA strategies require the stereochemical proximity of specific water molecules (active water) in the endonuclease-mRNA-ASO/siRNA complex. We will present compelling evidence that specific hydration level around phosphate ester change upon complexation and subsequent structure reorganization ensures acceleration of the mRNA cleavage/degradation. This presentation will address and provide some direct experimental evidence in support of the fact that water deprivation in the RNA duplexes retards its cleavage/ degradation rate. A phosphodiester bond of target RNA do not cleave if there is no water around it. Using carba-LNA modified oligo, we have enhanced the cleavage rate of the target mRNA by 7-8-fold compared to the native counterpart by recruiting water.

PL-2

A ChemogenomicInsight into the Discovery of Single and Dual-Stage Antimalarials

Rui Moreira

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Antimalarial drugs currently in use engage a reduced number of validated targets, and their efficacy is being undermined by the spread of parasite resistance. In addition, chemical diversity among these drugs is limited, which also contributes to the emergence of cross-resistance. Antimalarial drug discovery has traditionally focused on the optimization of known lead compounds to achieve efficacious drug exposures with the lowest possible dose. Recently, ligand- and structure-based design approaches complemented by cell-based screening have been developed to identify innovative and readily synthesizable hit and lead compounds. Here, we review how

low molecular weight as well as chimeric compounds have been designed and synthesized to engage different molecular targets in malaria parasites, enabling efficient elimination of parasites both in vitro and in vivo. In addition, we will report how structure-based design and target agnostic cell-based screening led to the discovery of novel small molecules that will help to overcome our limited understanding of *Plasmodium* biology.

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PL-3

Enaminones in the metal-free synthesis of polysubstituted heterocyclic systems. [2+2] cycloadditions, ring expansion reactions and other transformations

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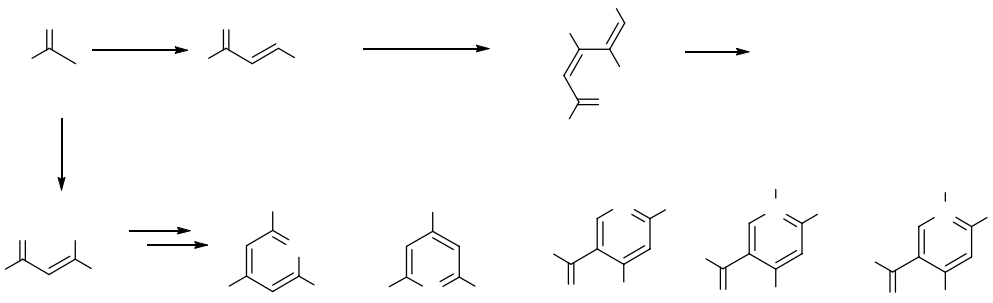
Enaminones and related compounds turned out to be extremely versatile reagents in the **metal-free synthesis** of many heterocyclic systems [1], including many nitrogen containing natural products and their analogues [2].

Regiospecific microwave-assisted [2+2], [4+2] cycloadditions and Michael additions of substituted 2-amino-3-(dimethylamino)propenoates and other enaminones, derived mostly from methyl ketones, with electron poor



acetylenes, such as acetylenecarboxylates, and azodicarboxylates, which gave highly functionalized 1-amino-4-(dimethylamino)buta-1,3-dienes as intermediates for the preparation of polysubstitutedpyrroles, azapentalenes, triazafulvalenes, 2-heteroarylpyridines and their *N*-oxides, 1-aryl (or heteroaryl)imidazol-2-ones and other heterocyclic systems [3] will be reported.[2+2]Cycloadditions of substituted acetylene iminium salts to enaminones, ring-expansion reactions, rearrangements of heterocyclic systems and other transformations will be preseted [4].

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PL-4

Hybrid structures herald new promises

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Chemical modifications of natural products to improve their selectivity, potency, or other physicochemical properties have made tremendous inroads in the drug discovery today. A logical extension of this exercise lies in the creation of natural product like *de novo* chemical entities using the fundamental building blocks of nature like amino acids, sugars and nucleosides to make hybrid structures with differentiated functional groups anchored on a single ensemble for easy assembly and manipulations. Our continued works on sugar amino acids (Saa) and related building blocks have led to the discovery of many interesting molecules with unprecedented structures and activities. Like, for example, a *cis*-Saa based foldamer exhibited an unusual conformational switch from its 10-membered H-bonded turn structure, when not appended with sugars, to an unprecedented 16-membered helical one when mannosyl units were grafted. The phenomenon, observed only in the *cis*-foldamer and not in its *trans* congener, were reflected in the contrasting interactions of these glycofoldamers with various biological targets suggesting that these differences may have their seeds in the underlying conformational preferences of these neoglycopeptides (*Angew. Chem. Int. Ed.* **2013**, *52*, 10221-10226). Our Saa-based cyclic cationic peptides continue to spring surprises showing excellent antimicrobial activities with much decreased, or no cytotoxicity (*Org. Biomol. Chem.* **2011**, *9*, 4806-4810). Cyclic oligomers of furan based unnatural amino acids led to the discovery of excellent and very selective G-quadruplex ligands that has been used extensively to modulate gene expression by targeting nucleic acid structures (*Biochemistry* **2014**, *53*, 3711-3718; *Biochemistry* **2014**, *53*, 1117-1124). Fully amide-linked RNA mimics of small oligos (*Tetrahedron* **2014**, *70*, 5455-5462) hold lot of promises for the future. Research activities in our lab in some of these areas and some recent results will be presented.

PL-5

[1,4]Thiazino[3,4-c][1,2,4]oxadiazol-3-ones: an examination of their reactivity and of their biological profile

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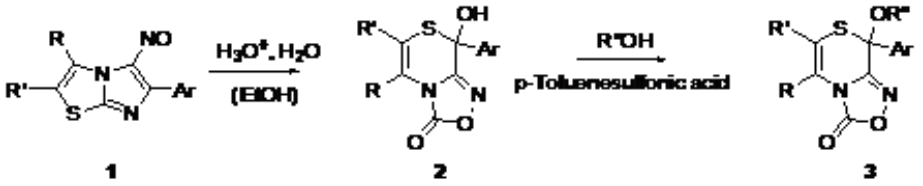
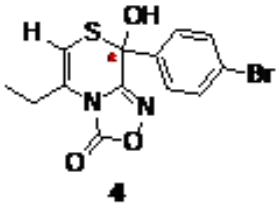
5-Nitroso-6-arylimidazo[2,1-b][1,3]-thiazoles (1) react with hydrochloric acid giving the 8-aryl-8-hydroxy-8H-[1,2,4]oxadiazolo[3,4-c][1.4]thiazin-3-ones (2), whose structures were determined by means of different spectrometric techniques (infrared, NMR, and mass) and confirmed by X-ray crystallography.1a,b Compounds 2 have been obtained with yields ranging from low (12%) to good (70%):1c they are hemithioacetals and contain a chiral 'unstable' center at C-8. Of course the relevant acetals (3) include a stable chiral center.2a-d Both hemithioacetals 2 and acetals 3 show very interesting biological features: as pointed out by some of us they are interesting hits thanks to their L type Calcium Channel (LTCC)2a-d and MDR activities.3a,b Because of this reason we have synthesized a lot of compounds 2 and 3 and we have obtained very promising results also with the help of in-silico predictions.2c,d; 3b

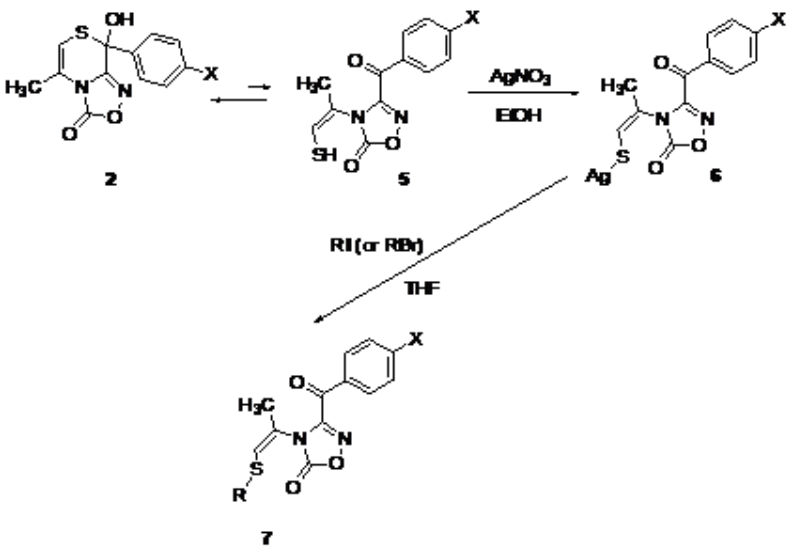


Scheme 1

In solid state hemithioacetals 2 exist as stable bicyclic compounds,1b in contrast in toluene at high temperature (383 K, following the process by 1H-NMR) we have observed that 5-ethyl-8-hydroxy-8(4-bromophenyl)-8H-[1,2,4]oxadiazolo[3,4-c][1.4]thiazin-3-one (4) leads to a R/S equilibrium at the C-8 chiral center.



The occurrence of the open-chain/thiazine equilibrium has been confirmed by freezing the open-chain structure.4



Scheme 2

We have obtained interesting information on the hemithioacetal ring-opening process from a DFT computational analysis of the corresponding potential energy surface. We have calculated that the cyclic structure is much more stable than the open one (?G° about 7 kcal mol-1). Also, we have identified a reaction path characterized by an energy barrier5 of about 23 kcal mol-1 which is consistent with the value determined by 1H-NMR experiments (about 20 kcal mol-1).6

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PL-6

Photoactivators, Photoswitches and Caged Biomolecules

Design, Synthesis and Mechanism of Photoreleasable Groups Used for the Caging of Drugs and Other Biomolecules

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Caging is a technique in which a bioactive molecule is rendered inactive by covalently linking it to a photolabile group, and when required the bioactive molecule is released from the cage in its active form in site-, time- and concentration-controlled fashion by photo-irradiation. Controlling activity of bioactive molecules with light in time and space is an important strategy in the processes as diverse as light-controlled enzymatic catalysis, activity of neurotransmitters, targeted drug delivery and development of pro-drugs, photo-control of drug and pharmacological activity, design of photoreceptors for opto-electronic applications, etc. Light-initiated cage release is also employed in the release of substances in building or isolating libraries in combinatorial chemistry, in photolithography, and in the photorelease of caged reagents in chemical transformations. The success of this strategy depends much on the availability of suitable chromophoric activators and switches that can be efficiently used under physiological conditions. Several types of photolabile groups including phenacyl , o hydroxycinnamoyl , coumarin , o nitrobenzyl esters and amides have been considered for caging applications. In recent times, the design and development of multi-photon sensitive photoreleasable groups has received a great deal of attention because of the improvement in spatial resolution for controlled release. We have examined the efficacy of new one-dimensional caging platforms based on nitro- and methoxynaphthyl, anthryl, azobenzene analogues, and phenacyl groups and noted that these chromophores are efficient phototriggers for caging of bioactive molecules. These cages are easily prepared and the release of bioactive component from the cage can be triggered by biologically benign visible light under physiological conditions. This lecture both reviews the recent accomplishments in the field of caged compounds and also looks forward to future inroads into other fields. In particular, it deals with the principles behind caging of bioactive molecules and photo-regulation of bioactivity, the challenges of molecular design of phototriggers, and the possible therapeutic scenarios. Synthesis and mechanism of light-induced activity of photoactivators and photoswitches designed in our laboratory, along with future prospects in the area will be discussed in detail.

PL-7

Collaborative Drug Research in India: The Current Contexts and Future Directions

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The drug discovery and development has taken a new dimension in last 15 years, as advancement of our understanding on several facet of medicinal chemistry has increased substantially. Several models were developed for drug discovery to hasten the process to rejuvenate the "dry" pipeline of new drugs. The R & D spending for "in house" new drug discovery by many pharma companies has to change their "strategy" and started finding out their strategic partners across the globe including India. Few success stories are noteworthy.

In last few years, Indian pharma companies, contract & clinical research organizations have contributed significantly towards new drug discovery by such alliances, but it is surprising that rarely two or three Indian pharma companies have join hands to march ahead in drug discovery.

Role from Indian subcontinent is somewhat restricted to be an "attached compartment of moving engine of fast speed train". Though India has many advantage of world class infrastructure at government and non government sectors, capacity building, huge trained pool of scientists from different disciplines of drug research, this potential is yet to tap.

This area is of grave concern, in spite of self reliance in many API & formulations of essential drugs due to concerted efforts between 1970-2005 for make them affordable and cheaper, not only in India but in exporting many third world countries.

We are yet to develop a robust chain without missing a single link with the help of all stakeholders under time bound schedule especially for malaria, tuberculosis, cancer, diabetes, obesity (and malnutrition too). A challenge is to create an appropriate techno-economic pathway for successful drug discovery in India.

PL-8

Complex Natural product Structures a Driving Force for Innovations in Organic Chemistry

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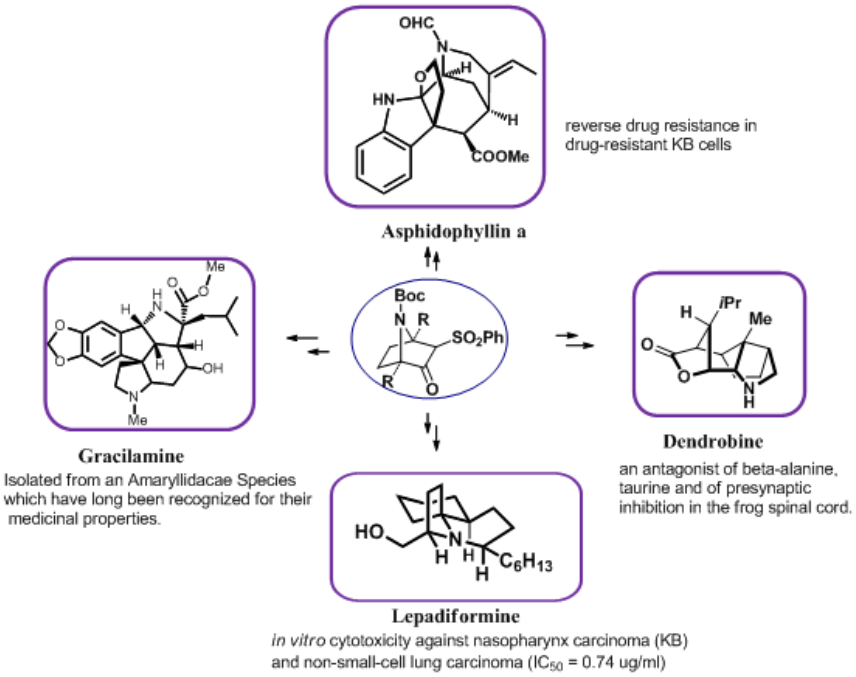
Unique and diverse natural products possessing high target affinity and specificity have been the richest source for novel modulators of biomolecular functions. Organic chemist has been intrigued over the years by the complexity of natural product synthesis which has also played essential role in drug discovery and chemical biology. With the introduction of novel, innovative concepts and strategies for synthetic efficiency, natural products synthesis is well poised to address the challenges and the complexities faced by natural products chemistry which would also be essential to the progress of biomedical sciences.

With above goal in mind, we have been focusing our activities towards developing novel synthetic route for the total synthesis of some biologically active alkaloids (Fig.1) from optically active azabicyclo[2.2.1] heptanone structural frameworks.



This approach will also be useful for drug discovery and chemical biology study with these molecules. Details of the concept and synthesis would be discussed.

INVITED

IL-1

Peptoids for organ targeted delivery of bioactive molecules

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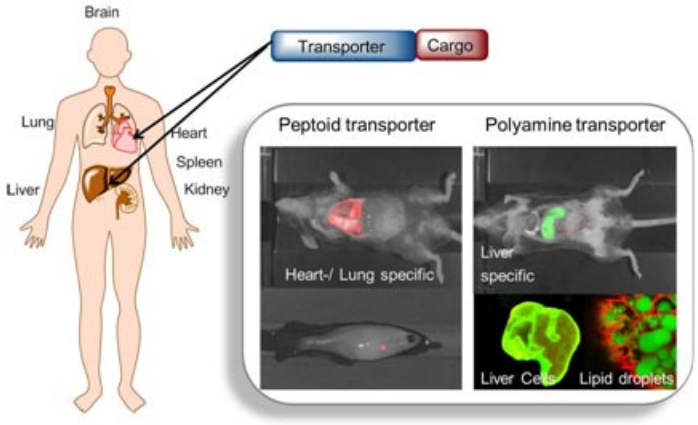
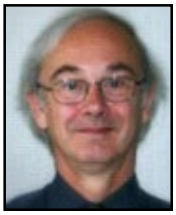
In order to deeply understand neural development and tissue regeneration and synthetic reconstruction we need to elucidate the role of key effector molecules. In order to understand these factors one has to manipulate them by using different tools. These tools can comprise bioactive molecules to downregulate or upregulate key molecules in cells and organisms such as siRNAs or morpholinos as well as peptides and proteins for the elucidation of biological mechanisms in neural development and tissue regeneration/reconstruction as well as the elucidation of factors that are involved in the response of the innate immune system during regeneration. How can we get those molecules and tools into cells and how do they specifically get into different organs such as brain, liver, muscle etc. We have been working since quite some time on the development organ targeting transport molecules on the basis of cell penetrating peptoids and polyamines, we are currently investigating tools to address organ specific delivery of bioactive molecules.Cell penetrating peptoids (CPPos) are potent mimics of the corresponding cell penetrating peptides (CPPs). The synthesis of diverse oligomeric libraries that display a variety of backbone scaffolds and side-chain appendages are a very promising source of novel CPPos, which can be used to either target different cellular organelles or even different tissues and organs.We have established a radiofrequency tag based combinatorial synthesis of different peptoid librariesin IRORI MiniKans to expand the amount for phenotypic high throughput screens of CPPos, where we systematically changed the properties of the peptoids.The libraries consisting of tetrameric to hexamericpeptoids [oligo(N-alkylglycines)] were established on Rink amide resin in a split and mix approach.Typically, they contain positively charged amino side chains which are synthesized via their protected analogues. To avoid the use of amine protecting groups a Click-chemistry based modular synthesis of novel hydrophilic as well as amphiphilic cell penetrating peptoids were developed to generate novel structures for drug delivery in organs. All CPPos of the presented library were fluorophorelabeled to allow for the monitoring of cellular uptake by fluorescent confocal microscopy or small animal imaging. So far, have already isolated heart/ lung, liver, brain and melanoma specific peptoids.



IL-2



The Antibacterial Drug, MGBBP3, from Discovery to Clinical Trial

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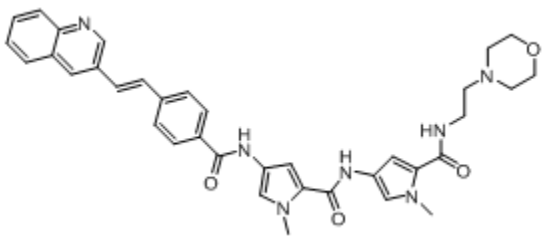
The need for new and effective anti-infective drugs, including antibacterial compounds, is recognized world-wide. In particular, compounds from new structural classes that work through new biological mechanisms are being sought so that the risk of early resistance emerging can be minimized. The oligoamide natural products, netropsin and distamycin, have been known since the 1960s to have a wide range of anti-infective biological activities but with limited selectivity and potency. These activities have been presumed to be a result of their ability to bind to the minor groove of DNA and to inhibit in some way the normal function of DNA, possibly by binding to transcription factor sites. With these compounds as starting points, a library of analogue minor groove binders (MGBs) has been prepared in which some of the N-methylpyrrole amino acid building blocks have been modified to increase the lipophilicity so as to increase hydrophobic interactions with the backbone of DNA. In addition, benzenoid aromatic groups have been introduced and most importantly, one of the amide links replaced by its isosteric alkene. Together, these changes have led to a family of MGBs with a wide range of anti-infective activities. Of these compounds, MGBBP3 is the most developed and will enter clinical trials for the treatment of Clostridium difficile infections in 2015.

MGBBP3 is highly and rapidly active against Gram positive bacteria and is superior to vancomycin in most measurements. Its development has been undertaken in partnership with a new Scottish company, MGB Biopharma, which has worked with the University and a number of CROs to produce clinically acceptable products. The property that dominated the development of MGBBP3 is its strong tendency to form head-to-tail dimers, a consequence of the lipophilic components of the molecule. Nevertheless, the laboratory synthesis has been scaled up to multi kilo scale producing API for clinical trial in greater than 99.5% purity (Almac, Northern Ireland). Formulations for both GIT and intravenous delivery have been developed (Aptuit, Scotland). The mechanism of action and selectivity of MGBBP3 are being investigated through cell biology studies of the transcriptome of Staphylococcus aureus when challenged by the drug and transport into and out of cells. It appears that a failure of energy production accounts for cell death in S.aureus. Cell wall and cell membrane transporters seem to be important in determining selectivity. The presentation will give an up to date description of the properties and mechanism of action of MGBBP3.



MGBBP3

IL-3

Designing multitarget drugs for neurodegenerative diseases

Maria Laura Bolognesi

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Despite the large research effort, for Alzheimer's and other neurodegenerative disease there is no cure. The molecular mechanisms of these diseases involve a complex array of processes operating simultaneously and synergistically, including: (i) protein aggregation; (ii) oxidative stress; (iii) mitochondrial dysfunction; (iv) unbalance of metal ions. Therefore, it is extremely challenging to develop therapies for major neurodegenerative diseases. The dominant drug discovery paradigm is 'one disease, one target, one molecule', which ignores the polyetiological nature of such maladies. Thus, this paradigm has been shown to be a possible factor in the ongoing failure of current neurotherapeutic drugs. An alternative approach involves single chemical entities that interact simultaneously with multiple targets, the so-called multitarget drugs. This polypharmacological approach is more promising because it is more adequate at addressing the multifactorial and progressive pathophysiological processes involved in neurodegeneration.

By way of illustration of this principle, in this lecture, using examples taken from my own research, I will propose MTDs as innovative tools for addressing the drawbacks and pitfalls of current drug discovery.

IL-4

Recent Developments in Aqueous Chemistry

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According to the green chemistry principles, organic chemists are deeply encouraged to develop environmentally-benign products and processes using ecologically friendly materials and solvents, with no or minimal amount waste generation. In this conference, conventional micellar catalysis and "magic" photochromic micellar catalysis [1,2] will be presented including:
reductive pinacol coupling affording 1,2-diols via C-C bond creation between two carbonyl compounds;
Barton decarboxylation affording new carboxylic acid or diacid via radical homologation;
Pd-catalyzed Tsuji-Trost reaction affording allylic analogues via C-C, C-N, C-S bond creations [2].
Conception, synthesis and physico-chemical properties will be detailed.

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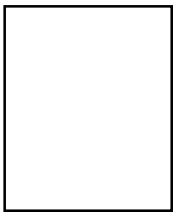
IL-5

Development of Some Novel and Green Protocols in Organic Synthesis



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In today's world, synthetic chemists in both academia and industry are constantly challenged to think about more environmentally benign methods for generation of the desired target molecules. As a result, green chemistry has attained the status of a major scientific discipline, leading to the development of cleaner and more benign chemical processes with many new technologies being developed each year. Microwave has emerged as a novel and benign source of energy for chemical reactions and has been extensively investigated in organic synthesis during recent years. Catalyst and solvent usage is often an integral part of a chemical or manufacturing process. Toward this end, considerable efforts have been devoted to develop and use nontraditional catalysts and solvents for chemical synthesis.

The development of novel chemical reactions and recuperating the reaction conditions to maximize product selectivity, energy efficiency, and environmental safety remains the main thrust of current chemical research. Direct formation of C-C and C-X linkage via carbon hydrogen (C-H) bond activation of hydrocarbons is of immense importance and has currently emerged as a challenging goal.

In view of the above and as a part of our ongoing research interest, some recent results on the development of some new and green protocols for the synthesis of useful organic compounds will be discussed.

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IL-6

Design and development of novel anti-Parkinsonian agents in the therapy of Parkinson's disease

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Parkinson's disease (PD) is a progressive, neurodegenerative disorder resulting from degeneration of dopamine-releasing neurons of the substantial nigra, one of the movement control centers of the brain. The balance between the excitatory effects of acetylcholine and the inhibitory effects of dopamine within the motor system are regulated, however, a state of dopamine depletion occurs in the nigrostriatal degeneration. Stimulation of striatonigral with dopaminergics and blockage of striatopallidal pathway with A2a receptor antagonists to release dopamine has potential to increase motor activity in PD patients. Rational design and synthesis of dopaminergics and A2A receptor antagonist has been carried to alleviate the symptoms of PD.

IL-7

Assessment of catalytic accessibility of nanomaterials towards the synthesis of pharmaceutically imperative heterocycles moieties.

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Wet chemical precipitation method has been explored for the synthesis of a wide variety of nanoparticles (NPs) including CuO, ZnS, CdS and dopped nanoparticles with excellent catalytic properties and high stability in water. Moreover, this promising green technique for synthesis of nanoparticles was extended for the synthesis of magnetically separable nanoparticles as well. The magnetic nature of these heterogeneous nanocatalysts allows for its easy separation from the reaction mixture by using simple bar magnet, which is an additional greener

attribute of this approach. The nano-sized tiny particles increase the exposed surface area of the active component of the catalyst, thereby enhancing the contact between reactants and catalyst dramatically and mimicking the homogeneous catalysts. Besides, tremendous efforts have been implemented in the development of catalytic processes by employing water as a medium to accomplish greener syntheses. Thus, we modified the laborious process of lead discovery by accumulating green methodologies and nanotechnology.

To further utilize the potential of the dynamic characters of nanoparticles for the construction of heterocyclic frameworks, we describe herein nanoparticles catalyzed one pot multi component chemo\region\diastereo-selective synthesis of library of spiro and annulated heterocycles in aqueous medium. These processes are capable of generating 2-3 chiral alongwith spiro centers in a single reaction which enhances the biocidal profile or may discover new medicinal properties. Greenness of the process was well instituted as water was exploited both as reaction media as well as medium for synthesis of various doped and magnetically separable nanocatalysts. The synthesized compounds were screened for various biological activities such as anti-microbial, anti-mycobacterial, anti-malarial, DNA cleavage, anti-hyperglycemic, anti-oxidant activity, etc.

Fig. 1 Few representative examples of synthesized heterocycles

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IL-8

Synthetic Analogues of Indole Alkaloids as Potent Tubulin Inhibitors

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Microtubules constituted by a dynamic polymerization and depolymerization of - and -tubulin heterodimers are known to play a pivotal role in the development and regulation of cell shape by involving in a range of cellular functions.1 Dynamic equilibrium of tubulin-microtubule are recognized as one of the important targets for the identification of potent anticancer agents.1 The structurally diverse natural and synthetic analogues capable of

modulating the polymerization or depolymerization of microtubules are of significant interest as chemotherapeutic agents. The three identified binding cites of tubulin are the vinca alkaloids, taxanes and colchicine sites. There are many microtubule targeting agents including taxanes, colchicine, podophyllotoxin, combreastatin and vinorelbine are known to induce cell death by affecting apoptosis.2 Anti-mitotic agents including taxanes and vinca alkaloids have been continuously used in the clinical treatment of various human cancers over the past decade. However, the development of drug resistance, lack of tumor specificity, complex synthesis, and low bioavailability make the available anticancer drugs suboptimum for the treatment of cancer. Indole is one of the important heterocycles found to as a part of numerous natural and synthetic compounds endowed with a range of biological activities such as antiproliferative, antimalarial, anti-inflammatory, antifungal and antibacterial activities.2 Over the last few years, many indole-based tubulin polymerization inhibitors have been discovered from natural sources or prepared by chemical synthesis. For example, 3-indolylphenylmethanones, diarylindoles, aroylindoles, arylthioindoles etc have been prepared as antitubulin agents.2,3 In view of interesting biological properties of indole alkaloids and related heterocycles, we have synthesized various azaheterocycles bearing indole scaffold and evaluated for their in vitro cytotoxic activities against a panel of human cancer cell lines. Further mechanistic investigation revealed that some of the potent analogues could inhibit the microtubule polymerization by binding to the colchicines cite and induce apoptosis in cancer cells. Design, synthesis and molecular target studies of novel analogues of indole alkaloids will be discussed in the presentation.

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IL-9

Some Application of Directing Group in the Synthesis ofFunctionalize Heterocycles

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Functionalized heterocycles is an important class of compounds that is present as a structural motif in natural products, and in several physiologically active agents such as nucleic acids, antibiotics, hormones. The synthesis of highly functionalized heterocycles, particularlyisoquinoline, benzoxazole, indole and indolizine derivatives, is highly demanding not only in the construction of natural products, but also in asymmetric syntheses, and

agrochemicals. In the recent years metal catalyzed direct C-H activation via five or six membered cyclic transition state emerged as powerful and handy tools for synthesizing the functionalized heterocycles. The most common strategy for C-H activation involve use of directing groups to facilitate transformation of the thermodynamically stable cyclic transition state that eventually leads to atom economical products. In spite of the various synthetic routes already developed towards the synthesis of pharmaceutically active heterocyclic compounds, there is still much need to address the problems associated with regio selectivity, atom economy and efficient directing group for their synthesis.Some of the application of directing group in the synthesis of functionalized heterocycles at IITPatnawill be presented. The scope and limitations of such chemistry will be discussed using selected examples.

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IL-10

Understanding of Molecular Recognition and Function of an Essential Enzyme for Antiviral Drug Developments

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Norovirus protease is an essential enzyme for a proteolytic maturation of norovirus nonstructural proteins. The protease, therefore, has been implicated as a potential target for antiviral drug development. Though high resolution X-ray structures have given wealth of information about how this protease interacts with its substrate, it is unclear how the fluidity of certain residues in binding pocket plays a role in substrate recognition as well as overall catalytic activity of norovirus protease. In our efforts toward the development of antiviral compounds we have performed structural, functional and inhibition studies of this protease using multidimensional NMR spectroscopy and fluorescence resonance energy transfer (FRET) assay in the presence of a synthetic protease inhibitor. The C-terminal domain, which is responsible for ligand binding, shows significant structural variation in our solution NMR structure when compared to crystal structures. Also 15N spin relaxation data analyses show wide range of time scale motion for residues in the C terminal domain. In particular, the long loop spanning residues T123-G133 shows fast motion (ps-ns), and the residues in the bII-cII region forming the large hydrophobic pocket (S2 site) undergo us-ms time scale motion indicative of conformational exchange on slower time scales. The results from our recent studies providing insight into ligand binding and suggesting a possible mechanism for how this enzyme recognizes multiple sites in the norovirus polyprotein will be presented.

IL-11

Towards New Pyrazoles of Potential Biological Activities

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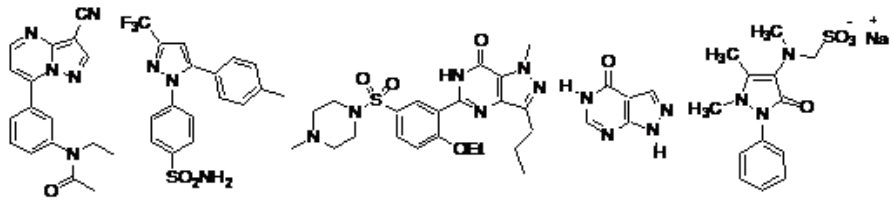
Pyrazole and its derivatives play an important role in medicinal and pesticide chemistry. They possess a wide range of bioactivities such as antimicrobial, anticancer, anti-inflammatory, antidepressant, anticonvulsant, antiparasitic, antipyretic, antiallergic, antihypertensive, antiviral activities [1-12] and as adenosine receptor antagonists [13].
Zaleplon [14], celebrex [15], sildenafil [16], allopurinol [17] and dipyrone [18] are some examples of pyrazole-based drugs which exist already in the market.



Zaleplon Celebrex Sildenafil Allopurinol Dipyrone

Many synthetic procedures exist for the synthesis of substituted pyrazoles. However, the development of simple, facile and efficient methodologies to get pyrazole derivatives and biologically active heterocycles containing the pyrazole moiety is always desired.

Several new pyrazole derivatives and pyrazole-containing heterocyclic systems have been synthesized using 1,3-disustituted-1H-pyrazol-5(4H)-one, or pyrazole aminonitrile and pyrazole aminoester derivatives as starting materials. Different synthetic strategies leading to different new pyrazole-based heterocyclic systems will be presented and discussed. The biological activities of some of the compounds prepared will be highlighted.

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IL-12

Chemo-enzymatic synthesis of biobased nitrogen containing bulk chemicals

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Nitrogen-containing compounds are produced on a huge scale by bulk chemical industry. They are mainly used as building blocks for polymers (e.g. acrylamide, acrylonitrile, caprolactam, 1,4-butanediamine) and as constituents of pharmaceuticals and agrochemicals (e.g. pyrrolidine, piperazine and derivatives).Their production implies the use of fossil resources, and of ammonia,which production is very energy-intensive. In nature, most nitrogen is stored in amino acids and proteins so we asked ourselves whether plant derived amino acids can be used as bio-based feedstocks for nitrogen-containing bulk chemicals. We have performed the following transformations of amino acids into nitrogen-containg bulk chemicalsusing enzymatic and chemical transformations:

- glutamic acid to N-methylpyrrolidone [1,2];
- glutamic acid to acrylonitrile [3]
- glutamic acid and glutamine [4] to 1,4-diaminobutane
- arginine to ornithine [5] to 1,4-diaminobutane [6]
- aspartic acid to ?-alanine [7] to acrylamide
- acrylates to ?-alanine derivatives [8]to polyamides [9]
- lysine to 5-aminovaleric acid [10]

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IL-13

Chemo-enzymatic Route to Therapeutically Important Sugar Modified Nucleosides

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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. C2?-endo (S-type) and C3?-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.

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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IL-14

Thiazole-based aminopyrimidines and n-phenylpyrazolines as potent antimicrobial angents. Synthesis and biological evaluation

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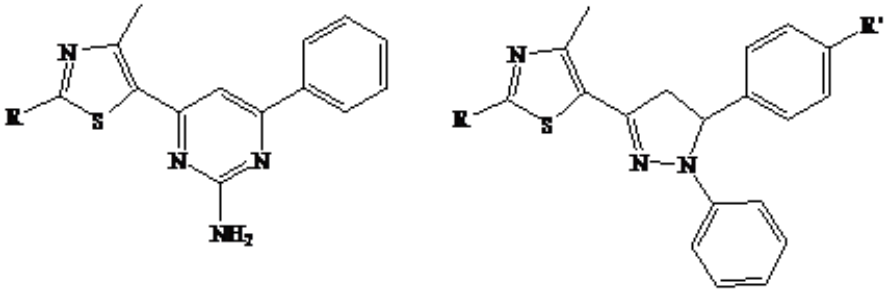
The treatment of infectious diseases still remains an important and challenging problem because of a combination of factors including emerging infectious diseases and the increasing number of multi-drug resistant microbial pathogens with particular relevance for Gram positive bacteria.1-5 The therapeutic problem has achieved increasing importance in hospitalised patients, in immuno suppressed patients with AIDS or undergoing anticancer therapy and organ transplants. In spite of a large number of antibiotics and chemotherapeutics available for medical use, at the same time the emergence of old and new antibiotic resistance created in the last decades a substantial medical need for new classes of antibacterial agents. Taking into account the interesting antimicrobial and chemical properties of thiazole, pyrimidine and pyrazoline derivatives, herein is presented the synthesis and evaluation of antimicrobial activity of the compounds presented in Scheme 1.



Scheme 1

The antimicrobial assay was carried out by microdilution method. For the evaluation of the antifungal activity of the compounds, the following fungi were used: A. ochraceus,, A. fumigatus, A. niger, A. versicolor, A. flavus, P. funiculosum, P. ochrochloron, T. viride, C. albicans and F. Sporotrichoides while for the antibacterial tests were

used Gram-negative bacteria E. coli, P. aeruginosa, S. typhimurium, En. faecalis and Gram-positive bacteria L. monocytogenes, B. cereus, M. flavus, En. cloacae and S. aureus. As reference drugs were used a) ketoconazole, bifonazole and b) ampicillin, streptomycin for the antifungal and antibacterial assays respectively.

The tested compounds exhibited outstanding antimicrobial activity, being in most of the cases more potent than reference drugs. Our promising findings lead the way for further investigation in order to unveil the mechanism of action at molecular level, responsible for the activity of the title heterocycles.

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IL-15

Targeted Synthesis of Natural Compound Analogs. Novel Reactions and Rearrangements

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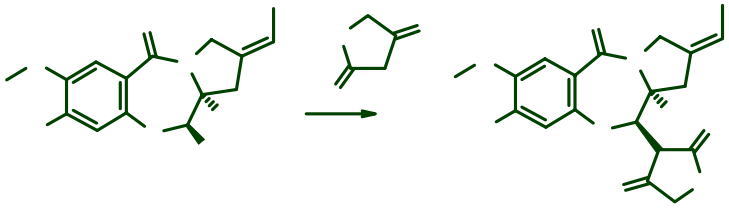
Several types of chemical reactions have been applied for modification of alkaloids in the frame of InterBioScreen' Project "Modification of Natural Products in Drug Discovery" . Below are some examples of these transformations: Mannich reactions (A), Addition reactions (B), Cyclocondensation reactions (C),T-Reactions (D) and New Hemiaminal rearrangements (E) etc.

A



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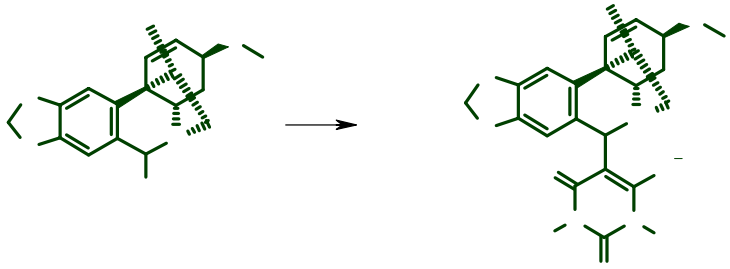

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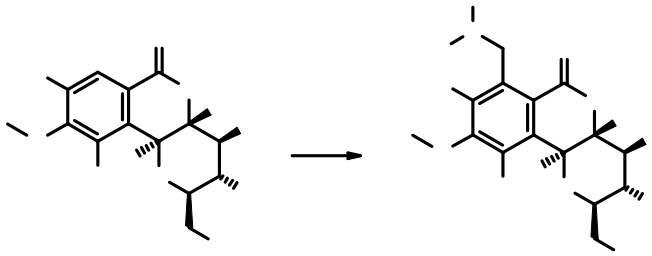
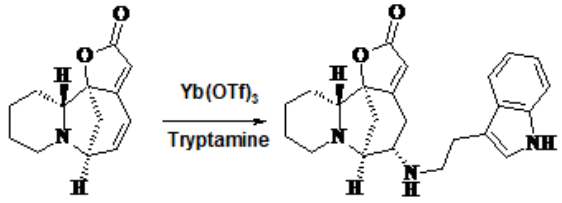


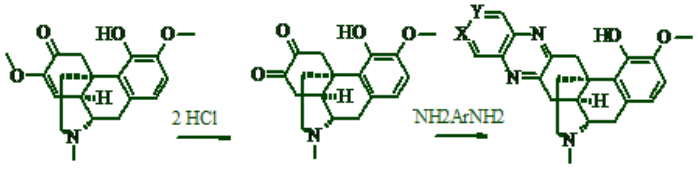
B



Securinine
from *Securinega spp.*

epi-Margaritarine
potent GABA blocker

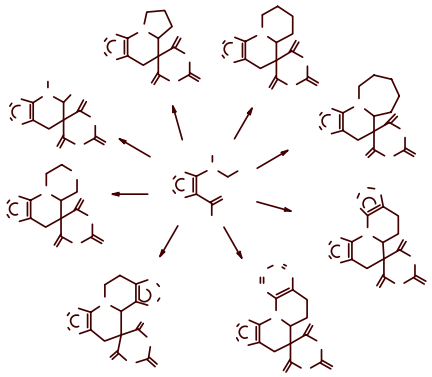
C



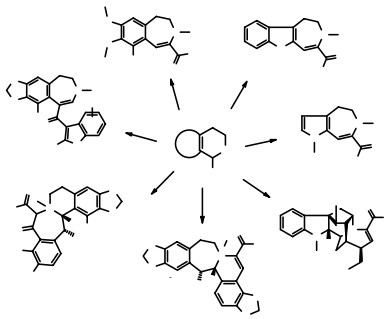
Sinomenine
from *Sinomenium acutum*

Potent antineoplastics

D



E



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IL-16

Molecular hybridization: a useful tool in the design of new drug prototypes

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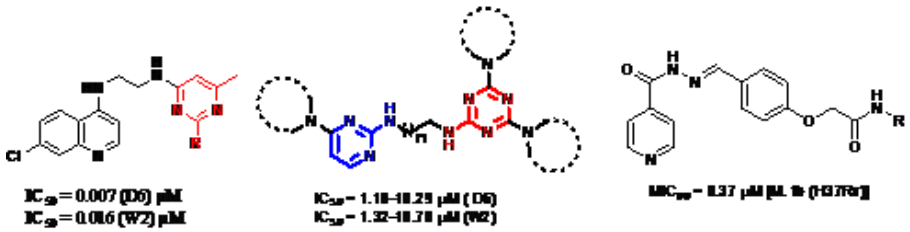
The design of new molecules with improved ADME properties along with effective pharmacologic potency and lack of toxicity for the treatment of infectious diseases has remained a big challenge for the scientific community. Molecular hybridization is a relatively new concept in medicinal chemistry, drug design and development which deals with the covalent hybridization of two or more distinct pharmacophores into a single molecule to produce a new hybrid compound with improved affinity and efficacy, when compared to the parent drugs [1-3]. Additionally, this strategy can result in compounds presenting modified selectivity profile, different and/or dual modes of action and reduced undesired side effects [4]. The development of such molecular frameworks with synthetic selectivity and economic viability still represents a big challenge for pharmaceutical sector and demands continuous efforts. Molecular hybrid is a structural modification strategy useful in the design of new optimized ligands and prototypes with new molecular architectures composed of two or more known bioactive derivatives, through the adequate fusion of these sub-unities. The molecular hybridization strategy is particularly interesting for the development of new prototypes for the treatment of infectious diseases where treatment is restricted to few commercial drugs or in the cases where compounds exhibit high toxicity or pharmacokinetic and pharmacodynamic restrictions. The advantage of using molecular hybridization is to activate different targets by a single molecule, thereby increasing therapeutic efficacy as well as to improve the bioavailability profile. Towards these goals we have synthesized various molecular hybrids and tested these for antimalarial, anti-TB and anti-cancer activities and efforts will be made to present our recent work [5-17].



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IL-17

Design and Synthesis of Metallic Potential Antitumor Agent, Characterization and in vitro Mechanistic Studies of Cancer Inhibition

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Medicinal inorganic chemistry is a multidisciplinary field combining elements of chemistry, pharmacology, toxicology and biochemistry. The clinical success of cisplatin and related platinum-based drugs, as anticancer agents that bind covalently to DNA, is severely affected by the serious side effects, general toxicity, and acquired drug resistance. This is an impetus to inorganic chemists to develop innovative strategies for the preparation of more effective, less toxic, target specific, and preferably non covalently bound anticancer drugs. Therefore, alternate strategies based on different metal ions, ligand functionality, shape or geometric requirement and stereo selectivity were opted to design new metal-based chemotherapeutic drugs.

New metallic complexes possessing CuII,SnIV/and RuIII bimetallic cores were synthesized by de novo design strategy involving a biologically active ligand scaffold. All the complexes were thoroughly characterized by elemental analysis and other spectroscopic data including 1H, 13C , 119Sn NMR and X-Ray crystallography Preliminary in vitro DNA binding studies viz. UV-visible, fluorescence, cyclic voltammetry and viscosity measurements were carried out. These complexes exhibit significant hyperchromicity on addition of DNA indicative of electrostatic mode of binding. Metal complexes have novelty due to molecular scaffold which ensures a dual mode of binding and preferential selectivity inside the cells copper ions specifically bind to N7 guanine residue of DNA while Sn(IV) ions prefer to bind the phosphate backbone of DNA helix. Furthermore, the bimetallic complexes exhibited avid DNA binding propensity as quantified by Kb, Ksv values and shifts in the peak potential values. DNA binding propensity of the complexes were also validated by its artificial nuclease

activity with supercoiled pBR322 DNA; complexes exhibits a remarkable DNA cleavage activity (concentration dependent) with pBR322 DNA and further it was observed that cleavage reaction involves various singlet oxygen species and hydroxyl radicals via hydrolytic cleavage mechanism.

IL-18

Molecular drug design, synthesis and a comprehensive biological insight of chiral metal-based antitumor chemotherapeutic drug entities: DNA binding profile, cleavage studies, in vitro cytotoxicity and in vivo systemic toxicity studies.

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Current interest in metal complexes is stemming from their potential use as antimicrobial, antiviral, antitumor agents, enzyme inhibitors, or chemical nucleases Recently, considerable research interest has arosen in metal-based compounds containing copper and tin which have exhibited promising chemotherapeutic potential that have different mechanism of action from platinum-based drugs .The fundamental role of copper and the recognition of its complexes as important bioactive compounds in vitro and in vivo is well-established and cooper is considered as potential drug for therapeutic intervention in various diseases. Furthermore, Sn and organotin complexes also gain attention due to their apoptosis inducing character.

Chiral drugs are at the forefront of pharmaceutical drug research as introduction of chirality not only enforces stereo-selective specific drug interaction but also promotes the formation of more active compounds with better therapeutic efficacy as biotargets viz., DNA which is the primary intracellular target is chiral in nature.

Copper and copper-tin heterobimetallic potential chemotherapeutic drug entities were designed, synthesized and evaluated for in vitro antitumor acitivity and their in vivo systemic toxic studies was also carried out. In vitro DNA binding profile of both (R)- and (S)-enantiomers of complexes was carried out to evaluate their enantioselectivity, exhibiting remarkable degree of enantioselectivity in their interaction with DNA, with the (R)-enantiomer exhibiting greater DNA binding propensity.

Apart from the modulation of the drug design, the possible role of dietary antioxidants (EVOO) in combination with anticancer agents can be promising to minimize or avoid primary genetic damage and therefore the effects of olive oil in the presence of the complexes which exhibited good cytotoxic activity and could be considered as potential chemotherapeutic drug candidate with CDDP have been evaluated. Considering the role of DNA damage in some diseases, the evaluation of the genotoxicity and protective effects of small molecules or therapeutic compounds has become very important. The micronucleus (MN) assay on peripheral blood or bone marrow cells is considered the primary assay for assessing in vivo genotoxic potential. The alkaline comet assay complements the MN test. We have analyzed the in vivo genotoxicity of these complexes by micronucleus testing on bone marrow cells and comet assay in peripheral blood lymphocytes.

IL-19

Contemporary Landscaping of 4-thiazodinones:
Synthesis and Biological Profile of Small and Hybrid Heterocyclic Molecules

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Heterocyclic compounds are an integral part of chemical and life sciences and constitute a considerable quantum of modern research that is being currently pursued throughout the world [1]. In this context, the diversity in biological response of 4-thiazolidinones has attracted an enormous amount of attention of many researchers to explore this framework for its potential. It is, therefore, of prime importance that the study of this topic and the development of new synthetic strategies should be based on the most recent knowledge, emerging from the latest research.

4-Thiazolidinone derivatives have attracted continuous interest over the years because of their diverse biological activities, such as anti-inflammatory, anti-proliferative, antiviral, anticonvulsant, anti-diabetic, anti-hyperlipidemic, cardiovascular, anti-tubercular, antifungal, and antibacterial. Compounds such as; ralitoline (anti-convulsant), etozoline (antihypertensive), pioglitazone (hypoglycemic) and thiazolidomycin (activity against streptomyces species), based on this pharmacophore are already in the market. In recent years, 4-thiazolidinone derivatives with antitumor activity on leukaemia, melanoma, lung, colon, CNS, ovarian, renal, prostate and breast cancer cell lines have become a promising area of research [2-6]. Our group has also been continuously involved in synthesis of small and smart hybrid motifs of this nucleus through chemical modifications with encouraging results [7-10]. The talk summarizes contemporary landscaping of 4-thiazolidinone synthetic chemistry and divulges the utility of this potent pharmacophore as a rich source of new compounds having promising biological activities. This assemblage recapitulates on going medicinal chemistry investigations worldwide, to explore novel chemical entities that can be useful in the treatment of many ailments.

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IL-20

Metal Based Drugs -An Under Explored Area

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In the recent years focus of research on developing drugs using different established moieties has enabled synthetic organic chemists to develop number of potential drug molecules. However, one area which is left under explored is drugs based on metal complexes. We have been working on biological activities of metal complexes and have tried to scrutinize metal complexes as potential drug candidates. Hydroxytriazenes and their metal complexes can be very potential anti-inflammatory agents as has already been established. The complexes vis-a-vis their parent ligands offer excellent area of research from activity point of view. This is the thrust of the present lecture.

IL-21

Chiral Catalystsfor Enantioselective Synthesis of -Aminoalcoholsfor Pharmaceutical Applications

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The role of chiral catalyst in the synthesis of pharmaceutically and biologically important organic compounds is ever increasing particularly in the area of asymmetric catalysisbecause one enantiomer of a chiral drug molecule is likely to show desirable therapeutic effects while other enantiomer can have a different or adverse biological response.1Among the various approachesto achieveenantio-pure -aminoalcohols, catalytic asymmetric meso-epoxide ring opening (ARO)2 and aminolytic kinetic resolution (AKR)3 of racemic epoxide with amine is of prime interest since it allows the formation of chiral -amino alcohol in a single step by the use of a small amount of chiral catalyst. This field has contributed significantly towards the requirement of enantiomerically pure -aminoalcohols particularly in pharmaceutical industry via designing of efficient chiral catalysts. Therefore, the present talk will outline our efforts in designing of chiral metal complexes/organocatalysts for the synthesis of -aminoalcohols as key intermediate for pharmaceuticals.

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IL-22

Societal Impact of Nuclear Energy and Radiation Technology

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Ever since its independence, India has achieved significant progress during the past six decades in various sectors such as agriculture, animal husbandry, industry, power, science and technology including the fields of space, nuclear energy and Radiation Technology.

Radiation Technology in Healthcare:

Radioisotopes and radiation have innumerable applications in health care including diagnosis, treatment and sterilization of healthcare products.

Radiation Technology in Agriculture and Animal Husbandry

Radiation technology is making significant contribution towardsfood security and safety through crop improvement, crop nutrition, crop protection and preservation of crop products.

Nuclear and Isotope Technology in Water Management

Nuclear techniques like isotope hydrology contribute to the overarching global goal of improving water quality, availability and its management. Isotope hydrology is an effective means ofidentifying, assessing and managing water resources.

Nuclear and Isotope Technology in Industries

Radiation and radioisotopes have diverse application in industries helping the industrial growth benefitting the society. There are four major areas in which nuclear technique contributes to industries - non-destructive evaluation and testing of equipment, Nucleonic control system, industrial process troubleshooting and optimization and radiation processing for material modification.

Radiationand Isotope Technology in Environment

Nucleartechniqueshave tremendous application in environmental conservation. Isotope tracer technique is widely used to trace origin of terrestrial and oceanic pollution as well as in understanding various environmental related cycles including ocean climate coupling and carbon cycling, enabling scientific prediction.

Radiation treatment offers an effective mean of mitigating pollution by radiolytic destruction of chemical and microbial pollutants. BARC developed radiation treatment technique is being widely used for sewage treatmentand its conversion into bio-fertilizer.

Nuclear technique also helpsfarmers to optimize their irrigation, fulfilling the vision of "MORE CROP PER DROP". Nuclear technique for pest control reduces use of pesticides which are harmful to environment.

Miscellaneous Application

Radiation based systems are widely used in security (access control); telecommunication, defence equipment etc.

Societal Contribution of Heavy Water Board through Isotope Technology

Towards societal commitment, Heavy Water Board (HWB) is engaged in production of stable isotopes like Deuterated compounds (NMR solvents), Boron-10, Boron-11 and Oxygen-18. Deuterium has numerous applications in high technology area and life sciences. Deuterium conditioning of optical fiber is a boon to Information Technology.

IL-23

Drug Discovery in organic chemistry labs: scope and limitations of academic compound facilities

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In 2009, the platform "ComPlat" has been installed at the Karlsruhe Institute of Technology (KIT) to enable collaborations of chemists with biologists and to join forces in the field of compound screening and drug discovery. The platform acts as a storage and management facility and offers know-how and capacity for organic synthesis. The libraries of the platform ComPlat have been initiated with the results of several natural product syntheses and projects with methodic background at the KIT. They cover now - due to the participation of collaborating groups worldwide - a variety of molecules with diverse origin and are offered to interested groups of external academic partner institutions as well. The platform benefits from a network of chemists and biologists and is able to conduct in vitro and vivo assays (including zebrafish and mouse model) in collaboration with the Institute of Toxicology and Genetics of the KIT.[1],[2] A selection of molecules will be given as result of the latest KIT-library screens and new projects will be shown to present some perspectives of an academic compound facility.

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IL-24

Chiral Catalysts for Asymmetric CyanationReaction

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The asymmetric cyanation across C=C, C=O and C=N bonds ranks among the most important and well-studied reaction in asymmetric catalysis to achieve useful chiral building blocks for pharmaceuticals, agrochemicals and specialty materials1,2. The asymmetric cyanation reaction demands careful selection of a chiral catalyst and a cyanide source. A number of efficient and successful synthetic strategies have been developed that include asymmetric cyanation utilizing enzyme, organocatalyst and metal complexes as catalysts3. As far as the source of cyanide is concerned, inorganic cyanides e.g., NaCN and KCN; and organic cyanides e.g., trimethylsilyl cyanide (TMSCN), alkyl cyanoformates, acetone cyanohydrin, acetyl cyanide, alkyl cyanophosphorylates etc. have been employed depending upon targeted substrates. We have developed a series of efficient recyclable chiral metal complexes and organo-catalysts for highly enantioselectivecyanation reaction of aromatic, aliphatic aldehydes and aldimines using different source of cyanide with added advantage of catalyst reuse. The catalytic system provides an efficient protocol for the synthesis of pharmaceutically active compounds.

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IL-25

Making Olefin Metathesis Work-Recent Results in Ruthenium Catalysts Design and Applications

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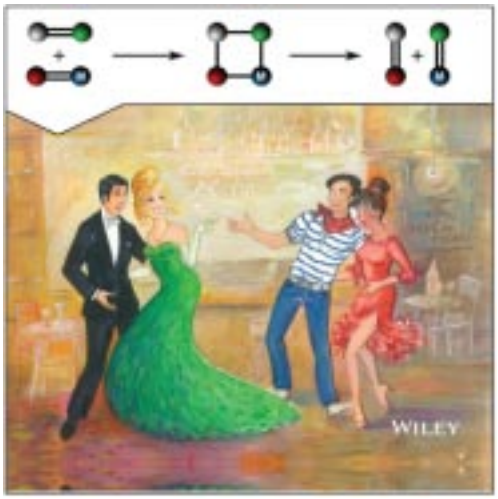
Ruthenium-catalyzed olefin metathesis reactions represent an attractive and powerful transformation for the formation of new carbon-carbon double bonds [1]. This area is now quite familiar to most chemists as numerous catalysts are

available that enable a plethora of olefin metathesis reactions [1]. However, formation of substituted and crowded double bonds, decreasing the amount of metal, using metathesis in medicinal chemistry, etc. still remain a challenge, making industrial applications of this methodology difficult [2]. These limitations can be solved by designing new, more active and stable catalysts and catalysts that can be easier removed / recycled [3].



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During the lecture a number of representative examples will be presented.

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IL-26

Gem-diphosphonates: the motif of diverse biological and medicinal importance

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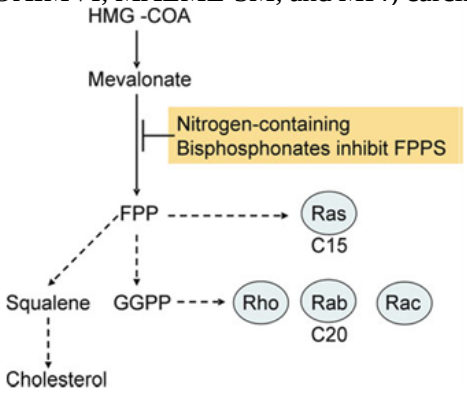
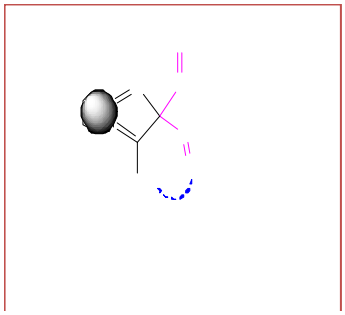
Bisphosphonates (BPs) are the most widely used and effective anti-resorptive agents for the treatment of diseases in which there is an increase in osteoclastic resorption. Recently, laboratory studies highly suggest that the third-generation of BPs, named N-BPs (e.g., ibandronate and zoledronate) can induce important antitumor effects in breast cancer cells in vitro by promoting apoptosis [1], and inhibiting cell adhesion and invasive potential. Nevertheless, it has been noted that the in vitro concentrations of N-BPs required inducing breast cancer cell apoptosis are higher than those required for osteoclast apoptosis. This recent discoveries of antitumor potency of N-BPs was attributed to the differences of their molecular mechanism of action. Thus, BPs can be grouped in two main different classes: first-generation is non-N-BPs and the second generation is N-BPs. First-generation of BPs, such as clodronate and etidronate, are metabolized intracellular to analogues of ATP by inhibiting ATP-

dependent enzymes. In contrast, second-generation N-BPs, such as pamidronate and zoledronate, interfere with mevalonate biosynthetic pathway, by inhibiting farnesyl diphosphate (FPP) synthase. Our recent [2, 3] and present work considered an elaboration of a novel series of nitrogen and/or sulfur containing BPs. Several of these N-BPs reflected remarkable antitumor activity against breast (especially MDA-MB-231/ATCC and BT-549), and myeloma (LOXIMVI, MALME-3M, and MI4) carcinoma cell lines.





Mechanism of action of N-BPs

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IL-27

Exploration of GPCR activation via protein dynamics and allostery, and its application to drug discovery

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G-protein coupled receptor (GPCR) is a major gatekeeper of extracellular signals on plasma membrane and activates the inside signal transduction pathways. Since this protein family is involved in many diseases, GPCR is one of the most important therapeutic targets for drug discovery. For deeper understanding of the regulation mechanism of GPCRs, the explanation of allosteric modulation and related intra-molecular signaling would be of a great help. To investigate the intra-molecular signaling of A2A adenosine receptor (A2AAR) which belongs to GPCR, we adopted network analysis to the apo and agonist-bound forms of the receptor. By analyzing graph representation of the structures, we calculated the maps of information flow and identified the important residues for intra-molecular signal transduction. Our analysis precisely identified the location of micro-switch residues,

which are critical to mediate signaling in GPCRs. It also showed that long-range communications exist between agonist-binding site and G-protein binding site.
Recently, we discovered novel A3AR modulators and found that minute chemical modifications crossover the boundary between agonistic and antagonistic effects. Using the A3AR homology models newly constructed based on multiple receptor conformations, we found out that the interaction with Thr94 plays a crucial role for agonistic effect of A3AR. Interestingly, this residue was also identified as an allosteric hot spot by our network analysis. Our new models constructed regarding the pharmacological profile of the ligands can facilely predict the boundary between agonist and antagonist in A3AR. Taken together, these structure-based modeling studies using MRCs and network analysis can provide valuable insights into the agonism and allosteric modulation of GPCRs, and they could be utilized as powerful tools in drug discovery.

IL-28

From Synthons to Bioactive Molecules: Efficient Stategies for heterocycle Synthesis

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'Small molecule heterocycles' play important role in both drug discovery and material science research providing one of the richest source of diversity, besides serving as rigid scaffolds for further display of a range of functionalities. Therefore design and development of new pathways leading to efficient synthesis of novel heterocycles, displaying skeletal and functional group diversity is emerging as an important area in both synthetic, medicinal chemistry and material science research.

For past several years, our research group has been engaged in design and development of new efficient methodologies for a wide range of substituted and fused five and six membered heterocycles utilizing organosulfur synthons such as polarized ketene dithioacetals and the corresponding N,S-acetals derived from them, as versatile building blocks. We have recently developed and synthesized new class of organosulfur synthons i.e. ?-(methylthio)-?-/?-aryl/ heteroaryl/alkyl acrylonitriles and utilized them for designing new reactions for diverse class molecular entities such as benzo[b]thiophenes, arylacetylenes, functionalized heteroarenes and other novel heterocyclic scaffolds of biological/material importance. Some of our recent results on these new synthetic methods derived from other easily accessible organosulfur building blocks involving organometallic methods, radical cyclizations, transition metal catalyzed intramolecular C-C, C-N and C-S bond formation, and cycloadditions of metalloisocyanides, domino reactions will be presented in the lecture.1

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IL-29

Micelles catalyzed chemo- and regio-selective synthesis of 1,4Naphthoquinones in H2O that potently induce apoptosis in cancer cells

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The extensive use of water as a medium for organic synthesis has been due to concept and language of Sharpless et.al.1 where reactions were carried out in aqueous solutions for cases where reactants are insoluble in water. The surfactant-type catalysts play a dual role both as a catalyst to activate the substrate molecules and as a surfactant to increase the concentration of organic reactants to form micelle particles in water which have been extensively used.In connection with our studies on the reactivity of naphthoquinones with nitrogen and sulfur nucleophiles in aqueous medium and the utility of surfactants in aqueous medium,we have carried out reaction of 1,4-naphthtoquinones and its derivatives with sulfur and nitrogen nucleophiles by economical green methodology approach using surfactant as a catalyst. The green methodology approach has led to synthesis of 1,4-naphthoquinone derivatives and polyheterocyclic compounds which have been evaluated for their anticancer activity against human cancer cell lines. The details of anticancer activity will be discussed.

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IL-30

Chemoenzymatic Synthesis of Amphiphilic Polymeric Architectures for Biomedical Applications

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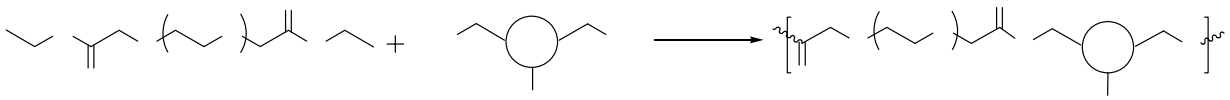
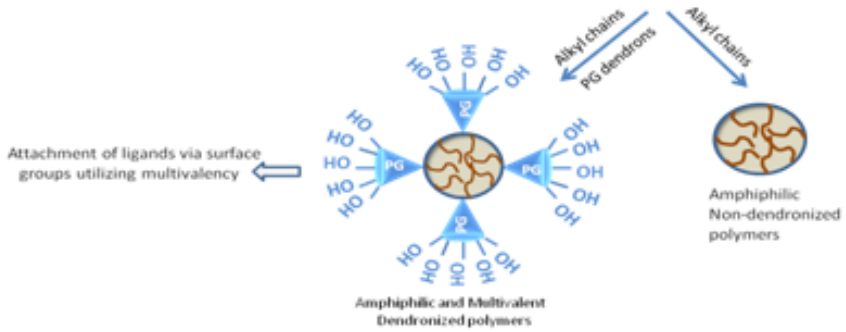
Nanotechnology is one of the most rapidly growing fields because of its ability to control the materials on the nanoscale. The amphiphilic polymers and dendritic scaffolds have been explored enormously for the transport of various bio-active components like genes, drugs, growth factors, antibodies and various others [1]. Over the past few years, significant progress has been made in the direction of synthesizing dendritic and multiarm polymeric scaffolds which act as unimolecular transport systems. Our group has also worked on the synthesis of amphiphilic dendronized [2] and non-dendronized [3] polymers and explored their transport potential. The dendronized polymers have an extra advantage of the multivalency provided by the surface functional groups of dendrons which provides amphiphilicity along with additional binding sites for various targeting groups and other imaging probes [1]. We have used poly(ethylene glycol) diethyl esters, azido glycerol and azido triglycerol as synthons for immobilized Candida antarctica lipase (Novozym 435) catalyzed polymerization reactions. All the synthons used are biocompatible, non-toxic, and readily available. The resulting co-polymers were then functionalized with alkyl moieties and regular and hyper-branched polyglycerol (PG) dendrons. The multiamphiphilic dendronized / non-dendronized polymers aggregate in aqueous medium to form well defined nanospheres which have been explored for their encapsulation potential using model dyes and drugs. The cyto-toxicity profile of all the resulting amphiphilic polymers was also studied and these polymeric systems were found to be non-toxic over a wide concentration range. The synthetic methodology, characterization and transport study results will be discussed during the symposium.





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IL-31

Synthesis of heterocyclic compounds via transition metal-catalyzed inter- and intramolecular direct arylation

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Transition metal-catalyzed coupling reactions have become an integral part of organic synthesis for the construction of carbon-carbon or carbon-heteroatom bonds. Over the last decade, new areas have emerged that challenge the frontiers of synthetic organic chemistry. Selective construction of C-C or C-heteroatom bond by activating a specific 'inert' C-H bond is an emerging alternative to the conventional cross-coupling reactions for such transformations.1 Considerable interest towards these methods is attributed to the fact that it can be efficiently utilized for the synthesis of molecules of importance in pharmaceutical and material chemistry. The direct functionalization of C-H bonds provides shortcuts compared with classical organic synthesis, thus rendering synthetic routes more straightforward and atom-economical.

Encouraged by the growing demand for environmental friendly and economical protocols for the synthesis of complex molecules, we explored transition metal catalyzed C-C and C-N cross coupling reactions based on C-H bond activation for the synthesis of novel heterocyclic compounds.2 The lecture will highlight recent methods developed for the synthesis of fused heterocyclic compounds of medicinal importance using transition metal-catalyzed inter- and intramolecular (hetero)arylation involving C-H activation and tandem reactions.

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IL-32

Chemistry of 2-Cyanomethylbenzonitrile

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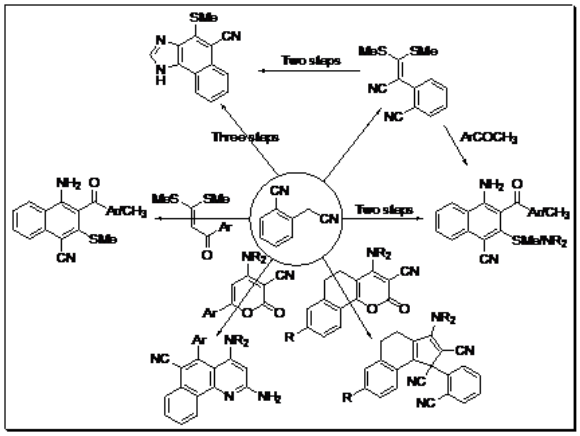

Various functionalized benzyl cyanides were used as precursor from several decades. Recently, we have picked up 2-cyanomethylbenzonitrile and used them as a carbanion source to explore their chemistry. We have synthesized various functionalized naphthalenes in good to excellent yield using 2-cyanomethylbenzonitrile.1,2 We have further explore 2-cyanomethylbenzonitrile as a carbanion source and isolated highly functionalized beno[h]quinolines on reaction with 2-pyranone.3 Interestingly, use of 2-oxo-4-secamino-1-yl-5,6-dihydro-2H-benzo[h]chromene-3-carbonitriles in lieu of 2-pyranone provides 1-(2-cyano-phenyl)-3-sec.amino-1-yl-4,5-dihydro-1H-benz[e]indene-1,2-dicarbonitriles.4 1H-Naphtho[1,2-d]imidazole were also synthesized in three steps involving 2-(1-cyno-2,2-bis methylsulfanyl vinyl)-benzonitrile1,5 as an intermediate obtained from 2-cyanomethylbenzonitrile.

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IL-33

A smart strategy for tuning the HOMO-LUMO gap

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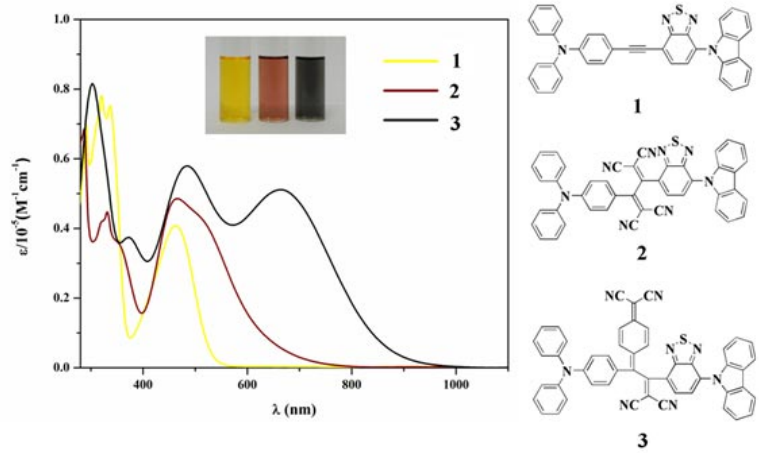
Low HOMO-LUMO gap materials are of wide interest due to their applications in optoelectronics such as organic light emitting diodes (OLEDs), organic photovoltaic devices (OPVs), organic thin film transistors (OTFTs), and non-linear optical (NLO) materials. Our group is involved in the design and synthesis of low HOMO-LUMO gap donor-acceptor molecular systems for photovoltaic applications.1,2 In view of this we have designed a smart strategy involving a click-type post-functionalization of acetylene ?linkers with tetracyanoethylene (TCNE) and 7,7,8,8-tetracyanoquinodimethane (TCNQ). The D-A system obtained through this strategy exhibits low HOMO-LUMO gap.3,4



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IL-34

Yoga of Chemistry and Commonsense: A Short-cut to New Drug Discovery

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New Drug Discovery is not simply to find a molecule possessing biological activity as perceived by most organic chemist involved in this activity. The fact is that New Drug Discovery followed by the registration, approval and launch in the world market requires involvement of Scientists (Molecular Biologists, Chemists, Microbiologists, Computer Scientists, toxicologists), Clinicians, Medical Practitioners, Statistician, Economists, Regulatory personnel, Engineers, Lawyers, Artists & Marketing Team to promote the drug and Pharmaceutical Industry have to overcome several hurdles, akin to a participants of a very long hurdle race, before the approved drug is able to see light of the day. In summary, the process of drug discovery & development is terribly complex and also needs few more things like passion, commitment and tons of money to reach the target.

Not only the success rate of any drug discovery / development is dismally very low but there are unlimited examples where an approved drug could not even generate enough revenue to meet the cost of development. And the worst happens when molecules are withdrawn from the market after successful launch due to some unfavorable outcomes leading to litigations & heavy payments to patients as compensation, putting unwarranted financial burden on the company.

The highlighted issues cannot be taken as deterrent or excuse for not involving in this important venture but are important for a company to assess their strength and weakness before taking the plunge. The best advice to the new players / aspirants, those they don't have enough experience and resources is to find out an innovative approach to start the activity which is likely to give guaranteed success in whatever they decide & do.

The talk will focus on a smart approach which not only has more that 99.99% chances of success but also requires much less time and money to discover and develop a novel drug. The case study taken for discussion makes use of the existing knowledge of the target coupled with awareness of inter-disciplinary areas of research and presence of mind to give highly rewarding outcome.

IL-35

Biomimiks™ as Chemosynthetic Livers: Predict, Prepare and Prove the Structure, Activity and Toxicity of Drug Metabolites

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We report advances in proprietary invitrogreen chemistry-basedBiomimiks™ technology, mimickingin vivo metabolism of several chemical entities used in pharmaceuticals, cosmetics, and agrochemicals. Biomimiks™ enables prediction of metabolism patterns and introduces new paradigms for drug discovery and drug-drug interactions for clinical diagnostics.

Metabolites are implicated in adverse drug reactions, and are the subject of intense scrutiny in drug R&D. Present-day processesinvolving animal studies are expensive, labor-intensive and chemically inconclusive.

Our catalysts (azamacrocycles) are sterically protectedand electronically activated, providing speed, stability and scalability. We predict structures of metabolites, prepare them on a large scale by oxidation, and elucidate chemicalstructures.Comprehensive safety evaluation enablesscientiststoconduct more complete in vitro

metabolism studies, confirm structure and generate quantitative measures of toxicity.Biomimiks™ is an animal-free platform that identifies a more complete set of safety-relevant drug metabolites while keeping up with the rapid pace of drug development.

Polypharmacy, involving co-administration of several drugs, is common among the elderly and chronically ill. It is a risk factor for adverse drug reactions (ADRs) and drug-drug interactions (DDIs). One plausible DDI occurs when a drug interferes with another, causing irreversible changes to formation of metabolites from one or both. Such suppression or attenuation of metabolism could cause variances in toxicity and efficacy. We report experiments to predict and confirm modulation of oxidative metabolites from several combinations of common drugs for cancer, diabetes, hypercholesterolemia and hypertension in the presence of each other. Recent papers indicate best evidence for the dimerization of some compounds in dilute aqueous solution or assorted complex formation between disparate compounds.

Biomimiks™ technology (in vitro and ex vivo) is designed to mimic the in vivo oxidative metabolism mediated by cytochromes P450. This can be applied at the individual patient level for chemistry-based diagnostics to determine comparative effectiveness and safety.

IL-36

Amino-catalyzed transformations of dicarbonyls: Synthesis of medium sized nitrogen heterocycles

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Organocatalysis has grown-up rapidly and applied successfully to several different enantioselective reactions in last one decade and therefore, now considered as the "*third pillar*" of enantioselective catalysis, together with biocatalysis and metal catalysis.[1] Additionally, nitrogen heterocycles constitutes a number of Small molecule natural products (SMNPs) acts as therapeutic agents for the treatment of a plethora of diseases that confront humankind in an age where the rapid emergence of multi-drug resistant forms of these are becoming an increasing threat. In the continuation of our interests,[2] recently we have developed new methods for the synthesis of heterocyclic SMNPs using amino-catalyzed transformation of dicarbonyls through D-A annulation approaches. Details of the D-A concept, design and synthetic strategy for medium sized nitrogen heterocycles as SMNPs will be presented here.

Figure 1: 1,3-and 1,4-carbon D-A annulation approaches for the synthesis of SMNPs

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IL-37

Using Technology to Improve Student Engagement and Success in a Flipped Classroom

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A subset of the biology faculty at University of Houston-Downtown has been collaborating in a Community of Practice as part of the CSSP (Comprehensive Student Success Program) grant from the Texas Higher Education Coordinating Board (THECB). Our goal has been to improve the ABC pass rate in the gateway biology courses, thus improving retention in the science majors. Additionally, our goal as educators was to improve engagement in the classroom and deepen learning. We have developed robust, challenging modules for Team-Based Learning (TBL) that were implemented successfully last year and are now practiced inmultiple classes. A feature of TBL is the readiness assurance process for team engagement in rich applications of this background. These curricular innovations have made use of several technologies: Blackboard-based readiness assurance tasks and scratch-off (IF-AT) cards for team that "flips" the background learning from the lecture hall to preparing before class. Now class time is used quizzes, and formative in-class assessment usingthe cloud-based Learning Catalyticsapplication on Nook devices." Preliminary results show TBL model improved retention and student engagement.

IL-38

Scalable Green Chemistry in Pharmaceutical Applications

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Green chemistry, also called sustainable chemistry, is a philosophy of chemical research and engineering that encourages the design of products and processes that minimize the use and generation of hazardous substances. Chemists and medicinal scientists can greatly reduce the risk to human health and the environment by following all the valuable principles of green chemistry. The most simple and direct way to apply green chemistry in pharmaceuticals is to utilize eco-friendly, non-hazardous, reproducible and efficient solvents, reagents, organic

targeting GPCRs and their signaling pathways. In this talk, I will present our recent findings on structural visualization of GPCR signaling complexes and highlight how we are using this information for novel drug discovery. I will also present our recent efforts to design a label free and cell free approach for discovering new pharmacophores for selected GPCRs and their subsequent validation in traditional cell based GPCR signaling assays. Finally, I'll highlight our recent efforts to design synthetic proteins for live cell delivery and their potential therapeutic utility in rewiring GPCR signaling.

IL-40

Design, synthesis and anti-proliferative activity of condensed 2H-4- heteroarylaminopyrimidines

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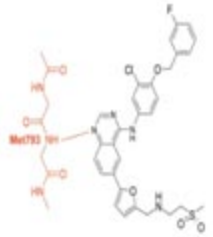
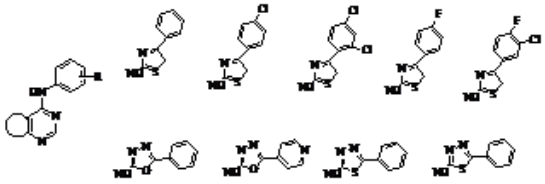
Bioisosteric condensed 2H-4- arylaminopyrimidines have been shown to exhibit selective receptor tyrosine kinase (RTK) inhibitory activities like the well known drug class of quinazoline drugs e.g., Gefitinib (Iressa). RTK's are inhibited by these molecules at the catalytic domain of their ATP binding site through . two key hydrogen bonds involving the amino group and the N1 pyrimidine nitrogen. The aniline moiety interacts with variable residues in this regions hydrophobic pocket. Thus, subtle variations of the 4-substituent of the 2H-anilinopyrimidine scaffold, like using hereoarylamino moieties may help in a) Modulation in selectivity of activity, b) Modulation in time duration of action. e.g., Lapatinib has prolonged effect at lower dose compared to Gefitinib.

Model of ATP- binding site of protein kinases



Lapatinib



Changes made at the 4-position w.r.t. replacing arylamino ring with various amino-heterocycles based on the principle of bio-isosterism.

A small, focused library of condensed 2H-4-heteroarylaminopyrimidines, with 3-diversity points, based on an initial design by molecular docking study of this scaffold at the active site of the EGFr Kinase domain (PDB-1XKK) was synthesized through a one-pot (MWI) green chemical synthetic protocol [1-3]. The screening of the synthesised compounds for antiproliferative activity was done on various cancerous cell lines like PC-3 (Human

Prostate Cancer), EAC (Ehrlich Ascites Carcinoma), A549 (Lung Carcinoma), HT-29 (Adenocarcinoma), MDA-MB 231 (Breast cancer) & HeLa (Cervix cancer). Ten molecules were found to be more potent against HT 29 cell lines, compared to gefitinib as revealed by their pIC50 values.

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ORAL

O-1

In-silico screening of chalcone derivatives as potent plasmepsin inhibitors

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Plasmepsin-II is an enzyme which catalyses the hydrolysis reaction of the bonds linking certain hydrophobic residues in hemoglobin or globin. It has also been identified to have extreme therapeutical implication, since its deactivation can be targeted in malaria disease organism, Plasmodium. This study includes molecular docking of chalcone derivatives with Plasmepsin II, followed by ADME toxicity analysis to understand the novel chalcone Plasmepsin II interactions. GLIDE module of Scrodinger suite was used for molecular docking and results obtained from this study also coincide with experimental findings. After molecular property analysis we found that given compounds also follows Lipinski's rule of five. Compound number 7 exhibited best Glide score (-5.87). Analysis of chalcone Plasmepsin II complexes ushered lipophilicity due to hydrophobic contact in inhibition and individual chemical scaffold on chalcone derivatives. This study can be used further for drug design against malaria.

Keywords: Chalcone derivatives, Molecular docking, Molecular property analysis, ADMET.

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O-2

Superoxide Ion Induced One Pot Synthesis of Benzo[c]acridine Derivatives

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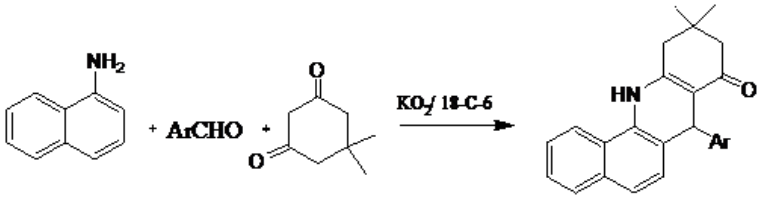
Superoxide chemistry is one of the most fascinating problems of current research. The use of this novel, innocuous and biochemical species has been demonstrated for achieving a number of organic transformations. Despite some progress made in the understating of the organic chemistry of superoxide ion, an important aspect involving the use of superoxide ion in multicomponent organic synthesis still remains untouched and warrants study in this direction.

Multicomponent reactions (MCRs) by virtue of their convergence, productivity, high yields and ease of execution have recently emerged as a valuable synthetic tool in modern organic synthesis. Due to their diversity and large unexplored chemical space, MCRs have been recognized as the most efficient approach to a variety of chemical synthetic problems. Some of the MCRs are important cornerstones in the diversity-oriented construction of molecular complexity due to their ability to incorporate, in a fast and efficient manner, three or more components into a single product.

Superoxide ion induced one-pot synthesis of benzo[c]acridine derivatives via the three-component condensation reaction of aromatic aldehydes, 1-naphtylamine, and dimedone using KO2 and 18-crown-6 under the mild reaction conditions at room temperature was studied.



Scheme

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O-3

Characterization of Indian Himalayan Medicinal Mushrooms

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Indian medicinal mushroom,Ophiocordyceps sinensis is popularly known as Yarsagumba (winter worm summer grass) in India, Nepal and Bhutan. It is one of the most-prized herbs of Ayurveda and is also known as Bhu-Sanjivani. Ganoderma lucidum is commonly known as"Lingzhi" in Chinese, "Reishi" in Japanese. Both the mushrooms have broad medicinal effects such as immuno-enhancer, antioxidant, anti-aging, tonic effect, hepatoprotective, neuro-cardioprotective etc.Rathor et al.[1, 2]; Singh et al. [3].

Here,for the first time we present the results of the proximate analysis of the crude powderof Cordyceps sinensisandGanodermalucidum(Indiacultured mycelium and fruiting body) in terms of various parameters such as Moisture content,Total ash, Protein,Crude Fat, Crude Fiber,Carbohydrate,Nitrogen and heavy metals. The Preliminary qualitative analysis of crude powder as well as water extract of C. sinensis and G. Lucidum revealed the presence of Alkaloids, Carbohydrates, Saponins, Proteins, Phenolic Compounds, Fat and Gums. Protein estimation of all these powders and extracts by 1-D electrophoresis indicated the presence of wide range of proteins. Further, HPTLC analysis also showed the presence of nucleotides and nucleosides in both the medicinal mushrooms.

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O-4

Epoxidation of Indene by a Plant Chloroperoxidase

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Enantiomeric pure epoxides are well recognized as extremely important building blocks in the fine chemical industry, particularly for the synthesis of biologically active compounds and pharmaceuticals due to the increasing demand for single isomers under legislative pressure for safety issues.1-4 The versatility of the epoxide is attributed to the oxirane function that can be opened by various nucleophiles or undergo elimination, reduction or rearrangements to a multitude of more elaborate intermediates with the retention or inversion of chirality.5-7 Therefore the development of efficient synthetic methods for enantiomeric pure epoxides has been of fundamental research interest in both organic synthesis and biocatalysis.

Chloroperoxidase is a potent epoxidation biocatalyst that displays moderate to high enantioselectivity on a wide variety of olefinic substrates8-12.This communication reports a crude preparation of Chloroperoxidase from Musa paradisiaca which can be conveniently prepared and used for the transformation of indene to its epoxide. This is the report of epoxide formation using a plant chloroperoxidase.

The method for the preparation of chloroperoxidase from the stem of Musa paradisiaca has been developed. The enzymatic characteristics like Km for the substrates indene and H2O2, pH and temperature optima of the enzyme have been determined. The enzymatic transformation of indene to its epoxide has been demonstrated. The results of the above studies will be presented in the conference.

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O-5

Murrayakoenigii (L.)Spreng. Ameliorates insulin resistance in dexamethasone-treated mice by enhancing peripheral insulin sensitivity

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Type 2 diabetes mellitus (T2DM) is the most common endocrine disorder, characterized by hyperglycaemia and insulin resistance[1]. The main patho-physiological feature of type 2 diabetes mellitus is insulin resistance, characterized by reduced ability of target tissues, such as the liver, skeletal muscle, and adipose, to respond to insulin. This includes impairment in the insulin stimulated translocation of GLUT4 to cell surface and resulting defect in insulin-stimulated glucose uptake in peripheral tissues. Hence, interventions with ability to stimulate glucose uptake might be important for the treatment of diabetes mellitus[2].The discovery of new drugs from traditional medicine is not a new phenomenon. Murrayakoenigii (L.)Spreng.is an important medicinal plant used traditionally as an antiemetic, antidiarrhoeal agent and blood purifier and as a medicine for a variety of ailment[3]. This study investigated the effects of ethanolic extract of M. koenigii (MK) on diabetes-associated insulin resistance induced in mice by chronic low-dose injection of dexamethasone.Mice treated with dexamethasone exhibited hyperglycaemia and impaired glucose tolerance. Treatment with MK reduced the extent of dexamethasone-induced hyperglycaemia and decreased insulin resistance as indicated by improved glucose tolerance and increased insulin-stimulated AKT phosphorylation in skeletal muscle tissue. Further evaluation in clonal skeletal muscle cell lines suggested that MK increased glucose uptake in L6 skeletal muscle cells by increasing cell surface GLUT4 density via an AKT-mediated pathway.

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O-6

Aegeline from Aegle marmelos stimulates GLUT4 translocation mediated glucose transport via activation of insulin signaling in the mouse skeletal muscle cells

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Aegeline is an alkaloidal-amide, isolated from the leaves of Aegle marmelos and have shown antihyperglycemic as well as antidyslipidemic activities in the validated animal models of type 2diabetes mellitus. The present work is undertaken to investigate the effects and the molecular mechanism of aegeline on the glucose transport for controlling the diabetes mellitus. Aegeline enhanced GLUT4 translocation mediated glucose uptake in both time and concentration-dependent manner. Glucose uptake was completely stymied by the transport inhibitors (wortmannin and genistein) in C2C12 myotubes. In vitro phosphorylation analysis revealed that, like insulin, aegelinealso enhances thetyrosine phosphorylation of the insulin receptor-? (IR-?), insulin receptor substrate-1(IRS-1) and the serine phosphorylation of Akt under both basal and insulin stimulatedconditions without affecting the total amount of these proteins. Taken together, these findings provide the ample evidence that aegeline stimulates GLUT4 translocation mediated glucose uptake by the activation of PI-3-K/Akt dependent pathway.

Keyword: Aegeline, Aegle marmelos, C2C12 myotubes, insulin resistance, glucose uptake

O-7

Facile Access to Substituted Dihydrothiopyrano[2,3-b]indoles via Sequential Rearrangements during S-alkylation and Gold-catalyzed Hydroarylation on Indoline-2-thiones

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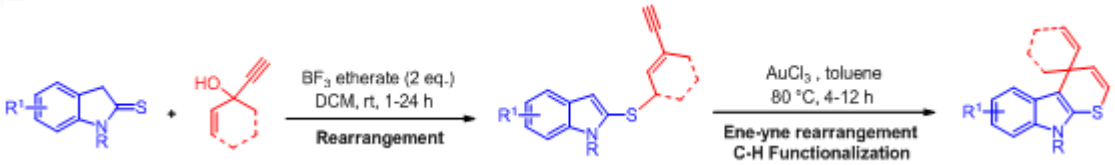
Transition metal-catalyzed hydroarylation reactions have been receiving considerable attention in recent years as an atom-economical approach for the functionalization of arenes, as well as for the creation of complex molecular architectures.[1] This ever-developing area has witnessed a remarkable growth in gold-catalyzed methodologies involving the addition of a wide variety of nucleophiles (C/N/O) to internal or terminal alkynes in an intra/intermolecular fashion.[2] Not surprisingly, this strategy has also emerged as a highly useful tool for the synthesis of novel heterocycles.[3]

In particular, chemicals possessing indole core are extremely desirable sub-class of heterocycles owing to a wide range of biological activity associated with them.[4] Literature survey suggests the chemistry of sulphur containing heterocycles, thiopyran and fused-thiopyrans, has not been explored to the same extent as that of their pyran analogs. Recent reports have associated substituted thiopyran and fused-thiopyran scaffolds to anti-inflammatory, anti-bacterial, anti-hyperplasia, antipsychotic, analgesic, estrogen receptor modulators, and anti-cancer activities.[5] Considering the importance of functionalized indoles, developing their efficient synthesis remains an intense area of investigation. Here, we wish to report a C-H activation-based two step synthesis of dihydrothiopyrano[2,3-b]indole ring system starting from indoline-2-thiones (Scheme 1). The newly generated indol-fused thiopyran devaritavies are structural analogs of biologically active carbazole skeleton.[6]



Scheme 1

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O-8

Curcumin ameliorates lipopolysaccharide induced allergic asthma exacerbations and structural changes in murine model

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Airborne lipopolysaccharide (LPS) is one of the most powerful pro-inflammatory factors and can induce rapid influx of polymorphonuclear leukocytes (PMNs) and release of inflammatory cytokines,reactive oxygen species and chemotactic factors causing acute pulmonary inflammation and lung injury. Curcumin derived from Curcuma longa has been investigated in balb/c (4-6 weeks) mice which were sensitized on 1st and 8th day with ovalbumin (OVA) and challenged with 1 % OVA (aerosol) from 9th to 15th day. Mice were exposed to LPS and curcumin 2 hr before each OVA challenge from 9th to 15th day. LPS induced asthma exacerbations were characterized by eosinophilic inflammation, histamine release and higher serum IgE level with elevated Th2 and Th1cytokine response in bronchoalveolar fluid BALF (IL-4, IL-5 and IFN-?). Extracellular matrix (ECM) degradation by matrix metalloproteinases (MMPs) activation is hallmark of airway remodeling in chronic asthma has also been revealed in LPS induced asthma exacerbations as revealed by gelatin zymography. Intranasal curcumin has ameliorated exacerbated asthmatic conditions by suppressing total and differential cell count in BALF by lowering eosinophils and neutrophils recruitment, histopathological changes in lungs, serum IgE level and significant supression in cytokine levels, whereas intraperitonael curcumin adminstration was not much effective. Being an antioxidant, curcumin may prove to possess immunomodulatory potential and effective in ameliorating LPS induced allergic asthma exacerbations.

O-9

Identification of Ferrochelatase as A Novel Therapeutic Target of Salicylic Acid using Highly Functional Magnetic Beads

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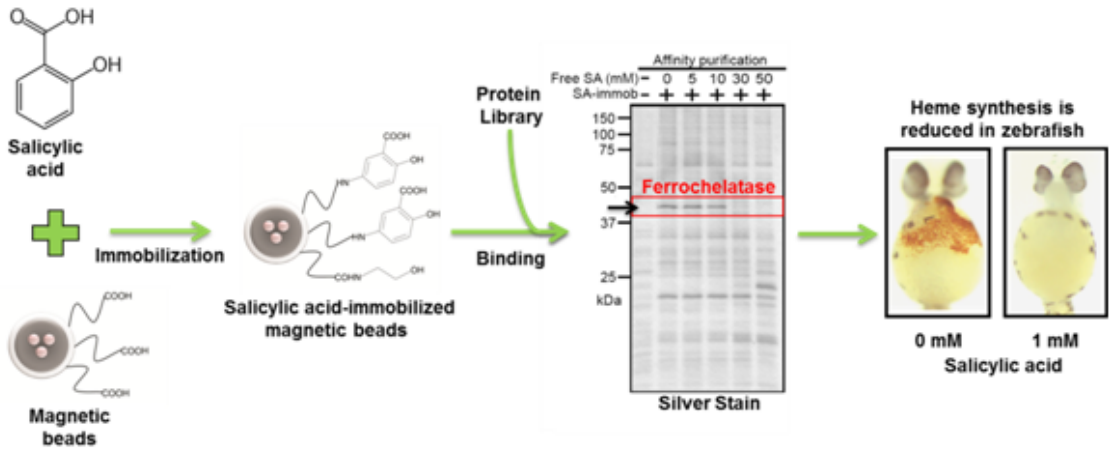
To better understand the mechanism of action of pharmaceutical drugs, it is important to identify the drug targets in vivo. Affinity purification is an old and reliable technique used to isolate and identify novel protein targets for active compounds from human cell extracts [1]. However, the classical technique is complex, less efficient and requires a considerable amount of time and effort. To overcome these challenges, we previously developed high-performance nano-sized magneticbeads that allow one-step affinity purification of drug target proteins from crude cell extracts [2]. We have used this methodology to identify new molecular targets of pharmacological drugs and elucidated novel cellular mechanisms responsible for their actions [2, 3, 4].Recently, we used this technique to isolate novel protein target of a classical non-steroidal anti-inflammatory drug, salicylic acid. Using salicylic acid-immobilized magnetic beads, we identified ferrochelatase (FECH), a terminal enzyme in heme biosynthesis pathways, as a novel protein target of salicylic acid[4]. Salicylic acid inhibits FECH activity inin vitro assay,cellular assay and animal model zebrafish. We further took this study and determined the cocrystal structure of FECHosalicylic acid complex showing that salicylic acid binds to the dimer interphase of FECH, causing allosteric inhibition of its activity. Thus, using our technique, we elucidated a novel aspect of the mechanism of action of salicylic acid.



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O-10

An enantioselective synthesis of an anti-hypercholesterolemic drug atorvastatin calcium (Lipitor) via direct catalytic asymmetric aldol reaction of thioamides

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Atorvastatin 1, an effective HMG-CoA (HMG-CoA=3-hydroxy-3-methylglutaryl coenzyme A) reductase inhibitor,1, 2 and the active ingredient in Lipitor, is in widespread clinical use for the treatment of hypercholesterolemia (Figure 1).3 Continuous demand of 1 is due to its reliable efficacy for lowering LDL (low-density lipoprotein) cholesterol and its established safety profile; the development of an efficient and scalable synthetic route to 1 is of sustained interest.4

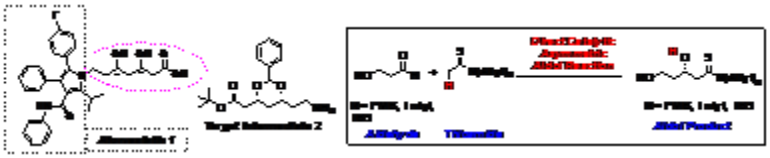

Figure 1: Structure of Atorvastatin 1 and its chiral target intermediate 2 as well as representative scheme for Direct Catalytic Asymmetric Aldol reaction of thioamides.

Extensive efforts have been reported to the synthesis of enantio-enriched target intermediate 2 and its related compounds, which are common intermediates for 1. Several synthetic strategies have been reported for the synthesis of the relatively simple compound 2, including syntheses through optical resolution and chiral auxiliary,2b,5 chiral pool methodology,6 enzymatic reactions,7 and asymmetric catalysis.8 Recently, Shibasaki et al. reported a concise Ist generation enantioselective synthesis of 1 in 11 steps with good ee, in which a direct catalytic asymmetric aldol reaction of thioamide was implemented as the key C-C bond forming reaction with the introduction of chirality (Figure 1).9 Herein, we will describe the IInd generation synthetic route to Atorvastatin 1 based on the direct catalytic asymmetric aldol reaction of a thioamide in 8 step with high ee in comparison to the Ist generation synthetic route.10,11

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O-11

Design, Synthesis and Anticancer Activity of Novel Pyrimidine Derivatives as CDK2 Inhibitors

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Cancer is one of the fatal diseases in world which leads to death when diagnosed at the latter stage. From many types of cancer, Skin cancer is one of the leading cause of death. Objective of present study was to develop new series of molecules targeting CDK2.[1,2] Here, we tried to develop the novel heterocyclic compounds which would act on the CDK2 to prevent skin cancer. Various computational tools were used for designing new molecules. Eight already published molecules, having remarkable activity on the CDK2 receptor, were selected to generate pharmacophore models by Sybyl. Best model, having 5 features viz. 2 donor atoms, 1 acceptor atom and 2 hydrophobic atoms, was taken as a query and virtual screening was performed using NCI database. PDB Id: 1AQ1 was used for molecular docking studies. Based upon docking data, pyrimidine core ring structure was considered for design of target compounds.[3] 14 novel substituted pyrimidine derivatives were designed, synthesized, characterized and evaluated for in-vitro anticancer activity on A-375 skin cancer cell line. Compound 4-anilino-6-(4-sulphanilamido)pyrimidine-5-carboxamide was found to be most potent compound and was selected for further in vivo study for skin cancer.[4] It was found that treatment with above compound showed favourable action against skin cancer. The designed series can further modified to discover novel lead for the treatment of skin cancer.

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O-12

An organocatalytic novel C-C bond forming approach for the direct syntheses of highly substituted tetrahydrocarbazoles and Carbazoles

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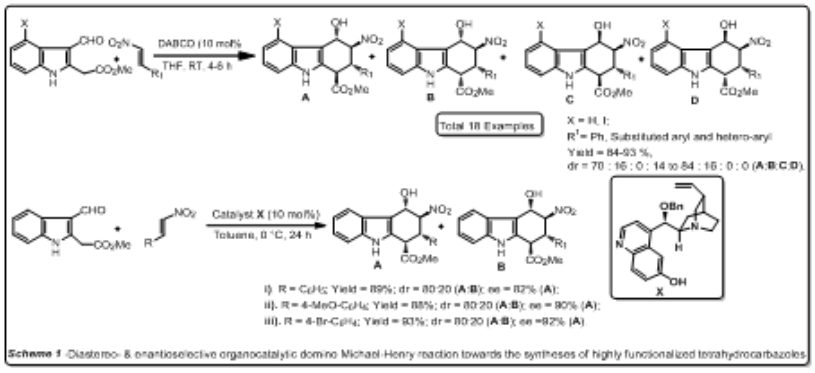
Development of a highly efficient method for the synthesis of functionalized tetrahydrocarbazoles (THCs) and carbazoles is a key research area in drug discovery as well as in medicinal chemistry because these moieties are present in a variety of drug candidates and natural products and many of them synthetic analogues showing potential biological activities. Towards this aim, several transition metal complexes catalyzed syntheses of both racemic and enantioselcetive versions of THCs and Carbazoles have been well documented. However, because of potential environmental concerns about metal catalysts in general, organocatalysis has been paid much attention in the context of green chemistry, as well possibly providing cost effective synthesis of optically active complex molecules from simple raw materials in a highly efficient manner.

In the view of above prospect, for the first time, a very simple, efficient, mild, organocatalytic and one- pot procedure for the synthesis of a series of densely functionalized 1,2,3,4-tetrahydro-9H-carbazole and highly substituted carbazole derivatives have been achieved via a domino Michael-Henry reaction of methyl 3-formyl-1H-indole-2-acetates with b-nitrostyrenes using DABCO as an organocatalyst. Furthermore, the high enantio- (upto 92% ee) and diastereoselective (upto 80:20 dr) synthesis of the title compounds have also been achieved with excellent yields using 9-O-benzylcupreidine (10 mol%) as a catalyst.



Scheme 1 -Diastereo- & enantioselective organocatalytic domino Michael-Henry reaction towards the syntheses of highly functionalized tetrahydrocarbazoles

We have also extended this optimized protocol for the synthesis of biologically important quinolinone and coumarin fused carbazole derivative along with the synthesis of biologically significant pyrimidocarbazole derivatives (topoisomerase II inhibitors). The detail of the study will be presented.

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O-13

Chalcones and its complexes in the treatment of diabetes

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NIDDM (Non-insulin dependent diabetes mellitus), a metabolic disorder leading to chronic morbidity and increasing mortality due to changing life styles particularly in urban Indian population. Different module of drugs targeting insulin modulation are known to treat the disease as insulin sensitizer and/or stimulator of insulin secretion. However due to non-responsiveness of patients after treatment for some time, requires drugs acting with some other mechanisms. Agonists of ?3-adrenergic and PPAR receptor modulators stimulate the oxidative pathway to dissipate heat without the synthesis of ATP and thereby lower plasma sugar and lipids profiles. Oxidative stress plays a key role in diabetes for macrovascular complications.

Flavonoids are polyphenolic compounds that are ubiquitous in nature and are categorized, according to chemical structure, into flavonols, flavones, flavanones, isoflavones, catechins, anthocyanidins and chalcones. The chalcones have aroused considerable interest recently because of their potential beneficial effects on human health. An imbalance between antioxidants and ROS results in oxidative stress, leading to cellular damage. Oxidative stress has been linked to different diseases. Chalcones are known to possess antioxidant property which therefore led us to utilize them for synthesis of hybrid molecules for the treatment of diabetes.

The inhibition of PTP-1B is a potential target for treatment of type-2 diabetes. V & Zn complexes have insulin-enhancing activities, and while vanadium compounds inhibit PTP-1B, little is known on the mode of action about Zn compounds.4 V is not only an important trace element for organisms but also the necessary element for human body. It has been demonstrated that many V-Compounds possess therapeutic effects as insulin mimetics.1, 2 Many clinical trials of V-compounds have also been reported3, 4 in which vanadium salts such as VOSO4 and NaVO3 were administered to diabetic patients. There are various V and Zn compounds have reported for anti-diabetic activity.

On the basis of above points, I have synthesized the chalcones and its metal complxes for antidiabetic activity.

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O-14

Comparative analysis of the in vitro antioxidant activities of three medicinal plants of North Eastern region of India

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Background: As a result of normal metabolic processes, the human body produces reactive oxygen species capable of oxidizing biomolecules that can damage DNA, cells, and contribute to chronic disease. This process can be attenuated or perhaps reversed by antioxidants that have the ability to scavenge reactive oxygen species.The present study is to measure the antioxidant properties of crude extracts of Amaranthus viridis (AV), Centella asiatica (CA) and Hydrocotyle sibthorpioide (HS).The antioxidant properties of three extracts were evaluated using different antioxidant tests, including 2, 2-Diphenyl-1-picrylhydrazylfree radical scavenging activity, reducing power, inhibition of lipid peroxidation, nitric oxide, ABTS, total polyphenolic and flavanoid contents. Quantitative phytochemical analysis of total phenol and flavonoids content showed that HS had the highest content of phenolic compounds followed by CA and AV. HS extract had effective DPPH free radical scavenging, nitric oxide scavenging, ABTS radical scavenging activity and lipid peroxidation inhibition activity. Meanwhile, CA had the highest reducing power activity followed by AS and HS. The present study demonstrates the antioxidative capacity of all the three plant species. Of all the plants, HS showed potentially a high antioxidant activity, with higher phenolic and flavonoids content. The data suggest that HS can be best utilized in developing bioantioxidants.

O-15

Synthesis of Curcumin Under Grinding Condition

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Curcumin is commonly known as diferuloyl methane and found in rhizome of the herb curcuma longa L. It is used as a dietary pigment spice and coloring agent and herb in traditional Indian and Chinese medicine Kuttan et. al (1). Curcumin is biologically active molecules and possess various pharmalogoical activities P. Anand et.al(2). Very few methods exist for synthesis of curcumin and synthesis of curcumin are reported by Paban(3), Paban et.al(4), K. V. D. Babu et.al(5), E. Venkata Rao et.al (6) However these reported methods suffer from drawbacks like low yield, harsh reaction condition, expensive and hazardous regents are used, and product isolation is a boring process. Therefore, there is scope to develop new methods for the synthesis of curcumin by using an inexpensive, safe, simple and eco-friendly catalyst. Recently S. Elavarasan et. al(7a) reported synthesis of symmetrical curcumin using calcium oxide under microwave condition and P. Kulkarni et. al reported using calcium hydroxide (7b). However this method also suffers from drawbacks like isolation of product require extraction process and long reaction time. Calcium is divalent in nature and it forms complex with acetyl acetone which protect middle methylene group and carried out condensation at terminal methyl groups to afford curcumin. In this method, we carried the synthesis of curcumin under grinding condition. The merit of this method is easily available, non toxic and inexpensive catalyst, short reaction time, yield is good, avoid use of solvent and electrical energy.

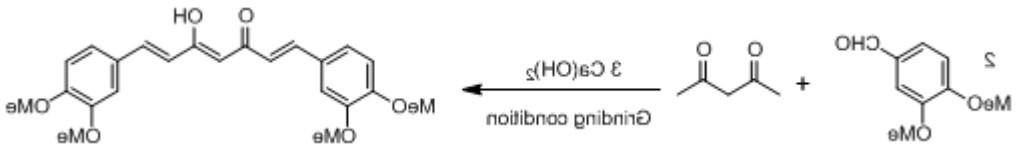

Figure 1 Synthesis of Curcumin using Calcium hydroxide as base under Grinding Condition

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O-16

Reaction of electron deficient olefins with diazo-compounds: metal-free stereoselective synthesis of cyclopropanes & regioselective synthesis of pyrazoles

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Diazo-compounds have been widely used for stereoselective cyclopropanation of olefins. Majority of such reactions are catalyzed by a transition metal catalyst that follows through metal-carbene intermediate and a mixture of diastereomers (cis/trans) are often obtained with varying degree of success. Additionally metal-carbene mediated cyclopropanations are usually successful with electron rich alkenes and only a few reports on electron deficient alkenes in such reactions are known. Generally diazo-compounds reacts with electron deficient alkenes in a manner of 1,3-dipolar cycloaddition to yield pyrazolines or pyrazoles and the success of reaction largely depends on the catalyst used or the leaving group present in the alkene. We realized the same in our attempt to achieve pyrazoles by reaction of EDA with doubly activated electron deficient alkenes such as arylidene-malononitrile or arylidene-ethyl cyanoacetate which failed and the same reaction exclusively yielded diastereoselective cyclopropanation of the alkene. Currently we are exploring the scope of the catalyst-free stereoselective cyclopropanation of electron deficient alkenes with diazo-compounds (Figure 1).1-4

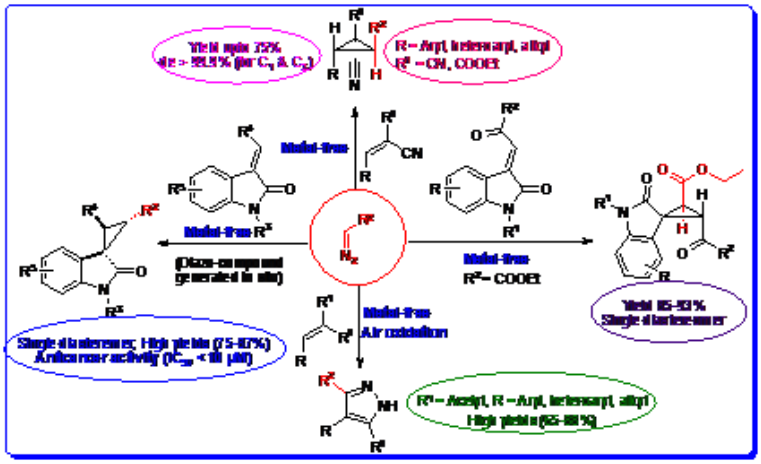

Figure 1. Transition metal-free stereoselective synthesis of cyclopropanes and regioselective synthesis of pyrazoles

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O-17

Homogeneous catalyst recycling: a continuous flow approach for metal catalyzed reaction

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Today, reuse and recycling of catalysts is receiving new attention as a critical component of emerging chemical technologies due to both environmental concerns and economic benefits. It is not surprising, therefore, that present industrial chemical processes are favoring heterogeneous catalysts which leads to efficient recycling and reuse. However, most heterogeneous systems require a filtration and/or a tedious workup of the final reaction mix-ture to recover the catalyst. A desirable system is one in which homogeneous catalyst is used and yet the catalyst is as easily recyclable as heterogeneous catalyst. One way of satisfying the desire involves use of a thermomorphic multicomponent solvent (TMS).1 In this TMS system, catalyst is soluble in one solvent and reactants/products are soluble in another solvent that is immiscible with the catalyst solvent. When supported metal catalysts are air and/or moisture sensitive, it is exigent that practical recycling processes must be carefully executed to avoid the deactivation via adventitious oxidation upon possible exposure.
Therefore, we envisage a closed and continuous flow reaction system without air and moisture exposure, which removes the limitation, with an efficient metal catalyst recycling loop. We have also developed a microfluidic loop system for continuous recirculation of polymer supported metal catalyst for novel cross coupling reactions under TMS condition.2 This approach takes full advantage of homogeneous catalyst system while retaining the advantage a heterogeneous catalyst system offers for easy separation and recirculation of catalyst. (Figure 1).3-5

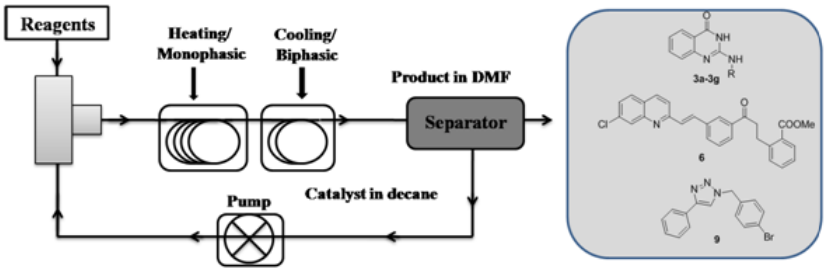

Figure. 1. Conceptual scheme for a continuous catalyst recycling microfluidic loop system via TMS separation.

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O-18

Synthesis and cytotoxic evaluation of novel thiazolederivatives bearing quinolone moiety

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One of the most frequently encountered heterocycles in medicinal chemistry is quinoline with wide applications including antibacterial, antifungal, antitumor, antimalarial, antiplatlet and antidepressant activities [1]. Quinoline and their derivatives are very important compounds because of their wide occurrence in natural products and biologically active compounds [2].

Pyrazole is another heterocyle that has widespread potential biological activities. Pyrazole derivatives have variety of applications in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals. Some of these are antitumor, antimicrobial, anti-inflammatory, antiviral, anticonvulsant, antidepressant and ACE-inhibitors[3].Thiazoles are one of the most intensively investigated classes of aromatic five membered heterocycles. The thiazole ring has been extensively studied and it forms a part of Thiamine (Vitamin B1) and penicillin and antibacterial thiazoles. Thiazoles serve in the study of polypeptides and proteins and occur as structural units in compounds of biological importance[4]. 1,3,Thiazole derivatives are found to possess a wide variety of applications ranging from bacteriostatics, antibiotics, and CNS regulants to high selling diuretics[5].
In the present work, we designed new series of compounds containing pyrazolo-quinoline derivatives incorporated with 1,3thiazole unit. 6/7 Substituted-2-chloro-quinoline-3-carbaldedhydes are prepared by Vilsmeir- Haack reaction The resultant quinoline carbaldehydes are hydrolyzed followed by the condensation with active aromatic ketones yield chalcones. The obtained chalcones are transformed into pyrazole derivatives by the interaction with thiosemicarbazide and resultant compounds are converted into designed title compounds. The newly synthesized compounds are characterized by spectral data. Antitumor, antibacterial and cytotoxic studies are in progress.

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O-19

An -L- rhamnosiadase from Penicillium greoroseum MTCC-9424

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?-L-rhamnosidase [EC.3.2.1.40] cleaves terminal ?-L- rhamnose specifically from a number of rhamnosides [1,2,3] and is widely distributed in nature[4].It has several potential applications and have been used for structural determination of biologically important glycosides, polysacrides and glycolipids [5,6]. It is also used for hydrolysis of rhamnosyl residues present in flavonoid glycosides, such as naringin, hesperidin, rutin and quercetrin. The hydrolysis of rutin and quercetrin, the most common flavonoids glucosides in the human diet, by bacterial ?-L-rhamnosidase have been reported [7].There are also several technological application of ?-L-rhamnosidase such as the removal of bitterness from citrus juices caused by naringin [8] and hydrolysis of hesperidin by ?-L-rhamnosidase to release L- rhamnose and hesperidin glucosides, which is an important precursor in sweetener production [9]. In addition, there is an industrial interest in ?-L-rhamnosidase for their action towards terpenyl glucosides in the application of enhancing aroma in grape juices and derived beverages [10]. The enzymes with different properties suit the different biotechnological applications. For example ?-L-rhamnosidase having pH optimum in 3-4 pH unit ranges are more suitable for debittering of citrus fruit juices which also have their pHs in the range 3-4 pH units. The enzymes with pH optima near neutral range are more suitable for the aroma enhancement of wine. Thus there is a biotechnological need to purify ?-L-rhamnosidases from different sources and to study their properties so that ?-L-rhamnosidases suitable for different biotechnological applications could be identified. In this communication, we report an ?-L-rhamnosidase from the culture filtrate of Penicillium greoroseum MTCC-9424 and have accessed its properties for different biotechnological applications.

Keywords: ?-L-Rhamnosidase. naringin. rutin. hesperidin .wine.

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O-20

Discovery and development of anti-hiv agents

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Acquired immunodeficiency syndrome (AIDS), one of the most devastating diseases currently affecting mankind, is caused by infection with the human immunodeficiency virus (HIV). Although there are over 30 clinically used drugs [1], the fast emergence of drug resistance and toxicity problems due to long-term use and drug-drug interactions have limited their long-term drug effectiveness. Therefore, studies aimed at the discovery of new anti-viral agents with novel structures or targets are still needed. Highly active antiretroviral therapy, involving the co-administration of nucleoside reverse transcriptase inhibitors (NRTI), and/or protease inhibitors, is a standard treatment regimen for human immunodeficiency virus (HIV) infections. This regimen suppresses the replication of HIV and controls disease progression in HIV-infected patients [2]. The anti-HIV chemotherapy era started a decade ago when suramin was found to protect human T lymphocytes against the infectivity and cytopathicity of human immunodeficiency virus (HIV). Suramin, as well as the polyoxometalate HPA were also the first antiviral agents shown to inhibit HIV replication in vivo, albeit in a limited number of AIDS patients. Meanwhile azidothymidine (AZT, zidovudine) had been discovered to inhibit the infectivity and cytopathicity of HIV at much lower concentrations than suramin. Shortly after AZT, two other 2',3'-dideoxynucleosides, viz. 2',3'-dideoxycytidine (DDC, zalcitabine) and 2',3'-dideoxyinosine (DDI, didanosine) were reported to inhibit the infectivity and cytopathicity of HIV. Recently, a series of extensive studies led to the development of a series of novel antiretrovirals with new mechanisms of action for anti-HIV therapy, including a fusion inhibitor (enfuvirtide) [3], an integrase inhibitor (raltegravir) [4], and a CC chemokine receptor type 5 (CCR5) antagonist (maraviroc) [5]. CXC chemokine receptor type 4 (CXCR4) antagonists, CD4 mimics, gp41-binding peptides small molecules [6,7] represent promising alternative anti-HIV agents. Unfortunately, however, an increasing number of patients with HIV infection/AIDS have failed to respond to the current antiretroviral therapeutics because of serious problems including the emergence of drug-resistant HIV variants and drug-related adverse effects. With this in mind, there is therefore a continuous need to develop novel anti-HIV drugs that are more effective against drug-resistant viruses and produce fewer adverse effects. We describe herein discovery and development of various anti-HIV agents of medicinal importance including mode of action of anti-HIV drugs.

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O-21

Identification of Lead Molecule of Biological Significance from Phlebophyllum kunthianum

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Traditional medicinal plants have considerable importance in medicinal chemistry as these provide the molecules with rich structural diversity and prominent pharmacological activities. Moreover, taking therapeutic applications in mind, many drugs used today are natural products or natural products derivatives. Their rich structural diversity and complexity has prompted synthetic chemists to optimize the activity by lead optimization of the active principle and it could be opening the door to a new era in the investigation of natural products in pharmaceutical industries. Keeping in view importance of natural products and in the continuation of our efforts to search and identify the lead molecules from traditional medicinal plants [1-2], recently, we have reported the antigiardial activity from the ethanolic extract of the aerial part of Phlebophyllum kunthianum [3,4] and subsequently, isolated and identified the active constituent from P. kunthianum, which displayed significant antigiardial activity in vitro against Giardia lamblia. The detailed bioassay guided extractions techniques, characterizations of the constituents by using various spectral data (1H NMR, 13C NMR, Mass, UV and IR) analysis and biological activity profiles of the active constituent will be discussed.

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POSTER

P-1

Novel Heterocyclic Schiff bases and 4-Thaizolidinones containing Iodohydroxy Biphenyl moiety

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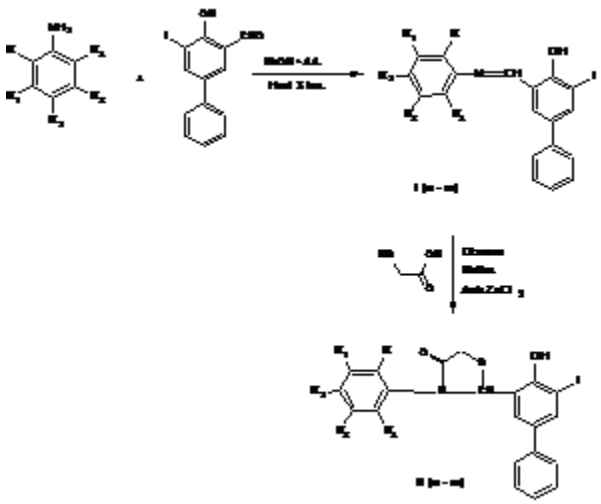
Some new heterocyclic Schiff bases I (a-m) were synthesized from 2-hydroxy-3-iodo-5-phenylbenzaldehyde moiety. Further, these Schiff bases were converted into 4-thiazolidinones II(a-m) by the action of mercaptoacetic acid. The structure of newly synthesized compounds characterized on the basis of elemental analysis and spectral data. The antimicrobial activity of newly synthesized Schiff bases and 4-thiazolidinones were studied by using different plant/animal pathogens.

Keyword: Schiff bases, 4-Thiazolidinones, Antibacterial activity, Antifungal activity.

Scheme:



Entry	R	R1	R2	R3	R4
Ia & IIa	H	H	NO2	H	I
Ib & IIb	H	H	I	H	NO2
Ic & IIc	H	H	I	H	Cl
Id & IId	H	H	Cl	H	I
Ie & IIe	I	H	CH3	H	I
If & IIf	I	H	NO2	H	I
Ig & IIg	CH3	I	H	NO2	H
Ih & IIh	H	H	COOH	H	I
Ii & Iii	I	H	COOH	H	I
Ij & IIj	I	H	H	NO2	H
Ik & IIk	H	H	H	Cl	I
Il & IIl	H	H	I	H	COOH
Im & IIm	Cl	H	I	H	Cl

P-2

Green Chemistry: A sustainable development in Organic synthesis

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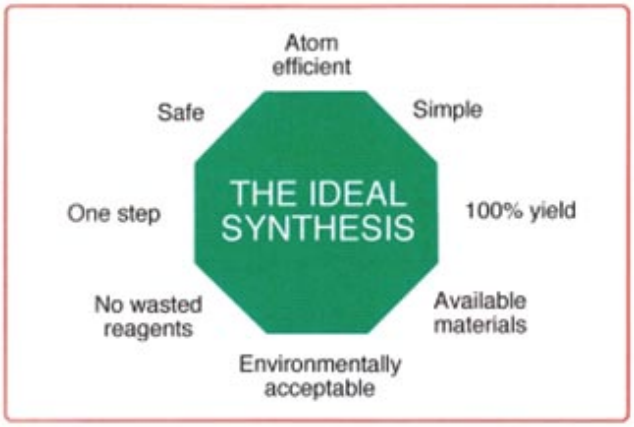
The term green chemistry is defined as: The invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances
Sustainable development, the keystone of technological progress in this new century, challenges chemical sciences to play a primary role in converting old technologies into new clean processes and in designing new products and new eco-compatible processes. Green chemistry, that is to say sustainable chemistry, is the new philosophy of chemistry, whose aim is to correct present practices in order to prevent problems in the future.
Organic chemistry chemicals are some of the important starting materials for a great number of major chemical industries. The production of organic chemicals as raw materials or reagents for other applications is a major sector of manufacturing, pharmaceuticals, pesticides, etc. Organic synthesis on a large scale, compared to the laboratory scale, involves the use of energy, basic chemical ingredients from the petrochemical sector, catalysts and after the end of the reaction, separation, purification, storage, packaging, distribution etc. During these processes there are many problems of health and safety for workers in addition to the environmental problems caused by their use and disposition as waste.
The ideal green chemistry will be combination of a number of environmental, health, safety and economic target.



Green chemistry essentially refers to the new sustainability priorities in technological and scientific innovation, on the basis of general rules stressing the need to abandon harmful products and processes.

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P-3

A Convenient synthesis and biological evaluation of novel fused pyrimido pyrimidine 3- carbonitrile and it's 2-substituted derivatives

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Pyrimidine moiety is an important pharmacophore in biological action. Synthesis of novel fused 6-hydroxy- 4-imino-8-methyl -2-methylthio-4H-pyrimido [1, 2-a] pyrimidine-3-carbonitrile (III) has been prepared by the refluxing of 2-amino-6-methyl 4-hydroxy pyrimidine (I) with 3,3'-bis-methylthio methylene malononitrile (II) for 5-6 hours in presence of anhydrous K2CO3 in DMF as solvent. Compound (I) has been prepared by the refluxing of Ethyl Aceto Acetate [AAE] and Gaunidine Hydrochloride in ethanol for 2-3 hours.

Compound (III) has methylthio functionality at 2-position, acts as best leaving group. Which was replaced / substituted by using selected different nucleophiles like substituted phenols/Anilines/heteryl amines/compounds containing active methylene group to afford 2- substituted derivatives of compound (III). All the synthesized compounds were characterized on the basis of spectral study.

All the synthesized compounds and it's 2- substituted derivatives were screened for their antibacterial activity, exhibited better antibacterial activity against Staphylococcus aureus (gram positive) and Escherichia-coli (gram negative) bacteria.

Keywords: Pyrimidine, pyrimido [1, 2-a] pyrimidine-3-carbonitrile, 3,3'-bis-methylthio methylene malononitrile, K2CO3, antibacterial activity.

P-4

Synthesis and anticancer evaluation of hybrid molecules of N-mustard and benzimidazoles and benzothiazoles

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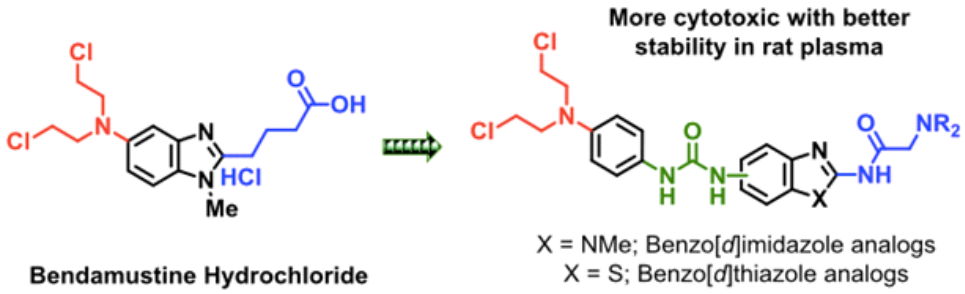
To improve the poor pharmacokinetic profile and enhance the antitumor activity of the anti- leukemia agent bendamustine, we synthesized a series of hybrid molecules comprising a phenyl N- mustard moiety and benzothiazole or benzimidazole scaffold linked via aureido linker. The antitumor characteristics of the new conjugates were evaluated. Preliminary studies revealed that these agents exhibited significant cytotoxicity against a panel of human lymphoblastic leukemia and human solid tumor cells in culture. Human lymphoblastic leukemia CCRM-CEM cells were the most sensitive to the tested compound. In general, the new hybrids are as potent as cisplatin but significantly more cytotoxic than bendamustine. Compounds 27d and 32b possessed significant cytotoxicity against the tumor cells tested. These two agents induced DNA interstrand cross-linking, arrested the H460 cell cycle at G2/M phase, and triggered cell apoptosis. We also demonstrated that the new hybrids were more chemically stable than bendamustine in rat plasma. Taken together, our results demonstrate that the newly synthesized hybrids are much more potent than bendamustine and more chemically stable in rat plasma.



P-5

Multicomponent synthesis of 5-substituted derivatives of phenyl-thidiazolo quinazoline

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Thiadiazzole is 5-membered ring system containing hydrogen binding domain, sulphur atom and two electron donar nitrogen system (N=C-S) that exhibit a wide variety of biological activity. It occur in four isomeric forms in the nature viz, 1,2,3-thiadiazole, 1,2,5-thiadiazole, 1,2,4-thiadiazole and 1,3,4-thiadiazole five member ring by Guost et al 1 .1,3,4-thiadiazole was first described in 1882 by Fischer and further developed by Busch and co-workers. Stelling et al 2, reported the advent of sulfur drug and the later discovery of mesoionic compound greatly accelerated the rate of progress in this field. In literature survey revealed that various thiadiazole have resulted in many potential drug and are known to exhibit a broad spectrum of pharmacological properties and biological properties such has antimicrobial 3, antituberculosis 4 , anti-inflammatory 5 , anticonvulsant 6 , antihypertensive 7 , antioxidant 8 , antifungal 9 , and anticancer activity10 . Anti tumor 11 (Zhang et al 2009), amoebicidal, antipyretic CNS depressant, antischistosomal 12 (Jain et al 2013), herbicidal 13 , Insecticidal, pesticidal 14 (Nadhi et al 2009) , Hypoglycemic 15 In view of the importance of 1, 3, 4-thiadiazole derivatives due to its pharmacological activities, its use in field of agro chemistry, medicinal chemistry, and several methods for their

preparation have been reported in literature.A mixture of 2- amino-5-phenyl 1,3,4-dithiazole and dimedone with different substituted aldehydes independently was refluxed in acetonitrile and iodine to isolate the respective 5-substituted derivatives of 8,9-dihydro-5-(4'-phhenyl)-8,8-dimethyl-2-phenyl-5H-[1,3,4]thiadiazolo[2,3-b]quinazolin-6-(7H)-one.

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P-6

Design and synthesis of Human P-Glycoprotein Inhibitors: Structure based drug designing approach

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In 2009, the first murine P glycoprotein was crystalized which kick started all attempts to predict structure of Human P glycoproteinhomology by homology modelling. Inspite of not all information were available in 3G5U structure were predicted based on the sequence similarity and published from 2009 to 2013. We have attempted to justify the role of template selection in predicting Human Pgp, which might not be accurate by just considering the highest similar murine structure. Comparative modelling approach was implied to execute the modelling of human Pgp by choosing a set of three templates. All modelled structure were investigated by the long molecular dynamic simulation, which give insight how stable modelled structure of human Pgp. Remarkably, the structure predicted with the template 3G5U or latest murine structure which published in 2014 not shown stability after long molecular dynamic simulation and these structures fails to provide linker region details. Structure with stable

linker region was taken for further design of inhibitors. Our own reported dihydropyrimidine (DHPM) structure was employed for further derivatization by isosteric, biosteric modification. Those structures were implemented for molecular docking study and reported best structure scrutinized by docking score and free binding energy, which were further synthesized in our lab. Moreover, Pgp inhibition assay and efflux rate of known inhibitor and design inhibitor will be compared in further wet lab research.

P-7

Microwave-Accelerated and Classical Synthesis of Pyrazolo[3,4-d]pyrimidines

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HClO4-Fuller's earth (heterogeneous acid catalyst) catalysed conventional and microwave accelerated one pot Biginelli type synthesis of pyrazolo-pyrimidine has been demonstrated. The conventional heating was carried out in acetonitrile and by using conc. HCl as the acid catalyst whilst the microwave assisted reaction was also carried out in acetonitrile but novel heterogeneous catalyst HClO4-Fuller's earth was utilized for the reactions. The compounds are characterized by 1H NMR, IR and Mass spectral techniques. The synthesis and various application of the catalyst have also been discussed in detail. In MAOS (Microwave Assisted Organic Synthesis), the overall yields of the products are higher than the conventional counterparts.

P-8

Synthesis and biological screening of 1-N-2'-(3'-methylbutanoicacid)-2-phenyl-4-arylidine-5-oxo-imidazolines

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1-N-2'-(3'-methylbutanoicacid)-2-phenyl-4-arylidine-5-oxo-imidazolines (3a-j) have been synthesized by the condensation of L-valine with different oxazolones. The products have been assayed for their antimicrobial screening against Gram+ve and Gram-ve bacteria. Some of the products showed moderate activity when compared with known standard drug viz. penicillin at the same concentration 50µg/ml. Sprctroscopic tequeniques are very good tools for the identification of compounds. The structures have been confirmed by 1H NMR, IR, and Mass spectral data.

P-9

Quantitative analysis of antiplatelet drug Ticagrelor in bulk and pharmaceutical dosage form by Validated UV-Spectroscopic method using green approach

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Ticagrelor is a platelet aggregation inhibitor drug. A rapid, specific and economic UV spectrophotometric method has been developed for the estimation of Ticagrelorin bulk and pharmaceutical dosage formulations. The optimum conditions for the analysis of the drug were established. The Ticagrelor content was determined using a greener solvent composed of 57:43 v/v methanol:water (pH-3.453 adjusted by Acetic acid). Maximum absorption found to be at max 222 nm. The method was validated based on ICH guidelines with respect tospecificity, precision, linearity and accuracy. The analysis data has been subjected to statistical analysis and the results of this study are validated. Beers law was obeyed in the concentration range of 8- 32?g/ml having linear equation of Y = 0.0946 x + 0.0239.The percentage recovery of Ticagrelor is between 97.08 to 98.07%. The results are simple, sensitive, reliable and reproducible, hence useful for the routine analysis of Ticagrelor.

P-10

Synthesis and Characterization of Ugi product by NMR and X-Ray Crystallography

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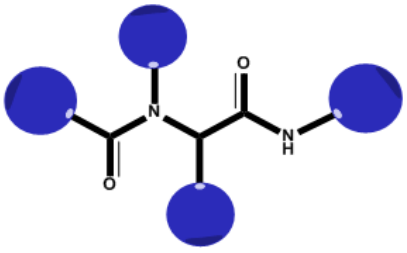
The study of crystal with the help of X-Rays is called X-Ray crystallography. When a beam of x-ray is allowed to fall on crystal, large number of images of different intensities are formed. The diffraction patterns produced by crystal, we can arrive at the detailed information regarding the position of particles in crystal. NMR spectroscopy is one of the most important technique for characterization of complex organic molecule. Besides X-Ray Crystallography plays equally important for the support of NMR data.



Multi component reactions are highly efficient in atom economical transformations in synthetic organic chemistry. They can be used for construction various libraries of compounds in medicinal chemistry. Ugi reaction, known as four component reaction, combines a carbonyl compound, an amine, a carboxylic acid and an isonitrile to afford highly functionalized molecules.

P-11

A validated hplc method for the estimation of a combination muscle relaxant drug: a stationary phase plays an important role in elution order during method transfer to uplc

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Validated RP-HPLC method was transfer to a new generation instrument UPLC using same mobile phase and column. The special characteristics of stationary phase such as carbon loading capacity, pore size and particle size of the stationary phase of same USP class of column take part in alteration of the elution order of the compounds. In the present work, sensitive isocratic RP- HPLC method was established and comprehensive validation study for the estimation of Tolperisone HCl and Paracetamol according to ICH guidelines. Simultaneous estimation was chromatographed using 0.1% ortho-phosphoric acid in water and acetonitrile (70: 30 v/v) as a mobile phase. Chromatographic separation accomplished isocratically on Waters HPLC Sunfire C18 (150 mm × 4.6 mm, particle size 5 µn) and Waters UPLC BEH C18 Column. The retention time was recorded according to HPLC and UPLC for Tolperisone HCl 1.95 and 2.62 and for Paracetamol 3.04 and 1.39 min, respectively. Based on the results, the validated method was effectively applied for the combined dosage form and in single pharmaceutical formulations of both the drugs.

P-12

Ultra performance liquid chromatographic method for simultaneous determination of five most potent antihypertensive molecules

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The present investigation describes the simultaneously development and validation of RP-UPLC assay method of Guanfacine hydrochloride, Sildenafil, Irbesartan, Losartan potassium and Indapamide in tablets by use of isocratic mobile phase. In present the method chromatographic analysis was performed using Acquity UPLC @ HSS C18 (50 X 2.1 mm id, 1.8µm particle size) column with 40°C column oven temperature. The isocratic mobile phase was consisted 0.1% OPA and Acetonitrile (68:32 V/V). The detection was monitored at wavelength of 211 nm. The flow rate was adjusted at 0.3 ml/min with 0.5 µl injection volume. The total analysis takes 3.5 minutes.

P-13

Cu(I)-Catalyzed Highly Efficient One-Pot Synthesis of Pyrazole Derivatives using Microwave Assisted A3-Coupling

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In recent years, one-pot microwave-assisted approach for the transition metal catalyzed A3-coupling reaction of an aldehyde, an amine and an alkyne has emerged as a powerful tool towards the synthesis of propargylamines. Moreover, the A3-coupling has employed as a key step for developing various nitrogen containing natural product analogues, and biologically active heterocycles. In this chapter, copper(I)-catalyzed one-pot coupling reaction of pyrazole aldehyde with various aliphatic amines and alkynes under microwave irradiation is described. Among the various catalyst used, Cu(I) bromide was found to be more effective catalyst for this coupling reaction. The reaction was fast and clean and the desire products were obtained in good to excellent yield and purity. All the synthesized compounds were characterized by various spectroscopic methods such as 1H NMR, 13C NMR and Mass spectroscopy. In addition, single crystal was developed to know the absolute configuration of the product.

P-14

Synthesis of Novel Chalcone Series and Their Mesomorphism Properties

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Novel homologous series of ?-4-(4'-n-alkoxybenzoyloxy) benzoyl-?-2''-thiophene ethylenes was synthesized and studied the effects of molecular structure on liquid crystal behavior of a substance with reference to steric

hindrance. Isotropic property shown in all homologues series and transition temperatures were determined by an optical polarizing microscopy equipped with heating stage. Transition curved of a phase diagram behaves in normal manner. Isotropic-nematic transition curve showed odd-even effect in very short range of temperature. Analytical and spectral data supported the molecular structures of homologues. Thermal stability is very low and the degree of mesomorphism is poor.

P-15

X-ray Crystallographic Study of Some Novel Mannich bases of 1,4-dihydropyridines

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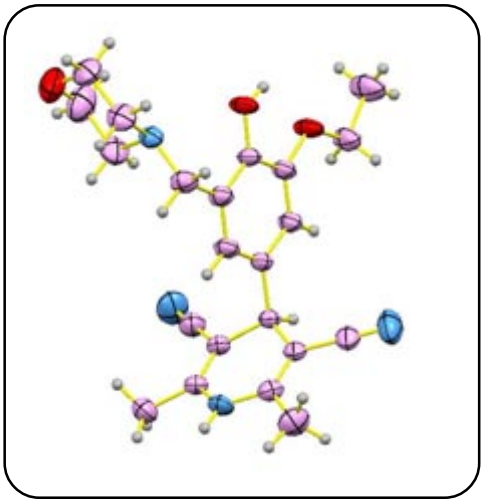
The novel mannich bases are synthesized by Mannich reaction of 1,4-dihydropyridines containing one hydroxyl group at C-4 position and one ethoxy group also introduced along with hydroxyl group on C-4 position of phenyl ring and various secondary amines.. Compound C22H26N4O3 crystallizes in monoclinic crystal system with P21/c (#14) space group and cell parameters a = 16.816(2) Å, b = 10.2851(8) Å, c = 12.6336(9) Å, ? = 92.801(2) o and Z=4. The ORTEP Diagram of the synthesized compound is given below along with CCDC number.



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P-16

An Isocratic UPLC Method for the determination of Levofloxacin Hemihydrate in Dosage Form: A Force Degradation Study

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A reliable and sensitive isocratic stability indicating RP-UPLC method has been developed and validated for Quantitative analysis and Content Uniformity study of Levofloxacin hemihydrate in tablets. An isocratic method for analysis of Levofloxacin Hemihydrate was archived on ACQUITY UPLC BEH C (100*2.1) mm particle size 18 1.7 µ columns within shorter runtime of 4 min with a flow rate of 0.400 ml/min and using a photodiode array detector to monitor the eluate at 294 nm. The mobile phase consisted of Acetonitrile-Buffer (23:77 v/v), (Buffer: 20mM K HPO + 1mL Tri Ethyl 2 4 Amine in 1L water, pH=2.50 by Ortho phosphoric acid). Response was a liner function of drug concentration in the range of 0.5-80 µg/ml (r2= 0.999) with a limit of detection and quantification of 0.1 and 0.5 µg/ml respectively. Accuracy (recovery) was between 99.77 to 101.55%. The drug was subjected to oxidation, hydrolysis, photolysis and thermal degradation. Degradation products resulting from the stress studies did not interfere with the detection of Levofloxacin Hemihydrate and the assay is stability- indicating.

P-17

Novel Aromatase Inhibitors in the Treatment of Breast Cancer

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Estrogens are a group of steroid hormones that are essential to normal female physiology and reproduction. Estrogen signaling pathway engages in several cellular processes particularly cell proliferation and cell survival. Estradiol is biosynthesized from androgens by the cytochrome P450 (CYPS) enzyme complex called "aromatase". The important approach for reducing aromatase is growth-stimulatory effects of estrogens in estrogen-dependent breast cancer. We have designed and developed a series of halogen derivative of benzonitrile or phenyl analogues of letrozole, bearing 1,2,3-triazole, imidazole and alkyl chain. Currently these new compounds are being screened for their anti aromatase inhibitors activity.

P-18

Synthesis and Characterization of Some Novel Coumarin Derivative

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Coumarin derivatives are well known to possess a diverse array of pharmacological and biochemical properties. Currently some Coumarin derivatives are available as prescription drugs, particularly as antibiotics such as novobiocin or clorobiocin. Coumarin Schiff base have great biological important also. So here we synthesize a new route of synthesis of Coumarin synthesis without forming aldehyde, using acetal of DMF (DMF-DMA) with 4-hydroxy Coumarin gives a adduct, which on further Nucleophilic attack of different aromatic amine lead to removing of good leaving group (N,N-dimethyl) and formation of Schiff base with high purity and less consumption of time.

P-19

Design and Synthesis of novel 2',6'-dimethyl-1',4'-dihydro-[3,4'-bipyridine]-3',5'-dicarbonitrile pyridinium bromide derivatives using structure base drug designing approach

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Dihydropyridine derivatives have shown diversed biological profile including anticancer activity and calcium channel blocker property. However, may of DHP derivatives were failed in clinical trials because of their poor solubility. Among the various techniques used, the preparation of water soluble prodrug or formation of various salts has often proved to be the most effective technique in improving the aqueous solubility of drug. A series of pyridinium bromide salt of dihydropyridine have been synthesized by the reaction of 2',6'-dimethyl-1',4'-dihydro-[3,4'-bipyridine]-3',5'-dicarbonitrile with various acetophenone. Various solvents were utilized as reaction media to validate the adopted reaction condition. All newly synthesized compounds were characterized by IR, Mass, 1H NMR, 13C NMR spectroscopy. In addition, the synthesized compounds were implemented for molecular docking study and reported best structure scrutinized by docking score and free binding energy when compared with previously synthesized DHP derivatives of our lab.

P-20

A convenient synthesis and biological activity of 3-amino- 4-imino 6, 9 dimethyl- pyrazolo-[3, 4-e] pyrimido [2, 3-b] [1, 3] benzothiazole

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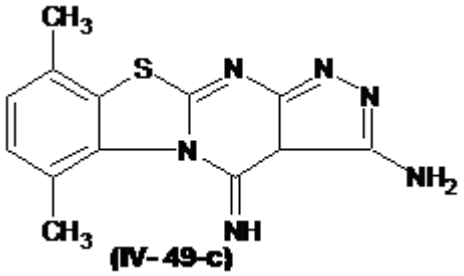
A convenient route to the synthesis of 3-amino-4-imino-6, 9-dimethyl pyrazolo [3, 4-e] pyrimido [2, 3-b] [1, 3] benzothiazole (IV-49-c) have been achieved in multistep reaction. Compound (IV-49-c) was prepared by the reaction of 3-Cyano -6, 9-dimethyl -2-methylthio -4-imino -4H-pyrimido [2, 1-b] [1, 3] benzothiazole (III) and Hydrazine hydrate (80%) in presence of anhydrous K_2CO_3 in DMF as solvent. The intermediate compound (III) was reported by the reaction of 2-amino 4, 7-dimethyl [1, 3] benzothiazole (I) and 3, 3' bismethylthio methylene malononitrile (II) under the same condition by using anhydrous K_2CO_3 in DMF as solvent. All the synthesized compounds were characterized on the basis of spectral analysis.
The reported compounds were screened for their anticancer as well as antibacterial activity; they exhibited better in-vitro anticancer activity against human 60 cell lines as well as antibacterial activity against gram positive and gram negative bacteria.

Keywords: pyrazolo-pyrimido-benzothiazole, bismethylthio methylene malononitrile, anticancer activity, antibacterial activity.



(IV-49-c)

P-21

Synthesis of Novel Aminopyrimido-triazoles Employing Click Chemistry

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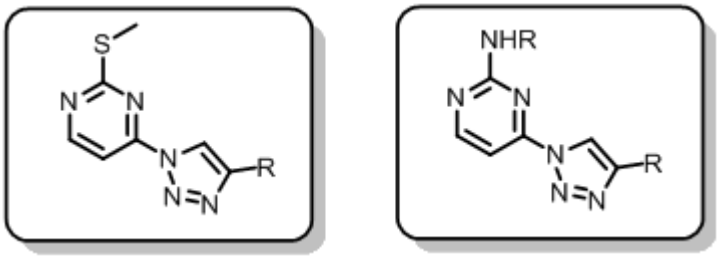
Nitrogen containing heterocycles are important class of compounds due to their role as potential pharmacophores. Among these, compounds containing pyrimidine moiety have been shown to possess wide range of biological activities such as anti-tumor, fungicidal, calcium channel blockers, -1a-antagonists, neuropeptide antagonists, adenosine receptor antagonists, CDK inhibitor etc. Marvaniya et al reported that transformation of arylpyrimidines to diaryl pyrimidines leads to improved anti-HIV activity with rilpivirine, etavirine etc.[1] Zeng et al. have showed that 1,2,3-triazoles show anti-HIV activities.[2] It has been also documented in literature that hybrid molecules of two different pharmacophores can lead to a bioactive compounds with improved activity and efficacy.[3] With this in mind, we have synthesized novel 4-(4-phenyl-1H-1,2,3-triazol-1-yl)pyrimidine-2-thiols and N-phenyl-4-(4-phenyl-1H-1,2,3-triazol-1-yl)pyrimidin-2-amines (Scheme 1) via click chemistry. Details of the synthetic scheme will be presented in the poster.



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P-22

Ionic Liquid-supported Azide: An Efficient Soluble Scavenger for Alkynes

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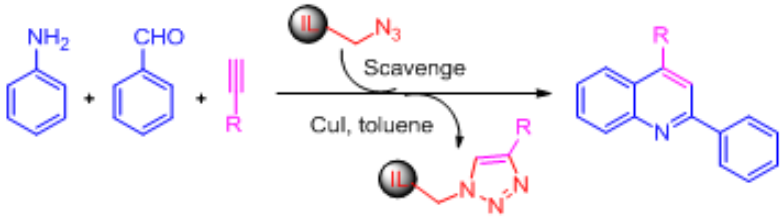
Scavenging is a significant technique in organic synthesis to remove the excess of reagent or byproduct from reaction mixture after the completion of reaction in parallel synthesis [1]. In synthetic chemistry, purification of the product is a remarkable and often challenging process. Although polymer supported scavengers are successfully used for purification process [2]; these scavengers suffers from several limitations such as limited mobility, biphasic reaction conditions, difficulty in reaction monitoring and requirement of large amount of solvent for swelling of resin. Several alternatives like PEG-supported, silica supported, fluorous-phase and aqueous phase scavengers have been developed to overcome some of these limitations [3]. In recent years, functionalized ionic liquids have emerged as potential liquid phase scavengers in parallel synthesis and combinatorial chemistry [4]. In continuation of our interest in ionic liquid supported scavengers[5] we have synthesized a novel ionic liquid

supported azide and exploited its application as a scavenger for an excess alkyne via click chemistry in copper catalyzed multicomponent reaction e.g. povarov reaction (Scheme 1). The salient features of this methodology includes high purity of product without need of column chromatography, requirement of minimum amount of solvent and scavengers, rapid scavenging process, easy monitoring over the polymer supported scavenger.



Scheme 1

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P-23

Imidazolium-Supported Sulfonyl Hydrazine: A Highly Efficient Scavenger for Carbonyl Compounds

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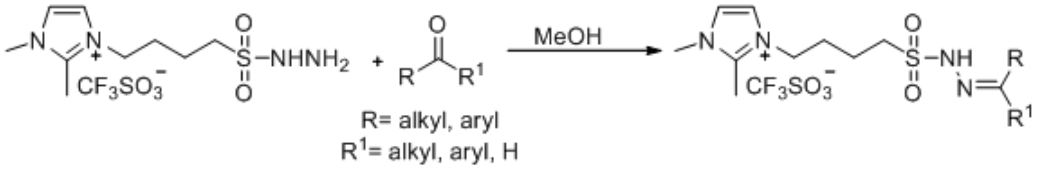
The progress of combinatorial chemistry over the past decade has expedited the development of new technologies that strive to eliminate the need for chromatographic separation of mixtures.[1] Consecutively, this led to the development of effective tools for impurity removal/product purification as polymer-bound reagents, and scavenging agents. Although these revolutionary tools are widely employed, they are limited by nonlinear reaction kinetics and their low-load parameters.[2] To address these issues the use of fluorous phase,[3] aqueous-phase,[4] polyaromatic and PEG-supported[5] reagents and scavenging agents has emerged as alternative. These newer strategy, however, have their own drawbacks, such as costliness, relatively low loading, and the need for large amounts of solvents. In recent years, functionalized imidazolium salts have been developed and utilized as alternative to other supported scavengers. The hallmark of these scavengers is a high site/material ratio (high loading), time saving, ease in monitoring, minimized solvents usage and recyclability.[6] In continuation of our

interest in imidazolium-supported reagents,[7] we have synthesized imidazolium-supported sulfonyl hydrazine and utilized it as scavenger for aldehydes and ketones in multicomponent reactions. The salient features of this strategy are high loading capacity, short sequestration duration, reusability, ease of scale up and ease of monitoring the scavenging progress.



Scheme 1: Scavenging of carbonyl compounds

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P-24

Ionic Liquid Phase Synthesis of 2-Aminothiazoles and Imidazo[1,2-a]pyridines

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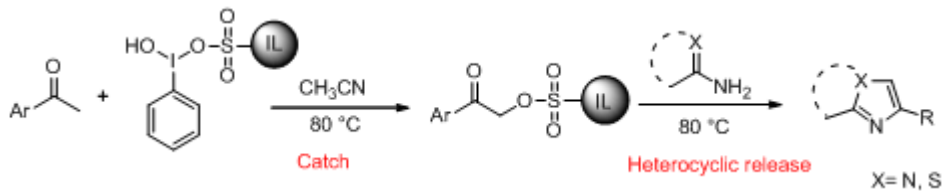
Aza heterocycles are important class of compounds due to their wide range of applications. They are predominant among all types of pharmaceuticals and agrochemicals.[1] Several synthetic methodologies have been developed for the synthesis of aza heterocycles.[2] The most widely used method for the synthesis of these aza-heterocycles is coupling reaction of ?-tosyloxycarbonyls/?-halocarbonyls with aza heterocycles.[3] However, this method requires isolation and purification of the intermediates and/or use of lachrymatory ?-halocarbonyls and thus novel method that can address these issues are desired for the synthesis of these aza-heterocycles. Alternatively some polymer supported hypervalent iodine reagents have been used to overcome these issues. Recently, ionic liquid-supported (diacetoxyiodo)arenes[4] and [hydroxy(tosyloxy)iodo]arenes[5] were prepared and used for oxidation and ?-tosylation respectively. In continuation of our interest in application of ionic liquids in organic synthesis,[6] we have synthesized a novel ionic liquid-supported hypervalent iodine reagent[7] and demonstrate its application for the synthesis of various aza-heterocycles via 'catch and release' strategy (Scheme 1). The procedure involves no chromatographic separation and gives product in good to excellent yield and high purity and thus makes the method greener. Details of the method will be presented in the poster.



Scheme 1

References

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P-25

Synthesis of Novel Azole Fused-Quinazolines via Tandem approach

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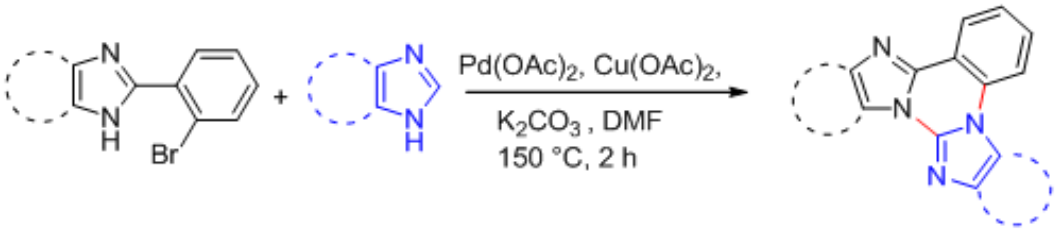
Synthesis of nitrogen containing heterocycles is an everlasting demand in organic chemistry as they are the basis for many natural products and pharmacologically potent molecules.[1] Transition metals catalyzed coupling reactions have emerged as efficient and straightforward strategy for the assembly of a variety of heterocycles starting from simple and commercially available non-preactivated starting materials.[2] These protocols gained an increased attention in recent years due to their advantageous features such as atom-economy and reduced by-product generation.[3] Quinazolines and their analogues are found to have considerable interest because of their wide range of biological properties such as antibacterial, antimalarial, anticonvulsant, antitumor, diuretic and antihypertensive.[4] We have developed an efficient one-pot method for the synthesis of novel azole fused quinazolines via Pd/Cu catalyzed coupling of 2-(2-bromophenyl)-1H-imidazole/benzimidazoles and azoles (Scheme 1).[5] Details of the protocol will be presented in the poster.



Scheme 1

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P-26

An Efficient Synthesis of Naphtho[1',2':4,5]imidazo[1,2-a]pyridines via Copper Catalysed Hurtley Coupling and Intramolecular Cyclocondensation Reaction

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Synthesis of aza-fused heterocycles have vital role in organic chemistry, which are found in many natural products,[1] agrochemicals,[2] and material sciences.[3] A great attention has been focused towards transition metal catalyzed synthesis of aza-fused heterocyclic molecules in last decade due to their biological activities and application in material science.[4] Naphtho-aza-fused heterocyclic compounds have been found evaluated as non-steroidal anti-inflammatory agents,[5] potential PTP-1B inhibitor.[6] These derivatives have also been studied for their photophysical properties.[7] In view of their biological importance, we have developed a simple and efficient copper catalyzed synthesis of naphtho[1',2':4,5]imidazo[1,2-a]pyridines which includes, initially C-C coupling in between substituted 2-(2-bromophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde and active methylene groups such as malononitrile and ethyl acetoacetate followed by intramolecular cyclocondensation reaction. Details of the protocol will be presented in the poster.

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P-27

Design, Synthesis and Application of Ionic Liquid linked Benzotriazole Reagents as Novel Greener Synthetic Auxiliaries

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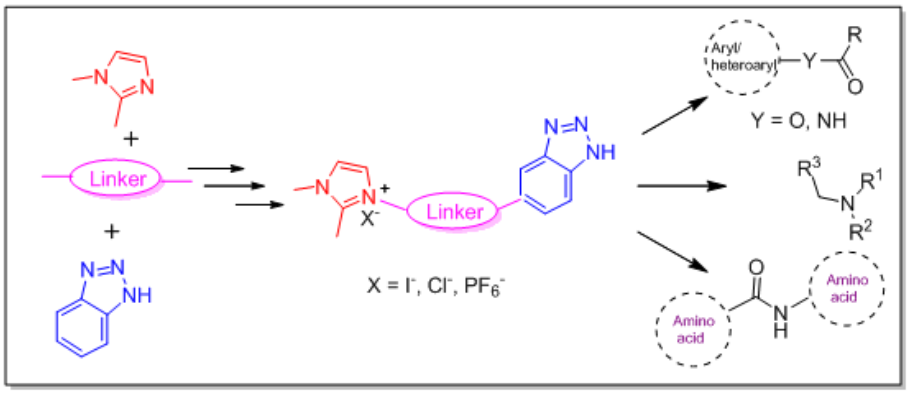
Benzotriazole is a versatile synthetic auxiliary for organic synthesis. Benzotriazole's ability to stabilize both ?-carbocations and ?-carbanions and, in addition, to act as a good leaving group has led to a wide range of valuable synthetic methods, for all major classes of organic compounds and biologically active heterocyclic systems.[1] However, removal of benzotriazole from the reaction mixture, after the completion of reaction is either preceded by acidification or basification, or by using column chromatography in presence of acid or base sensitive substituents that requires large volumes of hazardous organic solvents, making the process unclean and expensive and also resulting in low yields of the expected products. Thus, the methodology requires an alternate solution to make the process 'Greener', at the same time retaining the reactivity of benzotriazole. In recent year ionic liquid has received a acme interest as a greener reaction media and alternative soluble support for organic transformation.[2] Linking benzotriazole moiety to appropriate ionic liquid is believe to increase/decrease the water solubility of benzotriazole without affecting the chemical reactivity of benzotriazole nucleus such that after the reaction, it could be easily removed from the reaction mixture; thus avoiding the use of expensive and hazardous solvents, acid and bases. In present work, we report the design and synthesis of different Ionic Liquid linked benzotriazole reagents, and their application in different organic transformations. Details of the methodology will be presented at the conference.



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P-28

Organocatalytic synthesis of densely substituted 3-formylpyrroles from imines and 1, 4-ketoaldehydes

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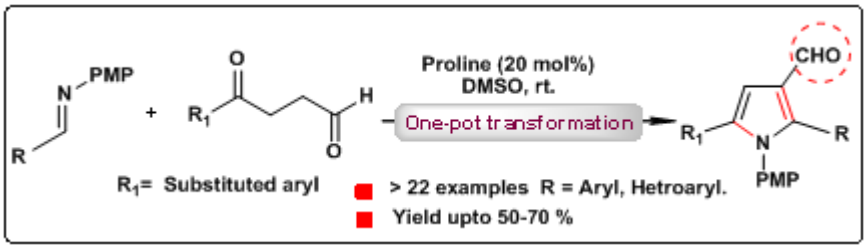
Heterocycles represent the most general structural units in several natural and synthetic bioactive compounds.[1] In particular, pyrroles are an interesting class of nitrogen-based heterocycles with diverse properties in pharmacology and materials science.[2] Organocatalysis has recently been used as an efficient strategy in various organic transformations other than Lewis acid and metal catalysis. In continuation of our interest in organocatalyzed reactions, [3] using linear dicarbonyl compounds as donor-acceptor precursors, presently we established the 1, 4-ketoaldehyde as a simple source of in-situ generation of 1, 3-carbon donor-acceptor precursors, we further extended the chemistry of 1, 4 dicarbonyls for the direct synthesis of densely substituted-3-formylpyrroles with formyl functionality at C3 position under mild conditions in high yields (upto 70%) [4]. The present idea of 1, 3- carbon donor-acceptor precursors is very compatible and even more greener as compared to the methods known earlier for the synthesis of substituted pyrroles from 1, 4-dicarbonyl compounds by Paal-Knorr strategy [5] and this method can be further utilized for the synthesis of some small molecule natural products. Details of this work will be presented here (scheme 1).



Scheme 1: In situ generation of 1, 3- carbon dipole from 1, 4-ketoaldehyde and application in 3-formyl pyrrole synthesis

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P-29

'Aggregation Induced Phosphorescence' Active 'Rollover' Iridium(III) Complex as Multi-responsive Material

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On reaction of 2,2-bipyridine with iridium(III), an 'aggregation induced phosphorescence (AIP)' active "rollover" complex [Ir(PPh3)2(bipy-H)(Cl)(H)], (bpy-H = ?2N,C-2,2?-bipyridine) or [Ir(bipy-H)] was obtained. The emission color changes from bluish-green to yellowish-orange and vice-versa after repeated protonation and deprotonation of [Ir(bipy-H)], respectively which invariably supports of its reversible nature. [Ir(bipy-H)] is sensitive to the strength of acids having different pKa values. The tuning of emission property has been demonstrated with respect to pKa of different acids. This behavior allow the complex, [Ir(bipy-H)] to function as a phosphorescence acid sensor in both its solution and the solid state as well as a chemosensor for detecting acidic and basic organic vapors. The protonated form, [Ir(bipy-H)]H+ which is generated after protonation of [Ir(bipy-H)] has been observed to use as a solvatochromic probe for the oxygen containing solvents, and also showing vapochromic property. The emission, absorption and 1H NMR spectra of [Ir(bipy-H)] under acidic and basic condition demonstrating its reversible nature. The DFT based calculations suggested that the change in electron affinity of pyridinyl ring is responsible for all the processes.

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P-30

An Expeditious Synthesis and Anticancer Activity of 2-Arylamino-5-(Indolyl)-1,3,4-Oxadiazoles

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Indole nucleus is one of N-containing privileged heterocycles which is widely present in most of the naturally occurring bioactive molecules with diverse therapeutic utilities [1]. It is found in many clinical therapeutic agents (e.g., indomethacin, indorenate and indoramin) and endogenous biologically active substances (e.g., serotonin, melatonin, tryptophan and brassinin) [2]. In the recent years, analogues of naturally occurring indoles namely Labradorins, Camalexin, Pimprinine, Topsentin and Meridianins have been prepared and evaluated for their anticancer activity [3]. Particularly, 2-arylamino-oxadiazoles (IMC-094332) and 2-arylaminothiadiazoles (FABT) exhibited remarkable anticancer activity against various cancer cell lines [4]. In view of interesting biological properties of indolylheterocycles, recently, we have identified bis(indolyl)-1,3,4-oxadiazoles, indolyl-1,3,4-oxadiazoles, bis(indolyl)-1,2,4-thiadiazoles, 2-arylamino-5-(indolyl)-1,3,4-thiadiazoles and 4-(3?-indolyl)oxazoles as novel anticancer agents [5]. With the successful identification of some indole-based potent analogues and in continuation of our efforts, we have designed and synthesized 2-arylamino-5-(indolyl)-1,3,4-oxadiazoles by incorporating bioactive arylamino-oxadiazole and indole units in the same molecule. A library of thirteen indolyl oxadiazoles have been prepared from cyclo-desulfurization of easily accessible acylthiosemicarbazides by employing hypervalent iodine (III) reagent [2]. Prepared 2-arylamino-5-(indolyl)-1,3,4-oxadiazoles were characterized by their IR, NMR and MS spectral data and screened for in- vitro anticancer activity against a panel of cancer cell lines. Synthetic protocol and anticancer activity studies of 2-arylamino-5-(indolyl)-1,3,4-oxadiazoles will be discussed during the presentation.

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P-31

Cu-Catalyzed Coupling of *N*-Tosylhydrazones with Amino Heterocycles: Synthesis of *N*-Benzylaminoheterocycles

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Amino heterocycles are known to possess a wide spectrum of biological properties such as anticancer, antimicrobial, antiviral and antihypertensive [1]. Some of these heterocycles have also shown promising applications in the field of materials science [2]. Due to the interesting applications of amino heterocycles it is important to develop a facile and efficient protocol for their synthesis. Several synthetic protocols have been documented for the construction of arylamino heterocycles. The most common route is the reductive amination of carbonyl compounds using metal hydrides [3]. However, reported methods require stoichiometric amounts of metal hydrides that generate various side products. N-Tosylhydrazones are well known precursors for in situ carbene formation and frequently used in metal-catalyzed cross coupling reactions [4]. In 2007, Barluenga and co-workers reported the first example of palladium catalyzed cross-coupling reactions of N-tosylhydrazones for the synthesis of polysubstituted arenes [5]. Recently, N-tosylhydrazones have received greater attention due to various applications in organic synthesis involving C-C, C-O, C-N and C-S bond formations [6]. To explore the chemistry of tosylhydrazones in the formation of C-N bond, we have developed an efficient protocol for the benzylation of various amino heterocycles by employing tosylhydrazones in the presence of a copper catalyst. Optimization of the reaction conditions, related mechanism and synthesized amino heterocycles will be discussed during the conference presentation.

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P-32

Design and Synthesis of Bis(indolyl)ketohydrazide-hydrazones as Potent and Selective Novel Tubulin Inhibitors

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Microtubules are composed of ? and ? tubulin heterodimers that play an important role in various cellular functions including mitosis, shape maintenance and intracellular transport [1]. Interference with microtubule assembly, either by inhibition of tubulin polymerization or by blocking microtubule disassembly, leads to enhanced number of cells in metaphase arrest. Inhibition of microtubule function using tubulin targeting agents is a validated approach to anticancer therapy [2]. Indole skeleton is frequently found in many natural as well as synthetic biologically important entities [3]. Among the indole-based heterocycles, bis(indole) alkaloids have drawn significant interest due to their diverse biological properties including antiviral, antimicrobial and anticancer [4]. Generally, these alkaloids are isolated from marine sources such as sponges, bryozoans coelenterates and tunicates. For example, Nortopsentins A-C, Topsentins, Hyrtinadine A, Coscinamides A-C were isolated from the marine sponges Spongosorites ruetzleri, Topsentia genitrix, Hyrtios sp and Coscinoderma sp, respectively [5]. Bis(indole) heterocycles containing linear chain spacers such as 1,2-diketo (Hyrtiosin B), glyoxylamide (Coscinamides A-C), enamide, hydrazide-hydrazone have also been reported to display interesting biological activities. Indolic enamides like Igzamide, Didemnidine B, Indibulin (D-24851) showed good in vitro cytotoxicity against the panel of cancer cell lines [6]. Recently, we have synthesized bisindoles with 1,2,4-thiadiazoles, 1,3,4-oxadiazoles, ?-cyano chalcones and hydrazide-hydrazone spacers and evaluated their in vitro anticancer activities [7]. In continuation of our efforts to identify potent indole-based anticancer agents, herein we report novel bisindoles by incorporating a ketohydrazide-hydrazone scaffold between the two indole rings while maintaining the crucial features of coscinamide, indibulin and bis(indolyl) hydrazide-hydrazones. A diverse series of ketohydrazide-hydrazones was prepared from the reaction of indolyl glyoxalylhydrazide with appropriate aldehydes. Some of the ketohydrazide-hydrazones were found to exhibit in vitro anticancer activity with IC50 values ranging in nanomolar concentrations against a panel of cancer cell lines. Details about synthesis and anticancer activity of ketohydrazide-hydrazones will be discussed during the presentation.

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P-33

Synthesis and in-vitro Anticancer Activity of ?-Cyano Bis(indolyl)chalcones

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Several natural and synthetic molecules containing the indole ring system have received increasing interest due to their potent anticancer properties [1]. Among the indole-based heterocycles, bis(indole) alkaloids have drawn significant interest due to their diverse biological properties including antiviral, antimicrobial and anticancer [2]. Bisindole alkaloids including Nortopsentins A-C, Topsentins, Dragmacidins, Hyrtinadine A and Coscinamides A-C have been recognized as one of the rapidly growing class of compounds isolated from sponge metabolites [3]. Chalcones, containing 1,3-diaryl-2-propen-1-one system, are known to play a vital role in the cancer drug discovery [4]. It is believed that ?-substitution imparts s-trans geometry to the molecule which may be responsible for the enhanced anticancer activity over unsubstituted analogues [5]. Recently, we have prepared indolyl chalcones as analogues of naturally occurring indolylazoles with excellent antitumor activities [6]. Similarly, we have also identified analogues of bisindole alkaloids with 1,2,4-thiadiazoles, hydrazide-hydrazones and 1,3,4-oxadiazoles spacers as potent anticancer agents [7]. In continuation of our efforts to find potent indole-based heterocycles as antitumor agents, we designed novel ?-cyano bis(indolyl)chalcones by incorporating important pharmacophoric features of chalcones and bisindole alkaloids in a single molecule.

A library of ?-cyano bis(indolyl)chalcones was prepared from easily available 3-cyanoacetyl indoles and indole-3-carboxaldehydes [8]. Some of the synthesized ?-cyano bis(indolyl)chalcones were found to exhibit in-vitro anticancer activity with IC50 values in low micromolar range against a panel of cancer cell lines. Details about synthesis and anticancer activity of ?-cyano bis(indolyl)chalcones will be discussed during the presentation.

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P-34

Synthesis and Photophysical Studies of Novel Triazolo-fused Porpyrins

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Porphyrins are an important class of aromatic compounds that exhibit interesting optical and electrochemical properties and have attracted much attention as key components of functional materials and supramolecular architectures [1]. Among the porphyrins, fused porphyrins have attracted considerable attention in recent years owing to their attractive properties such as red-shifted absorption and emission profiles, intriguing nonlinear optical properties, high electron mobilities, multicharge storage capabilities and photosensitizers [2]. Simple porphyrins shows absorption in Soret band (380-500 nm) and weak Q band (500-700 nm) [3]. Porphyrins with extended -system or conjugated with a fused peripheral heterocycle moiety offers the possibilities for modulation of photophysical properties of the parent macrocycles [4, 5]. On the other hand, fused-triazoles are well known for their diverse application in medicinal chemistry as well as in materials science [6]. In continuation of our efforts to identify novel porphyrin derivatives with improved photophysical properties, we have developed an efficient protocol for the synthesis of meso-? fused triazoloporphyrins by incorporating bioactive fused-triazole and porphyrin units in the same molecule. Various triazolo-fused porphyrins were prepared by the oxidative cyclization of hydrazones using iodine (III) reagent and followed by mild acid catalyzed oxidative C-C coupling reaction. meso-? Fused triazolo-porphyrins exhibited significant red shift compare to the parent porphyrins. The Synthesis and photophysical studies of meso-? fused triazolylporphyrins will be discussed during the presentation.

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P-35

Synthesis of some biological active novel ?-diketones containing pyrazole moiety

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Reaction of substituted pyrazole-1-acetyl chloride (3) with acetophenone derivative (4) in presence of sodium methoxide in dry toluene led to the synthesis of substituted ?-diketones containing pyrazole moiety (5a-l). All the newly synthesized compounds were confirmed by elemental analysis and IR, 1H, 13C NMR and mass spectral studies. The synthesized compounds (5a-l) were evaluated for their antibacterial and antifungal activities. The results indicate that these compounds were moderately active against various bacteria such as (S. aureus, K. pneumoniae) and fungi (A. niger, C. albicans). Compounds (5b, 5d, 5f, 5h, 5j, 5l) showed good activity against S. aureus, K. pneumoniae and compounds (5b, 5d, 5f, 5h, 5j, 5l) showed good activity against A. niger and C. albicans.

Keywords: Acetophenone derivative, pyrazole-1-acetyl chloride, 1,3-diketones, sodium methoxide, antibacterial, antifungal activity.

P-36

Alkaloids of Annona squamosa as Anti-ulcer agents

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Phytochemical investigation of Annona squamosa twigs, resulted in isolation and identification of twelve known (1-12) compounds. Their structures were elucidated using 1D and 2D NMR spectroscopic analysis. The isolated compounds (2-8, 11) were evaluated for H+ K+-ATPase activity. Three of these compounds (+)-O-methylarmepavine (2), N-methylcorydaldine (3), isocorydine (6) showed promising anti-ulcer activity. Activity of these compounds, comparable to the standard drug omeprazole is novel to our finding. Moreover, there is no information accessible regarding the pharmacological effect of A. squamosa on the gastrointestinal system. This study is the first of its kind to show the significant anti-ulcer effect of A. squamosa. The present study aimed to

evaluate the gastroprotective effect of A. squamosa (AS) and to identify its active constituents. Anti-ulcer activity was evaluated against cold restraint (CRU), pyloric ligation (PL), aspirin (ASP), alcohol (AL) induced gastric ulcer and histamine (HA) induced duodenal ulcer model and further confirmed through in vitro assay of H+ K+-ATPase activity and plasma gastrin level. AS and its chloroform and hexane fraction attenuated ulcer formation in CRU, PL, HA model and displayed anti-secretory activity in vivo through reduced free, total acidity and pepsin in PL, confirmed by in vitro inhibition of H+ K+-ATPase activity with corresponding decrease in plasma gastrin level. Cytoprotection of AS was apparent with protection in AL, ASP models and enhanced mucin level in PL.

P-37

Green chemistry based optimization of the synthesis of the scaffold of 3-benzyl-5-hydroxymethyl-1,3-oxazolidin-2-one by using microwave method

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Oxazolidinone is a five-member heterocyclic ring used as scaffold for the synthesis of various ligands for different targets. This fragment could be seen in antibiotics like Linezolid and is utilized as a privileged structure because of its occurrence in ligands for anti-muscarinic, anti-inflammatory targets etc Osa et al. [1], Pandit et al. [2]. Many synthetic approaches have been made available for this fragment, however they were found to be either time/energy consuming or multistep. The synthetic methodology involved conventional heating for more than 12 hrs. Green chemistry concept was applied by utilizing microwave method P.Lidstom et al. [3] in order to synthesize N3-substituted oxazolidinone alcohol wherein a benzyl amine was reacted with the carbonate salts and epichlorohydrin, in presence of base and solvent. The reaction was optimized for various parameters such as carbonate salts, base, starting material, solvent, time, temperature, power, ratio under open and close vessel microwave system. The time and the yield were found to be successfully optimized [1].

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P-38

Antiarthritic activity of hydroalcohol extract of Litchi chinensis Gaertn

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Rheumatoid Arthritis is a chronic inflammatory disease characterized by synovial inflammation and subsequent tissue damage, which leads to functional decline and disability as well as increased mortality (Abreu et al, 2005). The litchi (Litchi chinensis Gaertn., Sapindaceae) is a tropical fruit tree that originates from southern china and is cultivated in semi- tropical areas world-wide (Gontier et al., 2000). Leaves of Litchi chinensis was extracted by using hydroalcohol (60:40, ethanol: water) and Wistar rats (150-170 g) were used for the study. Arthritis was induced by complete Freund's adjuvant and different doses (100, 200 and 400 mg/kg) of HALC was used for the study. Change in Body weight, haematological parameters, paw volume and paw thickness was measured to assess antiarthritic effect. Treatment with 200, 400 mg/kg of HALC produced significant weight gain. The percentage decrease in WBC count and percentage inhibition of ESR was found to be 7.22%, 27.29% and 36.45% and 29.33%, 34.88% and 56.86% respectively at 100, 200 and 400 mg/kg. The percentage increase in Hb level was found to be 2.4%, 4.33%, 6.53%. The HALC extract significantly reduced the paw volume and paw thickness. These results indicate that HALC could be beneficial in the management of arthritis.

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P-39

Screening for antibacterial activity of leaf extracts of Datura inoxia: A study for its compound analysis

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Antimicrobial agents from plants are considerably useful and have enormous therapeutic potential. Due to the alarming incidence of antibiotic resistance in bacteria of medicinal importance, there is an urgent need to develop alternative antimicrobial drugs from natural sources. In present study, the antibacterial activity of different extracts of Datura inoxia leaf was investigated against Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli using hexane, ethanol and aqueous solvents. The extracts showed inhibitory effect against Staphylococcus aureus and Escherichia coli, while no antibacterial activity was observed against Pseudomonas aeruginosa. Column chromatography was performed to purify the ethanolic extract as this showed maximum antibacterial activity. All the fractions showed minor to significant antibacterial activity against the tested strains. The most active fraction was further analyzed through LC-ESI-MS and NMR techniques to identify compound from it. Our findings confer the utility of this plant in developing novel broad spectrum antimicrobial agents.

Key words: Datura inoxia, antibiotic resistance, antibacterial activity, column chromatography, LC-ESI-MS, NMR.

P-40

Sonochemical synthesis and characterization of novel oxadiazole derivatives

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Sonochemistry is a new trend in organic chemistry, offering a versatile pathway for a wide variety of synthesis. A large number of organic reactions can be carried out under ultrasonic irradiation in high yield, short time and mild conditions [1]. Different Oxadiazole derivatives were synthesized by reaction between aryl aldehydes and semicarbazide. The completion of organic reaction and purity of compounds were checked by TLC and the structures of synthesized compounds were confirmed by spectroscopic analysis using IR and 1H NMR. A series of novel oxadiazole derivatives were synthesized using sonochemical synthesis technique in lesser time with higher yields. A class of novel oxadiazole under sonication condition were synthesized successfully.

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P-41

Ionic Liquids a Promising Podium for Medicinal Chemistry

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The pharmaceutical industry of today is unquestionably facing number of challenges. Though many of these challenges involved current business strategies and model, but the lake of innovative and new effective drug therapies are another frontier of the challenges for the pharma industry. This declares the urgent need for new science to bring forward innovative and effective solutions for the safer drug formation and use for the existing therapies. In fact industrial synthesis protocols of pharmaceutical compounds often employ organic solvents which mostly concerned for various reasons such as cost effective procedure, ease of handling and temperature to be applied. But most of the times, these reaction media are accountable for organic contamination of the final product of pharmaceutical importance. This contamination usually referred as 'residual solvents' or 'organic volatile impurities". Pharmacopoeias and the International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use[1], given the guidelines for the acceptable

limits for contaminants resulting from the entire drug product manufacturing process. The ICH guideline makes a distinction and describes the four classes of residual solvents in drug substances as:

Solvents to be avoided,
Solvents to be limited,
Solvents with low toxic potential and
Solvents without adequate toxicological data.

Geno-toxic impurities (GTIs) are regarded as the most dangerous contaminants for human health. Exposure of such impurities even at very low levels in the final active pharmaceutical ingredient (API) can cause/resultant into genetic mutations and may potentially be the cause of cancer in humans. Conversely, regardless of the solvent type and class, it is essential to explore the other promising opportunities to reduce or avoid the use of unsafe solvents in the manufacturing process of pharmaceutical ingredients Bouder et al. [2].

In last two decades Safer Chemistry becomes an intriguing and more demanding science to produce outstanding results while preserving many safety concerns and pharmaceutical concern integrated. In this perspective, ionic liquids have gained excellent reputation as a possible 'green' substitute to more volatile organic solvents. Wilkes et al. [3],. It provides the revolutionary concept of environmentally benign synthetic medicinal procedures. Ionic liquids (ILs) are liquid at room temperature principally Ionic liquids (ILs), solvents composed entirely of paired ions made of ions and short-lived ion pairs. They have unique combination of physical and chemical properties which are not always associated with molecular solvents. ILs are known designer solvents, they are promising molten materials and used in variety of applications in pharmaceutical and biotechnology fields. Wells et al. [4]

The Applications of ILs includes i) avoid polymorphism of crystalline solids, ii) stabilizes labile biopharmaceutical products for therapeutic use, iii) convert s active pharmaceutical ingredients to liquids with benign counter-ion, iv) as anti-biofilm agents and. v) as preferred solvent system for synthesis and stabilization of nanoparticles and in drug delivery techniques for new controlled-release dosage. It is also reported that enzymes showed enhanced enantio-selectivity without losing any significant activity while coated with an ionic liquid. Moreover employment of the chiral ionic liquids may give improved methods for synthesis of chiral products or the manufacture of single enantiomer drugs for the pharmaceutical industry. Above mention data reveals that Ionic liquids have the potential to become an imperative part of the drug development tool-kit mainly for biocatalysis, mass extraction and vessel cleaning. This study will provide the extensive information of ionic liquids for its use at Industrial level with special reference to the APIs synthesis and nanoparticles synthesis. Sekhon et al [5].

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P-42

Evaluation of natural product with novel approaches for preventing cancer

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Cancer is a leading cause of deaths worldwide including India. Cancer cells are mainly characterized by uncontrolled cell growth due to slow apoptosis and high cell survival signaling. Thus, anticancer strategies generally target these signaling events in cancer cells. Natural products have been great source of molecules with putative anticancer activities. However, the demand of day is to target specific signaling events in the cancer cells with minimal effects on non-cancerous environment. Various plants based products have shown specific targeting mechanism in cancer cells. Such as, resveratrol found in grapes seed activated lipid-raft dependent CD95/FasL mediated cell death in human colon cancer and leukemia cells. Quercetin, a flavonoid, induced cell death in lung cancer cells by enhancing p53 expression. Andrographolide, a diterpene lactone, downregulated PI3K/Akt signaling and suppressed c-Jun?c-Fos in human cancer cells. Recently, we have identified that a medicinal edible mushroom Inonotusobliquas suppresses intestinal inflammation and colorectal carcinoma through novel mechanism. Cedrol, a sesquiterpene alcohol from cedar wood oil, inhibited the growth of human leukemia and colorectal cancer by the destabilizing plasma membrane lipid raft. In this presentation, we have focused on to highlight some important medicinal plant with novel therapeutic approach.

Keywords: natural products, anticancer, apoptosis, novel mechanisms

P-43

In vitro evaluation of carboxymethylated bael fruit gum as excipient for F4 fimbriae oral formulation

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In the present study, carboxymethylated bael fruit gum (CBFG) was investigated as a novel excipient for oral tablet formulation of F4 fimbriae vaccine to ensure its protection in the stomach and permit its consequent release in the intestinal fluid. Carboxymethylation of Bael fruit gum was achieved by reacting it with monochloroacetic acid under alkaline conditions. F4 fimbriae, thus formulated with CBFG as tablets showed a higher stability in gastric fluid containing pepsin after 2 h of incubation than the free, F4 fimbriae in solution which in these conditions digested completely. In simulated intestinal medium containing pancreatin, the F4 fimbriae were liberated from CBFG tablets over a period of 6 h based on the fast swelling during its passage from gastric acidity to alkaline intestinal medium, enzymatic hydrolysis triggering their rapid, almost total dissolution. Thus, F4

fimbriae formulated with CBFG showed higher survival rates in acidic gastric conditions and for extended periods than the free F4 fimbriae in solution.

P-44

Novel synthetic ester of Brassicasterol, DFT investigation including NBO, NLO response, reactivity descriptor and its intramolecular interactions analyzed by AIM theory

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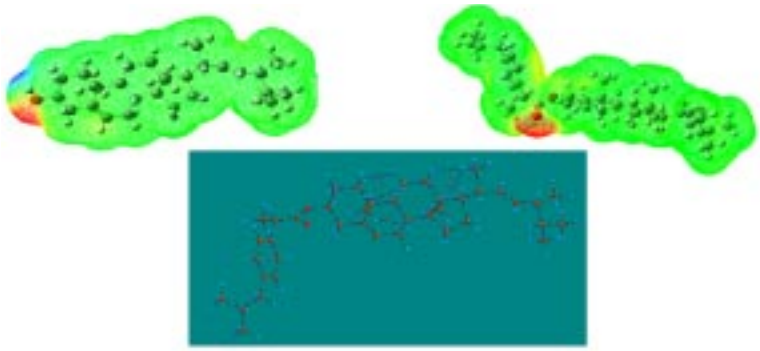

Different extract of the flowers of Allamanda Violacea viz. petroleum ether extract, ether extract, chloroform extract, chloroform:methanol (4:1) extract, chloroform:methanol (3:2) extract were prepared and first subjected to biological screening (Anti-hyperlipidemic, anti-oxidant, anti-diabetic activities). Chloroform extract showed significant biological activities hence evaluated for the presence of steroidal derivatives. With the help of repeated column chromatography using n-hexane/ ethyl acetate as eluent and thin layer chromatography, a novel sterol, Brassicasterol (compound 1) was isolated (25 mg) as needle shaped crystals. Compound 1 was esterified with the well known NSAID ibuprofen by Steglich esterification yielding a novel steroidal ester, 3?-(2-(4-isobutyl phenyl) propionoxy) 24 methyl cholest-5, 22-dien (compound 2). Identity of synthetic derivative was done with the help of modern spectroscopic techniques like, 1H NMR, IR and UV as well as mass spectrometry. Molecular geometry and vibrational frequencies of compound 2 were calculated using density functional method (DFT/B3LYP) and 6-31(d,p) basis set. NMR chemical shifts of the compound were calculated with GIAO method. Electronic properties such as HOMO-LUMO energies were measured with the help of time dependent DFT method. Natural bond orbital (NBO) analysis was carried out to study hyperconjugative interactions. Non linear optical (NLO) response of compound 2 was also evaluated. Molecular electrostatic potential (MEP) surface has been used to indicate nucleophilic and electrophilic sites. Global reactivity descriptors of compound 1 and 2 were also calculated. Intramolecular interactions were analyzed using Atoms in molecule (AIM) theory.

P-45

Spectroscopic investigation of novel 2[(3-? acetoxy) pregn-5 ene-20-one-16-thio] propanoic acid synthesized via thia-Michael addition, its molecular structure, vibrational assignments, NBO analysis, intramolecular interactions studied by DFT and AIM approach

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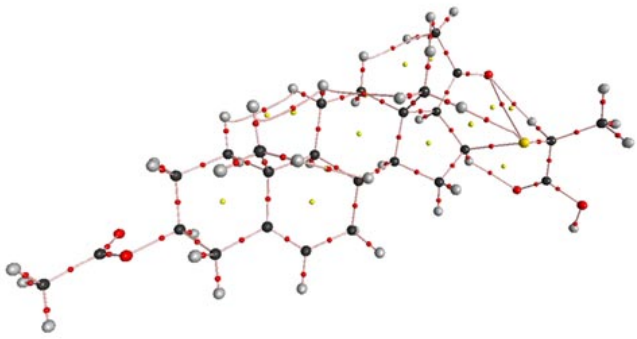
Pregnane derivatives have been reported to possess anti-inflammatory, anti-asthmatic, anti-feedant, anti-dyslipidimic, anti-oxidant and anti-viral properties. Taking this into account, we planned to synthesize a novel 2[(3-? acetoxy) pregn -5 ene -20-one -16 -thio] propanoic acid (compound 2) and characterized with the help of 1H, 13C-NMR, IR, UV and mass spectrometry. The molecular geometry of compounds was calculated in ground state by density functional theory (DFT/B3LYP) using 6-31G (d, p) basis set. 1H and 13C-NMR chemical shifts were calculated using Gauge-Including Atomic Orbital (GIAO) approach. The electronic properties such as HOMO and LUMO energies were calculated using time dependent density functional theory (TD-DFT), showing n? ?* and ?? ?* transition. Stability of the molecules as a result of hyper conjugative interactions were analyzed using natural bond orbital (NBO) analysis, showing ? ? ? *, ? ? ?*, n? ?* and n ? ? * hyper conjugative interactions, point to the stabilization of the molecule. The topological parameters were analyzed by 'Atoms in molecules' AIM theory and it was found that all the intramolecular interactions are weak. The intramolecular interaction energy of compound 2 was calculated as -18.76 kcal / mol using AIM calculations. Local reactivity descriptors like Fukui functions (fk+, fk-, fk0), local softness (sk+, Sk-, Sk0) and local electrophilicity indices (?k+, ?k-, ?k0) analysis have been performed to find out the reactive sites within the molecule confirming that C-16 site in compound 1 is more prone for nucleophilic attack than C-17, which leads to the formation of the desire compound.



Molecular graph of compound 2 at B3LYP/6-31G (d, p) level using AIM program: bond critical points (small red sphere), ring critical points (small yellow sphere) and bond path (pink lines).

P-46

Synthesis and characterization of novel steroidal derivatives, their theoretical study by DFT and AIM approach

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Steroid derivatives have been found to possess anti-inflammatory, anti-dyslipidimic, anti-allergic, anti-bacterial, lipid lowering, anti-cancer activities. Hence we synthesized novel steroid derivatives like 16?-methoxy pregn-5-ene-20-one-3yl -2-(4-iso butyl phenyl) propanoateand3?-2-(6-methoxynapthalen-2-yl)propioxy-16?-methoxy pregn-5-ene-20-oneby Steglich esterification on 3?-hydroxy16?-methoxy pregn-5-ene-20-one. Esterification reaction on steroid moiety was achieved in high yield using N, N'-Dicylcohexylcarbodiimide (DCC) as a coupling reagent and 4-Dimethylaminopyridine (DMAP) as a catalyst.The synthesized compounds have been characterized with the help of modern spectroscopic techniques like 1H, 13C NMR, FT-IR, UV-visible spectroscopy and mass spectrometry. Quantum chemical calculations have been performed by density functional theory (DFT) using B3LYP functional and 6-31G (d, p) basis set. 1H and 13C-NMR chemical shifts have been calculated with gauge-including atomic orbital (GIAO) approach. The electronic properties such as frontier orbitals and band gap energies have been calculated using time dependent density functional theory (TD-DFT). Stability of the molecules arising from hyperconjugative interactions and electron delocalization has been analyzed by natural bond orbital (NBO) analysis. The strength and nature of weak intramolecular interactions have been studied by AIM approach. The vibrational wavenumbers have been calculated using DFT method and assigned with the help of potential energy distribution (PED). Global and local reactivity descriptors have been computed to predict reactivity and reactive sites in the molecule. First hyperpolarizability values have been calculated to describe the NLO property of the synthesized compounds.

P-47

Synthesis of prodrug 3-cholesteryl 2-(6-methoxynaphthalen-2-yl)-propionate, its spectroscopic characterization, experimental and quantum chemical computational studies

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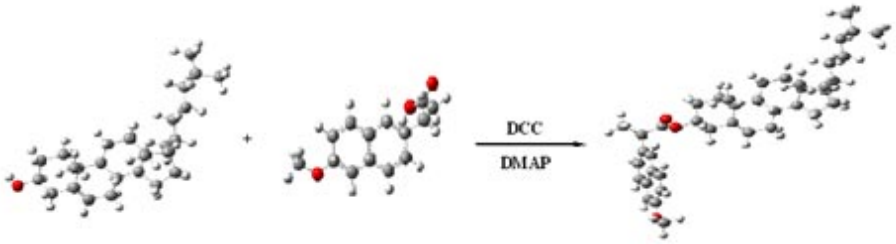
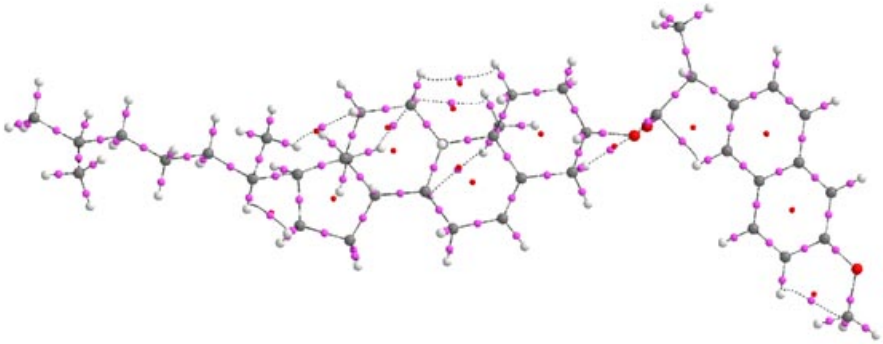
A steroidal-NSAID prodrug 3-cholesteryl 2-(6-methoxynaphthalen-2-yl)-propionate (2) was synthesized using cholesterol and naproxen by adopting Steglich esterification. Compound (2) was characterized by 1H NMR, 13C NMR, FT-IR, UV-Vis and Mass spectrometry. The molecular geometry, IR frequencies, gauge-independent atomic orbital (GIAO) 1H and 13C NMR chemical shift values of compound (2) were theoretically calculated in the ground state with the help of density functional theory (DFT) level of theory using B3LYP functional and 6-31G (d, p) basis set. The calculated values were found to be in good correlation with experimental data. The time

dependent density functional theory (TD-DFT) was used to evaluate various electronic transitions such as HOMO and LUMO energy within molecule. With the help of calculated HOMO and LUMO energy values, charge transfer within the molecule was indicated. Stability of the molecule as a result of hyperconjugative interactions was analyzed using natural bond orbital (NBO) analysis. NBO analysis resulted in ???*, n? ?* and n??* electron delocalization. Additionally, to investigate geometrical parameters (bond length), topological parameters for bonds of interacting atoms which include electron density (?BCP), Laplacian of electron density (?^2?(BCP)), electron kinetic energy density (GBCP), electron potential energy density (VBCP), total electron energy density (HBCP) at bond critical point (BCP) as well as estimated interaction energy (Eint) AIM (Atoms in molecules) approach was considered. AIM approach helped in studying intramolecular hydrogen interaction and ellipticity, indicated C3…H26, H4…H31, H36…H23, H30….H37, C62…H60, H89…H42, O94…H40 were weak interactions and ?-character of bond in aromatic ring.



Scheme of reaction between cholesterol and naproxen using DCC, DMAP in CDCl3 at room temp.



Molecular graph of compound 2 at B3LYP/6-31G (d, p) level using AIM program: bond critical points (small pink sphere), ring critical points (small red sphere), and bond path (black lines)

P-48

Protective effects of aqueous and alcoholic extracts of piper longum in experimental rodent models of seizures

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Epilepsy affects 5 to 10 per 1000 of the general population. It is the third most common neurological disorder after stroke and Alzheimer's disease. Available anti-convulsant drugs effectively control epilepsy in about 50% of the patients. Many epileptic seizures are refractory to current anti-epileptic drugs and safety of the anti-epileptic drugs has always been a concern. Herbal drugs may serve as the alternative for some such patients. Many plants have been used for the treatment of epilepsy in traditional system of medicines have shown useful anti-seizure activity. Herbal remedies have become popular, due in part to the lower risk of adverse reactions. Thousands of plants have been used traditionally to treat various diseases. Among them, species of the genus Piper are important medicinal plants used in various systems of medicine. The Piper longum fruit has been used in traditional medicine, including the Ayurvedic system of medicine.[1] Although there are numerous indications for its use and plant contains many active constituents, controlled trials are needed to determine its anti-epileptic efficacy in small animals.[2-4] The present study was done to evaluate anti-seizure activity of fruits of Piper longum on animal models of seizures and also to find out effectiveness of aqueous and alcoholic extract .

Keywords: anti-oxidant action ; anti-seizure activity; fruits ; piperine ; traditional medicine.

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P-49

Synthesis of Curcumin Under Grinding Condition

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Curcumin is commonly known as diferuloyl methane and found in rhizome of the herb curcuma longa L. It is used as a dietary pigment spice and coloring agent and herb in traditional Indian and Chinese medicine Kuttan et. al (1). Curcumin is biologically active molecules and possess various pharmalogoical activities P. Anand et.al(2). Very few methods exist for synthesis of curcumin and synthesis of curcumin are reported by Paban(3), Paban et.al(4), K. V. D. Babu et.al(5), E. Venkata Rao et.al (6) However these reported methods suffer from drawbacks like low yield, harsh reaction condition, expensive and hazardous regents are used, and product isolation is a boring process. Therefore, there is scope to develop new methods for the synthesis of curcumin by using an inexpensive, safe, simple and eco-friendly catalyst. Recently S. Elavarasan et. al(7a) reported synthesis of

symmetrical curcumin using calcium oxide under microwave condition and P. Kulkarni et. al reported using calcium hydroxide (7b). However this method also suffers from drawbacks like isolation of product require extraction process and long reaction time. Calcium is divalent in nature and it forms complex with acetyl acetone which protect middle methylene group and carried out condensation at terminal methyl groups to afford curcumin. In this method, we carried the synthesis of curcumin under grinding condition. The merit of this method is easily available, non toxic and inexpensive catalyst, short reaction time, yield is good, avoid use of solvent and electrical energy.

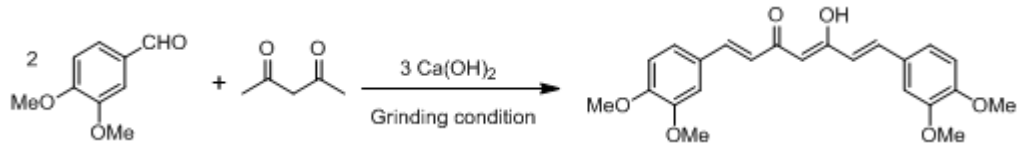

Figure 1 Synthesis of Curcumin using Calcium hydroxide as base under Grinding Condition

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P-50

Rational Design of small molecule inhibitors targeting Hup-dimerization and Hup-DNA Binding Interaction in Helicobacter pylori

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Helicobacter pylori (H. pylori) is the etiological agent of several human stomach illnesses including gastritis, duodenal/peptic ulcers, and gastric cancer [1]. The pathogen colonizes under harsh acidic and oxidative stress conditions of human gastrointestinal-tract (GI) and can survive there for infinitely longer durations of host life.

This happens because of several harbinger proteins the bacterium expresses to facilitate its persistent colonization under such harsh conditions. One such protein in H. pylori -crucial for its survival and pathogenesis- is the Histone like DNA binding protein [2]. Theprotein -referred here as Hup- is known to exist as a homo-dimer and this homo-dimeric form is crucial for its efficient binding to H.pylori genomic DNA. Several molecular biology and biochemical studies have revealed that Hup-DNA bindinginteraction is crucial for genomic-DNA compaction and in all DNA dependent cellular activities highlighting theimportance of this protein as a potential therapeutic target[2]. Thein vivo activity of Hup can be suppressed by the application of small molecule inhibitors.Working within this framework, the structural and mechanistic investigations have beencarried out using solution NMR (Nuclear Magnetic Resonance) spectroscopy in combination with various biophysical,biochemicaland bioinformatics methods. The resulted mechanistic and structural information isfurther used to identify small molecule inhibitors following the rational (structure-guided-computer-aided) drug discovery approach. The inhibitors has been designed targeting either Hup-dimerization or Hup-DNA binding interactionsand have been evaluated for their activity in solution using NMRin combination with various biophysical and biochemical methods.

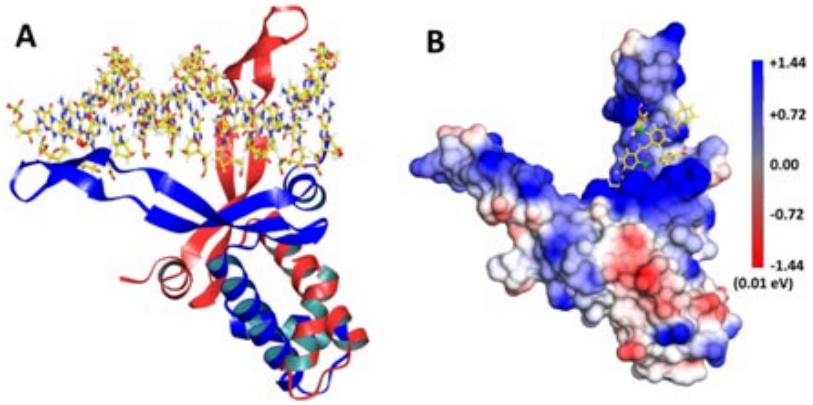

Figure: (A) Energy minimized Helicobacter pylori homo-dimeric Hup in its DNA bound form and(B) Small molecule inhibitor identified using virtual screening of compound libraries and docked to DNA binding site. The Figure also highlights that the DNA binding site on Hup is largely positively charged.

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P-51

Preferential Recognition of DNA G-Quadruplex Topologies by TMPYP4

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Nucleic acids containing successive runs of guanines (G) tend to self-associate into a four stranded G-quadruplex (G4) structure stabilized by Hoogsteen hydrogen -bonding under some monovalent cations [1]. In recent years,

these structures have attracted intense interest because of their role in potential biological functions, such as gene regulation, gene expression and antitumor potential [2]. G-rich sequences are unevenly distributed on some regions of the human genome, including telomeric ends, immunoglobulin switch regions and regulatory elements in some gene promoters, such as c-myc, c-kit, and so on [3, 4]. G-quadruplexs are considered to be promising targets for antitumor drug design. Several classes of small molecules that are able to selectively bind to G-quadruplexes have been known. The cationic meso-tetrakis (4-(N-methylpyridiumyl) porphyrin (TMPYP4), as a potential inhibitor of telomerase activity, has been the subject of extensive investigations [5].
We report here on the interaction of G-quadruplex binding ligand (TMPYP4), with G-rich sequences of various genomic locations. The sequences primarily adopt parallel as well as antiparallel quadruplex structures in solution containing monovalent K+ cation. Circular dichroism spectra of TMPYP4 complexes with all the G-rich sequences suggest a preferential destabilization of quadruplex with parallel topology while the TMPYP4 induced formation of antiparallel G-quadruplexes. To best of our knowledge this is the first report on preferential destabilization and stabilization (induction) of DNA G-quadruplex topologies, by, a quadruplex specific ligand TMPYP4.

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P-52

Tumor-Accumulating Ruthenium Complex for Tumor Hypoxia Imaging and Photodynamic Therapy

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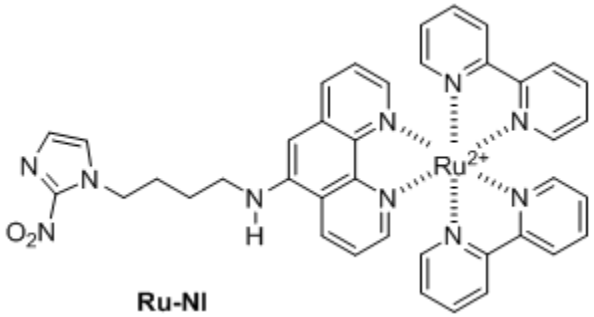
Photodynamic therapy (PDT) is a powerful tool to treat cancer without side effects, and has been successfully applied in the treatment of various cancers. Some researchers have already reported the applications of ruthenium (Ru) complexto PDT because of its long lived triplet state that led to produce reactive singlet oxygen species with high efficiency to kill cancer cells. [1, 2]However, these Ru complexes did not accumulate in tumor by itself, and therefore, itmay cause serious side effects.Herein, we proposedruthenium complex possessing nitroimidazole

unit (RuNI, Figure 1), which not only achievesfull PDT effects but also accumulates in tumor tissue. This accumulation arises from the tumor-specific reduction of nitroimidazole under hypoxic conditions by nitroreductase. In vivo experiment using tumor-bearing mouse actually showed that Ru-NI selectively localized at hypoxic tumor tissue. Photoirradiation at tumor tissue of mice resulted in a tumor-specific apoptosis and cell death without any side effects.In addition, Ru-NI showed strong phosphorescence specifically in a hypoxic region. This means that simple and single molecule, Ru-NI enables us to easily visualize multiple tumors by monitoring of its phosphorescence emission. Thus,Ru-NI provided a promising function for imaging and treatment of cancer.



Ru-NI

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P-53

Genome wide identification and In-silico characterization of Mn-peroxidase in plants

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Manganese peroxidase, MnP [E.C.1.11.1.13], a ligninolytic enzyme first reported [1] in the lignolytic culture of Phanerochaete chrysosporium, has been shown to occur in a number of fungi [2].It is a biotechnologically important enzyme [3]. Iimura et al [4] have expressed the MnP gene from Coriolus versicolor in transgenic tobacco plant and have found that it is a potential tool for phytoremediation of pentachlorophenol. The authors have been guided by the idea that if MnP containing natural plants could be identified, it may turn out to be better agents for phytoremediation. So far MnP is reported only in fungi and there is only one report of MnP in a plant [5].In order to identify other plant sources, the authors have used bioinformation techniques to search for the gene of MnP in 29 plants, the genome sequences of which are available [6].The results have indicated the possibility of the presence of MnP genes in 7 plants belonging to 6 plant families. Experimental studies have confirmed the presence of MnP in seven plants. The results of the studies will be presented in the conference.

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P-54

Heat of Formation (Hf): A Predictive Tool For Anti HIV-5-Phenyl-1-H-Imidazole Derivative

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Quantitative structure activity relationship (QSAR) model of a series of 40 antiHIV-5-phenyl-1-H-imidazole derivative were developed with the help of Quantum chemical descriptors. Molecular modeling and geometry optimization was carried out with CAChe prosoftware .Calculation of descriptors and multilinear regression analysis was done using Project Leader software. Various QSAR model of different combination for each set were developed and five model has been selected on the basis of correlation coefficient .Among them the best model is judged on the basis of values of statistical parameters such as Standard error (SE), Standard error of estimation (SEE), t-value, p- value and Degree of freedom (DOF) that were calculated by Statistica and secondly a direct relationship between heat of formation and observed activity is reported. Heat of formation (Hf) can alone be helpful for searching of antiHIV-5-phenyl-1-H-imidazole derivative of reliable activities before their synthesis.

Keyword: QSAR, AntiHIV activity, Heat of formation, Degree of freedom.

P-55

Molecular interaction of anti-cancer drugs, methotrexate with human orphan GPR87: a docking study

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GPR87 is an orphan G-protein coupled receptor (GPCR) which may be a potential molecular target for the treatment of squamous cell carcinomas (SCCs) or adenocarcinomas in lungs and bladder. A 3Dstructure of GPR87 is constructed by homology modeling, by using crystal structure of CXCR4 chemokine receptor (PDB ID: 3ODU|A) as a template. The modeled structure of GPR87 was further validated by comparison with structural features of templates through Verify-3D, ProSA and ERRAT scores. In this research hypothesis, we study the structural and functional of GPR87 protein by homology modeling and docking analysis to obtain more selective and potent drugs. The DRY-motif (Asp-Arg-Tyr sequence) showed at the end of transmembrane helix3, where GPCR binds and thus activation of signals were transduced. Molecular dynamics and docking studies were also used to search the various active sites, get their dynamics information and further recognizes the significant amino acids that plays important role in ligand binding mechanisms. Docking analysis with various anti-cancer drugs has been carried out, and finds that best ten anti-cancer drugs which shows that the better interaction with GPR87 are shown in Figure1. Finally, the docking study of methotrexate (MTX) an anticancer drug have highest dock score (153.663) and H-bonding i.e. 46 in 10 different conformation (poses) and involves amino acids are Lys247, Arg319 and their atom involves OG and HZ3 revealed ion-pair interactions with MTX atoms are O18 and O16 respectively. Our model can serve as a valuable reference for explored for drug targeting by design of suitable inhibitors for SCCs.

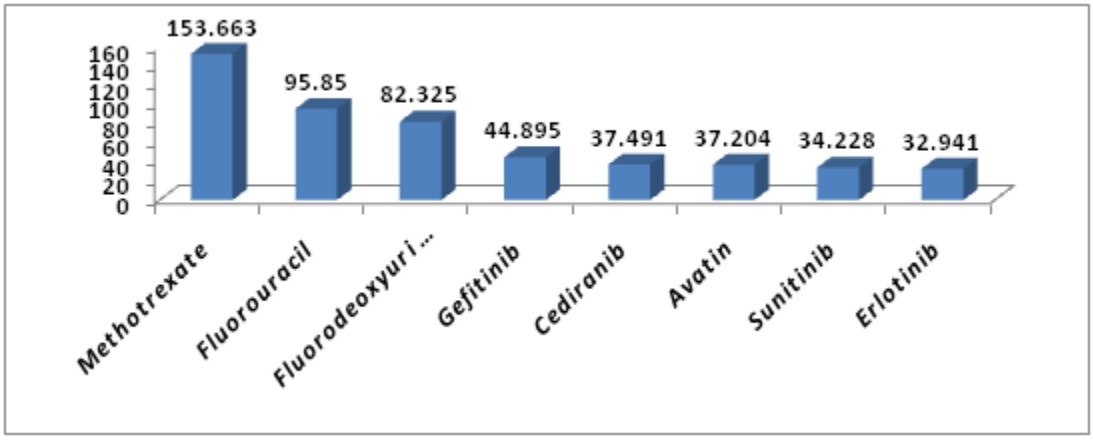

Figure 1: It shows the best ten anti-cancer drugs which have the better interaction with GPR87 protein.

Keywords: GPCR, GPR87, Docking, Methotrexate, anti-cancer drugs

P-56

Bile Acid Receptor Agonist GW4064 elicits multiple signaling cascades through modulation of G-Protein coupled receptors

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GW4064, a synthetic isoxazole was developed as an extremely potent specific FXR agonist [1] and has been widely used as pharmacological tool to decipher FXR physiological and cellular functions. Earlier we identified GW4064 as an agonist for estrogen receptor related receptor (ERR) demonstrated its ERR-mediated regulation of PPAR gamma coactivator 1 alpha [2]. However, during this study, we observed GW4064 also significantly activates number of empty luciferase reporters in FXR-deficient cells. We postulated that this activity of GW4064 might be routed through as yet unknown cellular target and took an unbiased approach to dissect the mechanism responsible for its FXR independent actions. Sequence analysis showed that GW4064 activate cAMP and nuclear factor for activated T cell -response elements present on these empty reporters leading to increase intracellular calcium level as well as soluble adenylyl cyclase dependent cAMP accumulation. Using dominant negative heterotrimeric G-protein minigenes, batteries of inhibitors and Radioligand binding study we showed that GW4064 interacted with multiple G-proteins coupled receptors and caused activation of Gi/o and Gq11 G-proteins. We also found that MCF-7 breast cancer cells, reported to undergo GW4064 induced apoptosis in an FXR-dependent manner [3], did not express FXR, and the GW4064-mediated apoptosis, also apparent in HEK cells, and could be blocked by selective histamine receptor-regulators. Together, we demonstrate identification of histamine receptors as alternate targets for GW4064, which not only necessitates cautious interpretation of the biological functions attributed to FXR using GW4064, but also provides important medical chemistry insight for designing of novel drugs related to histamine.

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P-57

Effective Binding Site Prediction, Multitemplate Homology Modelling of P4H Transmembrane Protein

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Prolyl 4 hydroxylase (P4H), a transmembrane protein of Homo sapiens, catalyzes the post-translational formation of 4-hydroxyproline in hypoxia-inducible factor (HIF) alpha proteins. P4H hydroxylates HIF1A at 'Pro-402' and 'Pro-564'. Koivunen P et al. [1]. This reaction, yields (2S,4R)-4-hydroxyproline (Hyp). The protein substrates for P4Hs are diverse. Likewise, the biological consequences of prolyl hydroxylation vary widely, and include altering protein conformation and protein-protein interactions, and enabling further modification. Kelly L et al. [2]. Prolyl 4-hydroxylases have central roles in the synthesis of collagens and the regulation of oxygen homeostasis. Myllyharju J. [3]. The Catalytic activity of P4H is -
HIF alpha chain L-proline + 2-oxoglutarate + O_2 = An HIF alpha chain trans-4-hydroxy-L-proline + succinate + CO_2.

Till date, there is no three dimensional structure of P4H protein, which is key part to study protein function and its family. Homology modelling is a computational method to model a protein structure on the basis of homologous protein structure. Claudio N et al.[4]

In this paper we have done homology modelling of P4H protein by schrodinger software using multiple template method. Schrödinger is a completely incorporated protein structure prediction program exclusively made for structure-based drug design. Sabita K et al.[5] The modelled structure was further validated by ramachandran plot, q mean analysis and anolea tool of expasy server. Further the modelled structure is used to identify the effective binding site using SITMAP program of schrodinger software. These binding sites can be used for molecular docking studies and hence provides an insight into structural and functional properties of an important trasnsmembrane protein.

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P-58

Prolyl 4-hydroxylases, key enzymes in the synthesis of collagens and regulation of the response to hypoxia, and their roles as treatment targets

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Prolyl 4-hydroxylase Prolyl 4-hydroxylases (P4Hs) have central roles in the synthesis of collagens and the regulation of oxygen homeostasis. May function as a cellular oxygen sensor and, under normoxic conditions, may target HIF through the hydroxylation for proteasomal degradation via the von Hippel-Lindau ubiquitination complex

An HIF alpha chain L-proline + 2-oxoglutarate + O_2 = An HIF alpha chain trans-4-hydroxy-L-proline + succinate + CO_2.

Posttranslational modifications can cause profound changes in protein function. Typically, these modifications are reversible, and thus provide a biochemical on-off switch. In contrast, proline residues are the substrates for an irreversible reaction that is the most common posttranslational modification in humans. This reaction, which is catalyzed by prolyl 4-hydroxylase (P4H), yields (2S,4R)-4-hydroxyproline (Hyp). The protein substrates for P4Hs are diverse. Likewise, the biological consequences of prolyl hydroxylation vary widely, and include altering protein conformation and protein-protein interactions, and enabling further modification. The best known role for Hyp is in stabilizing the collagen triple helix.

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P-59

Ultrasonic Studies on binary mixtures of Flavoured compounds and some hydrocarbons

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Ultrasound velocities (u) and densities (?) for the binary mixtures of flavoured compounds viz. butylethanoate and 3-methylbutyl ethanoate and several hydrocarbons viz. cyclohexane, benzene,1,4-dimethylbenzne and 1,3,5-trimethylbenzene have been measured at 308.15K. Adiabatic compressibilities (?ad), acoustic impedances (Z) and available volumes (Va) for all the mixtures have also been evaluated at entire concentration range. Ultrasound velocities increase as mole fractions of hydrocarbons increase in all the binary systems. Adiabatic compressibilities decrease with increase in volume fractions of hydrocarbons for the binary mixtures of ethanoates with aromatic hydrocarbons while it increase first, reaches a maximum values at around 0.6-0.7 mole fractions of cyclohexane and then decrease for the binary mixtures of ethanoates and cyclohexane. Deviations in ultrasound velocities (?u) and in adiabatic compressibilities (??ad) from the linear blending rule have been reported for all the studied binary mixtures. The results are discussed in terms of the unlike molecular interactions present in the binary systems.

Keywords: Ultrasonic velocities, flavoured compounds, binary liquid mixtures, adiabatic compressibilities.

P-60

CaCO3 microspheres/Ciprofloxacin HCl Loaded Macroporus Gelatin Scaffolds for Therapeutic Intervention of Osteomyelitis

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Osteomyelitis, a historic infection caused by a wide spectrum of bacteria, is an inflammatory bone disorder leading to necrosis and destruction of bone. It remains challenging and difficult to treat, despite of advances in antibiotics and new operative techniques due to long duration of therapy, frequent dosing, high doses, adverse effects associated therewith and non availability of localized drug delivery systems[1]. Here, an attempt has been made to fabricate a novel macroporus gelatin scaffold embedded with calcium carbonate microspheres

and ciprofloxacin HCl using glutaraldehyde as crosslinker via cryogelation technique for sustained and localized drug delivery[2]. This biodegradable and cytocompatible cryogel due to its unique porosity and mechanical strength forms a beneficial system as bone implants. Box- Behenken design was employed to optimize the formulation for desired properties. The prepared cryogels were characterized for pore volume, porosity, swelling index, swelling kinetics, breaking strength and in vitro degradation, FTIR and XRD. The surface morphology was observed using digital microscope and AFM. Fluorescent microscope was used to analyze the pore distribution on and inside the cryogels. The drug release study was carried out in PBS pH 7.4 buffer and showed sustained release of drug upto 15 days[3]. The in-vitro cytocompatibility assay performed on mice osteoblasts using MTT dye and hemolytic study on rat RBCs showed that the cryogels were not cytotoxic rather they provide a conducive environment for cells to grow and multiply. The in-vitro anti bacterial studies performed by serial transfer technique using two bacterial strains i.e. S. aureus (gram +ve) and E. coli (gram -ve) showed significant killing of both bacterial strains upto seven days. So it could be inferred that cost effective and industrially scalable cryogels possessing good mechanical properties, showing sustained release and significant killing may emerge as a promising delivery system for therapeutic intervention of osteomyelitis.

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P-61

Effective Binding Site Prediction, Multitemplate Homology Modelling of P4H Transmembrane Protein

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Prolyl 4 hydroxylase (P4H), a transmembrane protein of Homo sapiens, catalyzes the post-translational formation of 4-hydroxyproline in hypoxia-inducible factor (HIF) alpha proteins. P4H hydroxylates HIF1A at 'Pro-402' and 'Pro-564'. Koivunen P et al. [1]. This reaction, yields (2S,4R)-4-hydroxyproline (Hyp). The protein substrates for P4Hs are diverse. Likewise, the biological consequences of prolyl hydroxylation vary widely, and include altering protein conformation and protein-protein interactions, and enabling further modification. Kelly L et al. [2]. Prolyl 4-hydroxylases have central roles in the synthesis of collagens and the regulation of oxygen homeostasis. Myllyharju J. [3]. The Catalytic activity of P4H is -

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P-62

Morpholin/piperidin-1-yl-carbamodithioates as promising Vaginal Microbicides with Spermicidal efficacy

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To develop dually functional spermicides having contraceptive and microbicidal efficacy against STDs is amongst the major attentions of the 21st century. In our ongoing efforts [1] to develop dually active vaginal micrbicidal spermicides, seventeen carbamodithioate esters have been designed as a molecular prototype targeting sperm and Trichomonas through a single chemical entity for prophylactic contraception. The study identified eleven dually active compounds with spermicidal activity ranging from 0.36-57 mM and anti-Trichomonas activity 0.07-0.268 µg/mL with apparent safety against human cervical cell line (HeLa) and compatibility with the vaginal flora, Lactobacillus. The plausible mode of action was confirmed through reduction in available free thiols on human sperm.

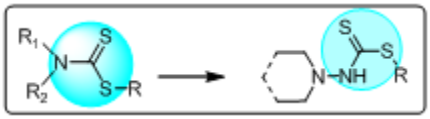

Figure 1: Designing of Novel Carbamodithioate Esters

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P-63

One-pot synthesis of steroidal thiophenes and assessment of their in vitro acetylcholinesterase inhibition activity

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The neurodegenerative disorder of the central nervous system is characterized by loss of cognitive ability and severe behavior abnormalities, resulting in the degradation of intellectual and mental activities. These symptoms are linked to a deficiency in the brain neurotransmitter acetylcholine and recognized as Alzheimer's disease (AD) [1-3]. According to the World Health Organisation (WHO), AD is one of the fastest growing health hazards because of its unknown etiology and irreversible progressive nature which ultimately results in the loss of thinking abilities [4,5]. Several efforts have been made in order to minimize the negative effects of the AD and carry out its preliminary diagnosis and therapeutic control. One of the emerging and reliable strategies is the enhancement of cholinergic neurotransmission which has been considered as one potential therapeutic approach against AD. One treatment approach is to enhance cholinergic function by the use of acetylcholinesterase (AChE) inhibitors to increase the amount of acetylcholine present in the synapses between cholinergic neurons [6]. AChE inhibitors like tacrine, one of the most extensively studied AChE inhibitors, have been shown to significantly improve cognitive function in AD. In this paper, the one pot three-component mixture of steroidal ketones, malononitrile/ethyl cyanoacetate and elemental sulfur were converted into the corresponding steroidal thiophenes in moderate to high yields with excellent selectivity. Moreover,all the synthesized compounds were screened for their acetylcholinesterase (AChE) inhibition activity.

Keywords: Steroids ,Thiophenes, In vitro, Acetylcholinesterase

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P-64

PTSA promoted solvent free Friedlander condensation Reaction: An efficient method for the synthesis of substituted 1,6-Dibenzonaphthyridines

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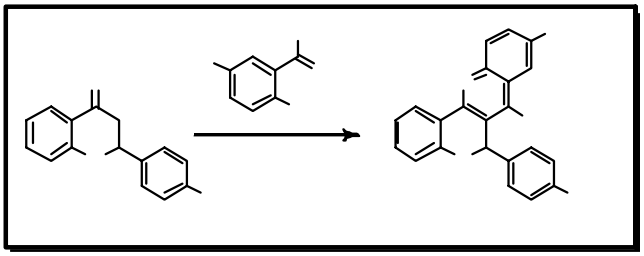
1,6- Dibenzonaphthyridines and their congeners have gained considerable attention due to their wide range of biological activities such as antibacterial, HIV integrase inhibitors, topoisomerase-I inhibitors, anti-proliferative, antitumor, anticonvulsive, p38 mitogen-activated protein kinase inhibitors, and spleen tyrosine kinase inhibitors. An efficient protocol has been developed for the synthesis of 1,6- Dibenzonaphthyridines from azaflavanones and 2-aminobenzophenones via PTSA promoted solvent free Friedlander condensation Reaction. This methodology was successful to access a wide range of 1,6-Dibenzonaphthyridines tetracyclic molecules with various substitutions.



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P-65

PAMAM Dendrimer - Mediated Solubilization, Synthesis and In Vitro Evaluation of Amphotericin B

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Amphotericin B is a polyene antifungal agent which is not freely soluble in water. The clinical use of amphotericin B is limited by nephrotoxicity and poor water solubility, which leads in some cases to permanent renal impairment, especially in the presence of other nephrotoxic drugs. PAMAM dendrimer provides a uniform platform for drug

attachment that has the ability to bind and release drugs through several mechanisms [1]. In the present study we investigated the potential of polyamidoamine (PAMAM) dendrimers to increase the solubility of amphotericin B. The experimental results suggested that the solubility of amphotericin B was greatly enhanced in the presence of PAMAM dendrimer solutions [2]. Results showed that the solubility of amphotericin B increased with increase in dendrimer concentration as well as generations. In vitro release behavior of amphotericin B in presence of G3 PAMAM dendrimers was performed by dialysis method [3,4]. Our work demonstrated that encapsulation of amphotericin B into dendrimers led to sustained release of the drug in vitro. The surface morphology of drug dendrimer conjugates were characterized by Transmission Electron Microscopy (TEM) studies.

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P-66

Identification and Characterization of DNA Quadruplex Element in the Human GRIN1 Promoter Region

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It is well known that G-rich sequences can fold into four-stranded secondary structures called quadruplexes. These structures are potentially useful therapeutic targets. N-methyl-D-aspartate (NMDA) receptor has been associated with many diseases that include Neurodegenerative disorders, Alzheimer's disease, Huntington's disease, but mainly the involved in Schizophrenia syndrome [1,2,3]. In the present study, we have focussed on the GRIN1 gene, which encodes NR1 subunit of NMDA receptor. Numerous single nucleotide polymorphisms (SNPs) have been identified in different regions of GRIN1 gene among schizophrenic patients of different parts of the world. While analyzing the promoter region of GRIN1, it was found out that G1001C polymorphism is associated with schizophrenia in the Italian population [4]. So, we have selected a 27-mer sequence of GRIN1 gene whose SNP has been associated with schizophrenia. With the help of different techniques such as Gel Electrophoresis, Circular Dichroism spectroscopy and Thermal-melting studies, we have indicated that this 27-nt sequence may possibly have Watson-Crick hydrogen bonding in addition to typical Hoogsteen hydrogen bonding of G-quadruplex. A truncated sequence GRIN15 from which bases that are involved in Watson-crick H-bonding are excluded is studied to further ensure the presence of tetramolecular G-quadruplex. Another sequence GRIN15M (a mutated version of GRIN15) has been employed to prove the non-existence of homo-duplex

structure formation by GRIN15 sequence. Experimental results conclude that the sequence under study forms tetramolecular G-quadruplex structure coexisted with Watson-Crick H-bonding underphysiological salt and pH conditions.

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P-67

Synthesis and Biological Evaluation of Indole based Triazoles

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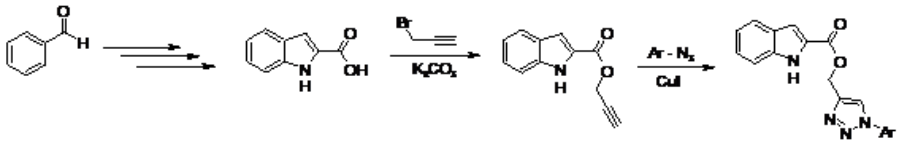
The Hemetsberger-Knittel reaction involves the base-mediated aldol reaction of aryl aldehyde with ethyl azidoacetate and subsequent thermal cyclization of 2-azidocinnamate, affording the corresponding indole-2-ester [1]. Hydrolysis of ester affords corresponding acid, followed by propargylation then click reaction.
In the recent advance of Cu(I) catalyzed condition affords superior Regioselectivity, high tolerance of other functionalities, and almost quantitative transformation under mild conditions [2].
1,2,3-Triazoles have gained increasing attention in medicinal chemistry since from the introduction of the so called Cu(I) catalyzed 1,3-dipolar alkyl azides coupling reaction[3], [4].



Key words: Click reaction, Regeoselectivity, K_2CO_3, N-Heterocylic compounds, 1,2,3-Triazoles, Biological activity.

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P-68

Solid Phase Extraction and Ultra Performance Liquid Chromatography-Tandem Mass Spectrometric Identification of Carcinogenic/Mutagenic Heterocyclic Amines in Cooked Camel Meat*

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The relationship between food content and human diseases like cancer is a major concern for human health [1]. Heterocyclic amines (HAs) are potent mutagens present at ppb levels in protein-rich cooked foods such as meat and fish [2], and play an important role in the etiology of human cancer [3]. In the present study, three kinds of camel (Mjahim, Mgatir and Humor) from Saudi Arabia have been studied for HAs contents in their cooked meat. The camel meats were cooked using common cooking practices such as frying, griddling, stewing and barbequing under controlled temperature. The investigated HAs were IQ, MeIQ, MeIQx, 4,8-DiMeIQx and PhIP. An analytical method based solid-phase extraction and ultra performance liquid chromatography-tandem mass spectrometry (SPE/UPLC-MS/MS) was used for the analysis of HAs in cooked samples. The level of IQ and MeIQ were found either below limit of quantification or not detected in all of the analyzed samples. The fried samples produced MeIQx, 4,8-DiMeIQx and PhIP, between 2.13 ng g-1 and 5.89 ng g-1, whereas, griddled and barbequed samples generated levels of MeIQx, 4,8-DiMeIQx and PhIP, ranging from 0.93 to 4.34 ng g-1. The stewing method applied to meat samples generated only PhIP at concentrations between 0.4 ng g-1 and 0.65 ng g-1, while MeIQx and 4,8-DiMeIQx were found below limit of quantification. The low levels of HAs in stewing method might be explained that the samples were not directly in contact with cooking pot or blaze which influences the formation of HAs. These outcomes suggest that camel meat is a significant dietary source of HAs and can be used in epidemiological studies to approximate HA exposure from dietary questionnaires.

Keywords: Heterocyclic amines; camel meat; cooking methods; SPE/UPLC-MS/MS

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P-69

Synthesis of nucleoside analogs and their biological activities

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Nucleosides are the essential building blocks of all living plants and animals. It is basically glycosylamines consisting of two types of nitrogenous base bounded together with either ribose or deoxyribose sugar via a ?-glycosidic linkage. When these nucleosides and heterocyclic ring with triazole molecules form a hybridized molecules there is alteration of the biological activity of such molecules towards antiviral and anticancerous agents. Nucleoside perform an important function of regulating enzymes, cell activities and controlling physiological blood pressure [1]. Capecitabine [2] Cladribine [3] Clofarabine [4] are some of the selected nucleoside possess anti-cancerous activities. Glycosyl and aglycosyl triazoles are important medicinal compounds. The azido sugars are the versatile starting materials in accessing numerous biologically active compounds which include amino sugars, nucleoside and many more glycosylated heterocycles. Carbohydrate based triazoles are endowed with many biological activities. Nucleoside analogs formed from such starting compounds are the prominent drugs use for the treatment of viral infections. Keeping in mind the above importance of such molecules sugar triazoles are synthesized and these sugars undergo acetylation to protect the hydroxyl groups and their coupling with silylated nitrogenous bases to form nucleoside analogs.

Scheme 1

Scheme 1

Keywords: Glycosyl donor, Glycosyl acceptor etc.

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P-70

Organocatalytic Asymmetric Mannich Cyclization of Hydroxylactams with Acetals: Total Syntheses of (-)-Epilupinine, (-)-Tashiromine, and (-)-Trachelanthamidine

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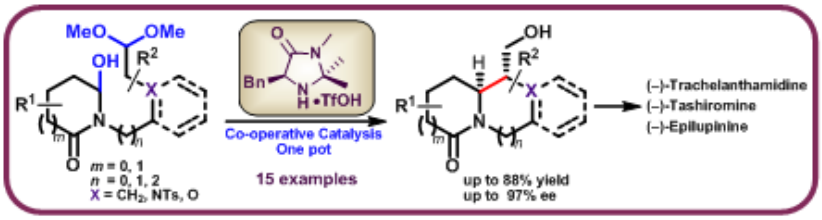
Naturally occurring izidine alkaloids (pyrrolizidine, indolizidine,and quinolizidine) and their synthetic variants are of considerable importance because of their diverse biological activities [1]. The syntheses of izidine alkaloids have been described using chiral-pool [2], chiral auxiliary [3] and catalytic approaches. But these approaches are defined and specific to syntheses of izidine alkaloids. Prompted by the biosynthetic pathway of pyrrolizidine alkaloids [4], here we report an asymmetric, organocatalytic, one-pot Mannich cyclisation between a hydroxylactam and Acetal with a Macmillan catalyst to offer fuse, bicyclic alkaloids bearing a bridgehead N atom. Both aliphatic and aromatic substrates were used in this transformation to furnish chiral pyrrolizidinone, indolizidinone, and quinolizidinone derivatives in up to 89% yield and 97% ee. The total syntheses of (-)-epilupinine, (-)-tashiromine, and (-)-trachelanthamidine also achieved to demonstrate the generality of the process.



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P-71

Effects of Food Additives on the Formation of Heterocyclic Amines in Cooked Meat and Determination by Liquid Chromatography-Tandem Mass Spectrometry

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Heterocyclic amines (HCAs) are known to be potent mutagenic and carcinogenic substances, formed in muscle meats during their cooking under normal conditions [1, 2]. In the present study, the effects of various food additives on the formation of HCAs in cookedmeat were investigated. The meat samples was subjected to pan-frying under controlled temperature, the amount of HCAs 2-amino-1,6-dimethylimidazo[4,5-b]pyridine (DMIP), 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx), 2-amino-3,4,8-trimethylimidazo[4,5-f]quinoxaline (4,8-DiMeIQx), 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), 1-amino-9H-pyrido[3,4-b]indole (Harman) and 9H-pyrido[3,4-b]indole (Norharman) were found between 1.20 ng/g and 5.31 ng/g, whereas, HCAs 2-amino-3-methylimidazo[4,5-f]quinoline (IQ), 2-amino-3,4-dimethylimidazo[4,5-f]quinoline (MeIQ), 2-amino-9H-pyrido[2,3-b]indole (A?C), 2-amino-3-methyl-9H-pyrido[2,3-b]indole (MeA?C), 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1), and 3-amino-1-methyl-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-2) were found either below limit of quantification or not detected in control sample. Nevertheless, in the samples cooked using food additives, the amount of HCAs (DMIP,MeIQx, 4,8-DiMeIQx, and PhIP) were obtained between 0.18 ng/g and2.85 ng/g, the harman and norharman were detected at higher concentration up to 8.21 ng/g while IQ, MeIQ found below limit of quantification and A?C, MeA?C, Trp-P-1, and Trp-P-2 were not detected in any analyzed samples. The obtained results demonstrated that the formation of HCAs (except harman and norharman) was decreased after the addition of food additives.

Keywords: Heterocyclic amines; Cooked meat; Food additives;Liquid Chromatography-Tandem Mass Spectrometry

Acknowledgments: This work was supported by NSTIP strategic technologies program number (12-AGR2594-02) in the Kingdom of Saudi Arabia.

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P-72

QSAR studies onaryl-N-(3-(alkylamino)-5-(trifluoromethyl) phenyl) benzamidesanalogues as potential TRPA1 antagonists

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Two dimensional quantitative structure-activity relationship studies using the multiple regressions analysis method was performed on a series of aryl-N-(3-(alkylamino)-5-(trifluoromethyl) phenyl) benzamides analogues as TRPA1 antagonists. The biological data set was chosen from a series of twenty three aryl-N-(3-(alkylamino)-5-(trifluoromethyl) phenyl) benzamidesanalogues reported by Laliberté et. al., [1]. The biological activity values [IC50 (?M)] reported in micromolar units were converted to their molar units pIC50 and subsequently used as

the dependent variable for the QSAR analysis.Where pIC50 is the -log of IC50 activity values and was taken as the dependent variable in the QSAR model development. The 2D structures of the chemical compounds and the template were drawn using Vlife Engine platform of VLifeMDS [2].They were converted to 3D by Vlife Engine platform of VLifeMDS and later energy minimized using the force field batch minimization utility with default parameters.The QSAR model was selected, having correlation coefficient r2 = 0.8955 and external predictive ability of pred_r2 = 0.8027 was developed. The study attempts to correlate the structural features of benzamides group with their biological activity based on a specified descriptors 2D-QSAR model. As a statistically robust model, it almost accurately predicts the biological activities of novel, congeneric benzamides derivatives. This study progresses the use of benzamides moiety as TRPA1 antagonists.

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P-73

General Neuropsychopharmacological Screening of Standardized Extract of Rosmarinus officinalis: an Experimental Study in Rodent

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Objective: Rosmarinus officinalis is an aromatic shrub, which has several therapeutic applications in folk medicine [1]. Considering the therapeutic application of Rosmarinus officinalis extract (RO) in management of neurological and psychiatric disorders [2, 3], the present study was designed to investigate its neuropsychopharmacological activities and provide scientific base through elucidation of its mechanism of action.

Materials and methods: Various neuropharmacological screening models i.e. potentiation of pentobarbital-induced sleep test [4], locomotor activity, Rota-rod test, pentylenetetrazol (PTZ) [5] induced convulsion in mice and maximal electroshock (MES) induced seizures in rats were used to evaluate neuro psychopharmacological activities of RO at doses of 30, 100 and 300 mg/kg, p.o., once daily for seven consecutive days.

Results: RO (30, 100 and 300 mg/kg) did not potentiate the duration of sleep in pentobarbital-induced sleep test. However, RO (100 and 300 mg/kg) significantly ($p<0.05$) reduced the locomotor activity and motor coordination. RO (30, 100 and 300 mg/kg) did not protect the rats from hind limb tonic extensor induced by MES but its 300 mg/kg showed a significant ($p<0.05$) decrease in duration of seizure in rats. Further, RO (300 mg/kg) significantly ($p<0.05$) delayed the occurrence of seizures but failed to protect the mice from generalized tonic clonic convulsions induced by PTZ.

Discussion: The observed finding suggests that RO did not showed protection against chemical and electric shock induced convulsions and it has no sedative effect. However, it could be use in ataxia because it alters the motor performance and locomotor activity as well.

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P-74

Synthesis of the pentasaccharide repeating unit of the O-antigen of Escherichia coli O175 using one-pot glycosylations and its conformational analysis

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Enteropathogenic Escherichia coli, Shigella, and Salmonella strains are commonly associated pathogens with the diarrheal infections. E. coli are member of facultative Gram-negative enterobacteriaceae and commonly found as commensal agents in the human colonic flora. However, very often they acquire virulent factors and behave as pathogenic organisms. Commonly found E. coli infections are (a) diarrheal or enteric disease, (b) sepsis and meningitis, and (c) urinary tract infections. E. coli O175 strain is responsible for acute diarrheal illness in the developing and industrialized countries. Recently, the structure of the cell wall polysaccharide O-antigen of E. coli O175 has been established by Svensson et al [1]. Bacterial cell wall O-antigens play important role in the host-pathogen interaction in the initial stage of infection. Several attempts were made in the past to develop glycoconjugate based antibacterial vaccine candidates for their use to control bacterial infections. Till now many vaccine have been prepared from the polysaccharides, isolated from the cell wall of bacteria. Isolation of the oligosaccharides from the bacterial cell wall in significant quantity with adequate purity is practically inconvenient. Hence, chemical synthesis is the best option to get large quantity of the particular oligosaccharide and its smaller fragments. We report herein a one-pot synthesis of a pentasaccharide as their 2-(p-methoxyphenoxy) ethyl glycoside corresponding to the O-antigen of Escherichia coli O175 (Figure 1) [2]. The synthesized pentasaccharide was also subjected to conformational analysis in aqueous environment using molecular dynamics (MD) simulation technique.

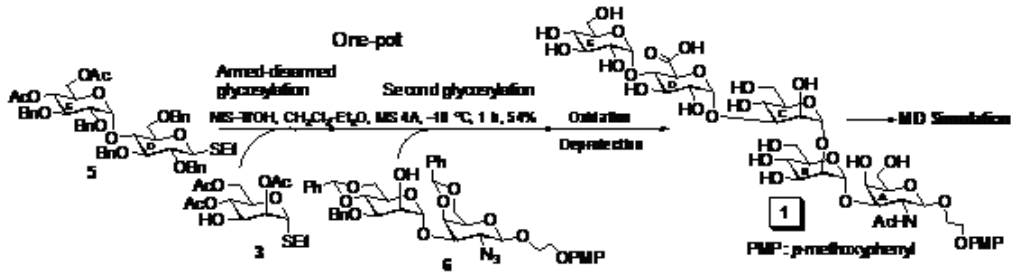

Figure 1: Synthesis of the pentasaccharide repeating unit of the O-antigen of E. coli O175.

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P-75

Identification and Characterization of Flavon-3-ols, Phenolic Acids and Triterpines in Terminalia arjuna using LC-QTOF-HRMS Technique

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Terminalia arjuna is known for its heart-health benefits in ayurvedic literature. It is important to characterise chemical constituents in different part of T. arjuna such as bark, fruit, leaf, root and stem. High performance liquid chromatography coupled with quadrupole time of flight mass spectrometry analysis of T. arjuna, confirmed that it contains flavon-3-ols (such as (+)-catechin, (+)-gallocatechin and (?)-epigallocatechin), phenolic acids (such as gallic acid, ellagic acid) and triterpines (such as arjungenin, arjunglucoside I, II etc) [1]. It was also observed that T. arjuna is rich source of polymer of flavanols i.e., proanthocyanidines (like procyanidin B1, procyanidin B1-3'-O-gallate etc). Proanthocyanidins have antioxidant activity and they play a role in the stabilization of collagen and maintenance of elastin. Given these results, it may be possible to attribute the heart-health effects of T. arjuna to these polyphenols which may be responsible for the endothelial benefit functions like tea [2].

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P-76

Efficient stereocontrolled synthesis of sitagliptin phosphate

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Sitagliptin phosphate 1 (Fig. 1) is an orally active, safe, selective, and potent DPP-IV inhibitor for the treatment of type 2 diabetes mellitus and has been approved by USFDA in October 2006 [1]. The key methods employed to install the correct stereochemistry of 1, using chiral auxiliary [1], transition metal mediated asymmetric hydrodenations [2], and biocatalytic approaches. The notable disadvantages of these methods are limited atom economy, and inherent drawbacks of metal mediated hydrogenation reactions such as specialized high pressure equipments, the use of precious metals, and possible metal contamination of the API. Here we report an asymmetric synthesis of sitagliptin phosphate 1, has been accomplished starting from the chiral synthon (1,4-bis[(R)-1-phenylethyl]piperazine-2,5-dione) 2 (Fig. 1), involving highly stereocontrolled (>98%) alkylation as a key step, in a good overall yield of 50% over six steps. This approach also reliable for multi-gram scale synthesis of target compound 1. In addition, this method uses inexpensive starting materials which could substantially cut the cost of the commercial synthesis of sitagliptin phosphate 1 (Fig. 1).

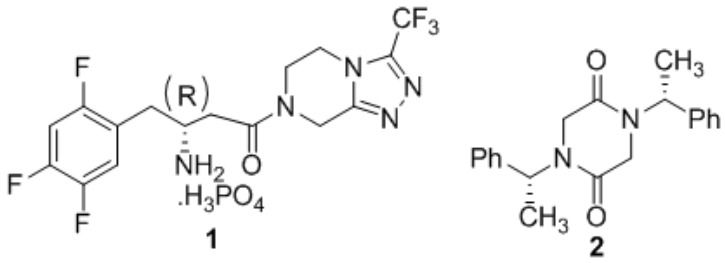

Figure 1. Sitagliptin phosphate **1**, and chiral synthon **2**

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P-77

Green Synthesis of Silver Nanoparticles and Study their Corrosion Inhibition Efficiency for Mild Steel

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The field of nanotechnology is one of the most active areas of research in modern materials science. Nanotechnology is concerned with the development of experimental processes for the synthesis of nanoparticles of different sizes, shapes and controlled disparity [1]. Nanoparticles exhibit completely new or improved properties based on specific characteristics such as size distribution and morphology. A number of approaches are available for the synthesis of nanoparticles for example, reduction in solution, chemical and photochemical reactions in reverse micelles, thermal decomposition of metal compound, radiation assisted, electrochemical, microwave assisted process and recently via green chemistry route [2]. The use of environmentally benign materials like plant leaf extract, bacteria and fungi for the synthesis of nanoparticles offers copious benefits of eco-friendliness and compatibility for pharmaceutical and biomedical applications as they do not use toxic chemicals in the synthesis protocols. The synthesis of nanoparticles from green chemistry has become the matter of great interest due to its various advantageous properties and applications in various fields. Though physical and chemical methods are more popular for nanoparticles synthesis, the green production is a better option due to eco-friendliness. In the present communication, we present the syntheses, characterization, and corrosion inhibition potentials of silver nanoparticles obtained from the reaction between silver nitrate and the fruit extract of Cordia Dichotoma. Corrosion control of metals is of technical, economical, environmental, and aesthetical importance. The use of inhibitors is one of the best options of protecting metals and alloys against corrosion. The environmental toxicity of organic corrosion inhibitors has prompted the search for green corrosion inhibitors as they are biodegradable, do not contain heavy metals or other toxic compounds [3]. In present research we aimed to focus on green synthesis of nanoparticles from plant extract and study their corrosion inhibition efficiency. The inhibition efficacy of extracts of Cordia dichotoma is temperature-dependent and its addition led to an increase of the activation corrosion energy. Higher values of activation energy Ea0 in presence of inhibitor supports that the inhibitor creates energy barrier for corrosion reaction.

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P-78

Development of a broad spectrum antimicrobial peptide from LCI, an anti-Xanthomonas peptide from Bacillus subtilis

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Antimicrobial peptides are naturally occurring defense molecules present in almost all living organisms as an essential component of their innate immune system. Today, due to the escalation of multidrug resistant organisms, existing antibiotics are losing their potency. Therefore, Antimicrobials are once again being looked at as the alternative candidates for classical antibiotics. Mishra et al. [1].

LCI is a 47 residue peptide isolated from a Bacillus subtilis strain A014 that exhibit high antimicrobial activity against the plant pathogen Xanthomonas campestris. Gong et al.[2]. As peptide synthesis involves some cost, it is always economical to design shorter peptides as potential antimicrobials. We designed a shorter C-terminal fragment of the LCI peptide, synthesized it using Fmoc chemistry, and characterized by HPLC and ESI-MS. Antimicrobial activity as well as salt sensitivity assay was performed against both Gram-positive and Gram-negative bacterial strains.

Peptide was found to be active against both Gram-positive and Gram-negative bacteria. In case of Staphylococcus.aureus and Pseudomonas.aeruginosa, the MIC of the peptide was 50 ?M and against Streptococcus.entericus it was observed to be 20 ?M. The peptide retained more than 90% activity against S.aureus in the presence of physiological concentrations of NaCl, MgCl? and CaCl?. Against S.entericus and P.aeruginosa, however, the peptide retained the activity in the presence of physiological NaCl concentration but the activity was compromised in the presence of divalent cations, Mg2+ and Ca2+. We aim to further optimize the activity of the peptide against broad range of microorganisms.

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P-79

An Exploration of in vitro DNA Binding Propensity & Cytotoxicity of Aromatic Organoselenium Derivatives

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A target synthesis of a library of symmetric aromatic diselenides was attempted to explore in vitro cytotoxicity, DNA binding ability and apoptotic potential aimed to generate anticancer lead compounds. Organoselenium compounds function as chemo preventives, as well as antitumor therapeutics, with the induction of apoptosis and inhibition of cell proliferation as the broader mechanisms in the cancer chemoprevention [1,2]. The synthetic methodology utilized is as shown in scheme 1 [3]

Thirteen synthesized molecules (1-13) were screened against a panel of human cancer cell lines (Leukemia HL-60 Epithelial OVCAR-5, Renal 786-O, Colorectal HT-29, Prostate PC-3). The compounds displayed a range of cytotoxicity towards these cancer cell lines. However the most impressive cytotoxicity was observed towards leukemia-HL-60 and prostate-PC-3 (with IC50 value of 8 and 13 µM respectively) for the lead compound.

Several apoptotic protocols like DNA cell cycle analysis, phase contrast and nuclear microscopy confirm good apoptotic potential of lead compound. DNA cell cycle analysis depict that the lead compound significantly inhibits S phase of the cell cycle and eventually trigger apoptosis in HL-60 cells through mitochondrial dependent pathway authenticated by the loss of mitochondrial potential. The DNA binding studies of lead compound depict it to be a minor groove binder where it is stabilized by hydrogen bonding and hydrophobic interactions.

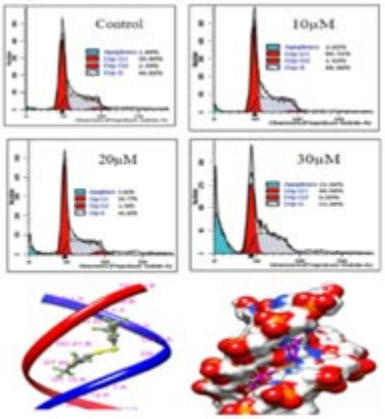

Fig.1: DNA cell cycle analyses of HL-60 cells in presence Mitochondrial of lead compound. Docked view of lead compound in with DNA dodecamer (1BNA.pdb)

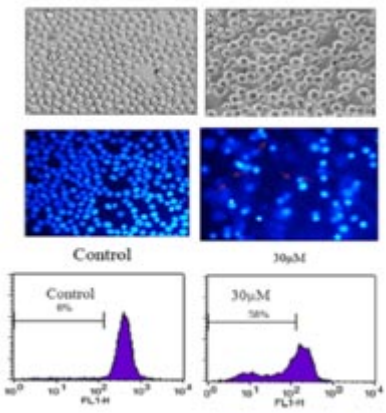

Fig.2: Cellular, Nuclear morphology & membrane potential analyses of HL-60 cells presence of lead compound

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P-80

Investigating structural features of huntingtin fibrils

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Huntington's disease (HD) is a neurodegenerative disease caused by misfolding and aggregation of mutated huntingtin protein. It is caused due to expansion of the PolyQ region (coded by tri-nucleotide CAG) in the Exon-1 region of huntingtin protein. The protein having >35 glutamines in the polyQ region aggregates and gets deposited as amyloid-like fibers. M A Poirier et al. [1].. The fibrils are very similar in morphology to those formed by other disease-associated proteins and peptide. Unlike all other disease associated peptides, however, the protein does not take a parallel in-register structure. C Bugget al. [2].It is therefore important to understand aggregate structure which can give insights into the aggregation mechanism of huntingtin and thereby therapy.

Till now, overall aggregation mechanism and structure of huntingtin aggregates are not properly understood. Several studies have been directed in this effort but most of them were conducted on small fragment of the protein. This study aims to understand the structural features through Fluorescence Resonance Energy Transfer (FRET) by incorporating the fluorescence donor and acceptor molecules at structurally relevant sites in huntingtin exon 1 domain.

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P-81

Characterization of diterpeniods and flavonoids in herbal medicinal Andrographis paniculata by LC/MS/MS

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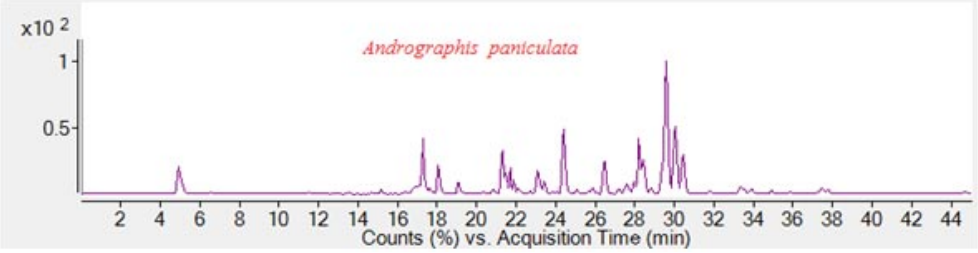
Andrographis paniculata(Burm. f.) Nees (Acanthaceae), commonly known as king of better a well-known herbal medicine, is found throughout southeast Asia, People's Republic of China and India (Committee of the National Pharmacopoeia 2005). It possess, antipyretic, anthelmintic, antifertility, antidiabetic, hypotensive, antihyperglycemic, antioxidant, antiviral, antifungal, anti-plasmodial, antioedema, analgesic anti-cancer, anti-HIV, hepatoprotective etc [1, 2, 3, 4]. The crude extract from whole plant has shown anti HIV activities [4].

The aim of this study is to develop a rapid liquid chromatography/tandem mass spectrometry (LC/MS/MS) method, using an ESI-QqTOF-MS/MS that provides accurate MS and MS/MS data to screen and identify known and unknown compounds from the crude extract of A. paniculata.



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P-82

A Chiron approach to the stereo selective synthesis of 2-epi-Jaspine B and its biological evaluation

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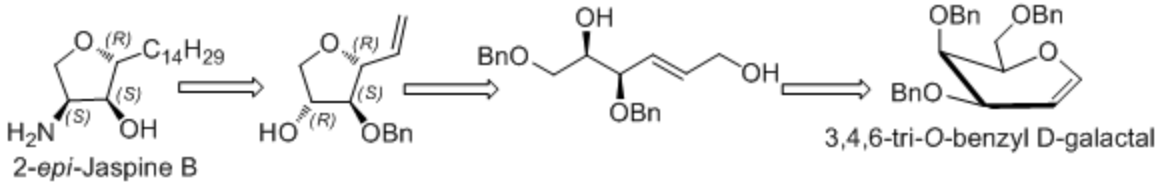
Higa and co-workers isolated an anhydrophytosphingosine derivative which they named pachastrissamine in 20021. A year later, Debitus et al reported the isolation of two anhydrophytosphingosines jaspines A and B from the marine sponge Jaspis sp.2 Jaspine B is the most potent compound against the A549 human lung carcinoma cell line till date. Owing to its wide range of biological activities, there has been a great deal of interest from synthetic chemists concerning the total synthesis of jaspine B, its C(2)-epimer (2-epi-jaspine B) and their analogues since its isolation. Herein we wish to present the total synthesis of 2-epi-Jaspine B. The iodocyclization of highly substituted enantiomerically pure allylic alcohol derived from the glycal was the key step to complete the synthesis of title molecule.



Scheme. Retro synthetic pathway of 2-epi-Jaspine B.

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P-83

Efficient Synthesis of the Pentasaccharide Repeating Unit of the Polysaccharide O-Antigen of Escherichia coli O166 Strain

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Diarrheal outbreaks and gastrointestinal complications are important health problems in developing countries as well as developed countries due to the intake of contaminated food and water and a lack of adequate sanitation. Among the several enteropathogenic microbes that are responsible for the diarrheal infections, pathogenic strains of E.coli merit particular attention. They can be classified as several pathotypes, such as enteropathogenic, enterohemorrhagic, enterotoxigenic, enteroinvasive, enteroaggregative. The E. coli O166 strain generally belongs to the enteroaggregative pathotype and causes diarrhoea in human by producing a heat stable enterotoxin. Cell-wall polysaccharides of virulant strains of bacteria play a vital role in the initial stages of bacterial infections in hosts. As a result researchers have focused attention on the characterisation of cell-wall polysaccharides from several bacterial strain. Recently Ali et al.[1] reported a structure of the pentasaccharide repeating unit (containing D-glucose, D-galactose and N-Acetyl-D-galactosamine moities) of the O-antigen of E. coli O166 strain.The specific polysaccharide O-antigens present in the cell wall of a particular bacterial strain provide the option of creating glycoconjugate vaccines. The polysaccharide fragments isolated from bacterial cell wall cannot provide the required quantity for their extensive biological evaluation. So, the development of a chemical synthetic strategy is useful for the preparation of the significant quantities of pure oligosaccharides with appropriate structures. In this context, we report herein a convenient synthesis of the pentasaccharide as its p-methoxyphenyl glycoside corresponding to the O-antigen of E. coli O166 strain (Figure 1) [2].

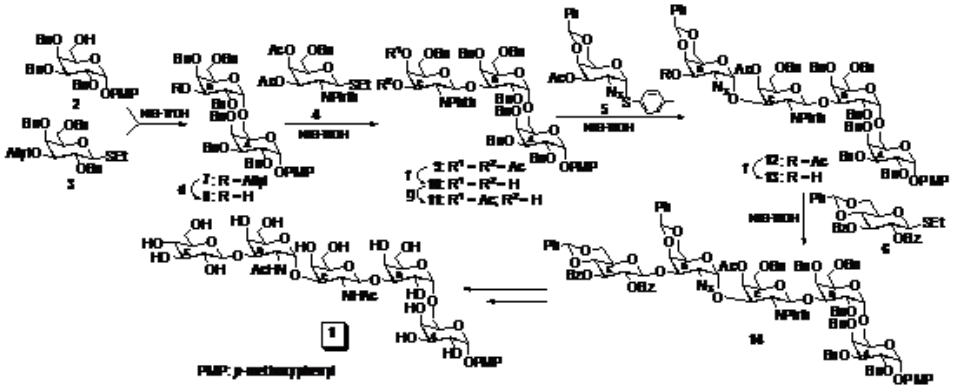

Figure 1: Synthesis of the pentasaccharide repeating unit of the O-antigen of E. coli O166.

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P-84

Efficient synthesis of the tetrasaccharide repeating unit of the O-antigen of Escherichia coli O174 strain

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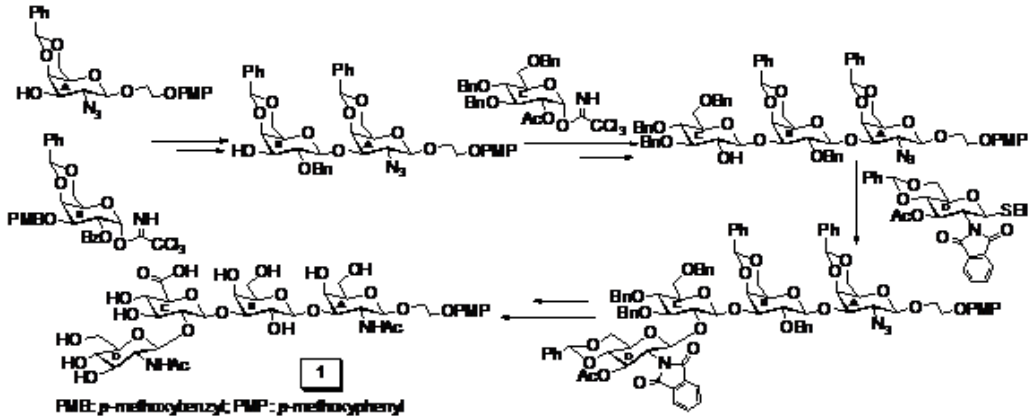
The major causes for the diarrheal infections recorded are due to the infections of pathogenic Escherichia coli, Shigella and Salmonella strains. E. coli strains associated with gastrointestinal infections, are classified into several pathotypes, among which verotoxin producing E. coli (VTEC) cause diarrhoea as well as life threatening hemorrhagic colitis and haemolytic uraemic syndrome. E. coli O174 strain belongs to the VTEC sub group. Since, the cell wall O-antigen is associated with the virulence factor of the pathogenic bacteria, the structure of the tetrasaccharide repeating unit of the O-antigenic polysaccharide of E. coli O174 has been established by Fontana et al. [1] Because of the important roles of the cell wall O-antigens in the initial stage of bacterial infections, it is quite pertinent to develop therapeutics based on the glycoconjugate derivatives related to them. However, it is quite difficult to isolate the sufficient quantity of the oligosaccharides from the natural sources (bacterial cell wall) with appropriate purity for their comprehensive biological studies. Therefore, development of efficient synthetic strategies for the chemical synthesis of the oligosaccharides is highly essential for getting access to the significant quantity of materials. Hence an efficient synthesis of the tetrasaccharide repeating unit of the O-antigenic polysaccharide of E.coli O174 is reported herein.[2]



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P-85

Molecular iodine promoted divergent synthesis of benzimidazoles, benzothiazoles and 2-benzyl-3-phenyl-3, 4- dihydro-2H-benzo[e] [1, 2, 4] thiadiazines

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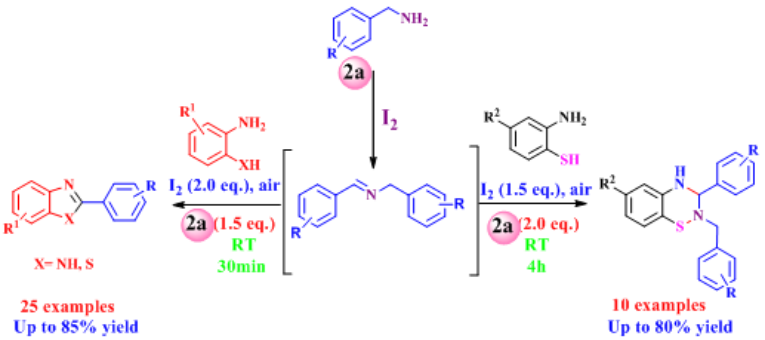
Benzimidazoles and benzothiazole are ubiquitous structural motifs found in many therapeutically useful compounds.For example, protonix, prilosec, nexium are representative drugs with benzimidazole skeleton and

5F203, PMX610 with benzothiazole skeleton [1]. Due to the biological importance of these motifs and inconvenient approach of existed methods the development ofefficient synthetic routs for construction of benzimidazoles and benzothiazoles are eternally fascinating.In this context we have developed a simple and novel protocol for the iodine mediated synthesis of benzimidazole and benzothiazole from readily available 2-amino/2-mercapto substituted anilines and various benzylamines. During this process an unprecedented formation of new class of 2-benzyl-3-phenyl-3, 4-dihydro-2H-benzo[e][1,2,4]thiadiazines has been discovered. This method involves metal-free C-N and S-N bond formation at ambient temperature to produce the products in good to excellent yields [2].1, 2, 4- benzothiadiazine derivatives are very interesting class of hetero cyclic motifs, which possess exciting biological activities. Various benzothiadiazine derivatives such as chlorothiazide (diuretic), cyclothiazide (diuretic and antihypertensive), and bendroflumethiazide are used as pharmaceutical therapeutics [3].



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P-86

A Facile Synthesis of 2-methyl-4-Hydroxyproline Diastereomers

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2-methyl-4-hydroxyprolines are structurally interesting variant of cyclic quaternary amino acids but remain unutilized for peptide engineering research due to limited availability of synthetic methodology [1]. The preparation of 2-methyl-4-hydroxyprolines diastereoselective synthesis is generally carried out starting from 4-hydroxyproline as a starting material [2]. In order to develop alternative route without using 4-hydroxyproline as a starting material, memory of chirality approach (MOC) has been utilized [3]. But there is still a large demand for its synthesis through novel approaches. Here we described a short and facile route for the synthesis of all diastereomers of the 2-methyl-4-hydroxyproline starting from alanine. Dihydroxylation of key intermediate (2S,4R)-Benzyl-4-allyl-4-methyl-5-oxo-2-phenyloxazolidine-3-carboxylate 8 (Fig.1) affords the lactone 9 via in situ lactonization.

Mesylation, hydrogenation followed by intramolecular cyclization during hydrolysis of 9 leads to 2-methyl-4-hydroxyprolines as a mixture of diastereomers. Appropriate protection followed by chromatographic separation results in isolation of diastereomers in optically pure form in overall 35-40% yield. Thus both the diastereomers of 2-methyl-4-hydroxyproline were prepared without use of any chiral auxiliary/induction. The other two diastereomers could be obtained by the same synthetic route by using D-alanine. Further, this will be useful for multi gram scale synthesis of all the 2-methyl-4-hydroxyproline diastereomers.

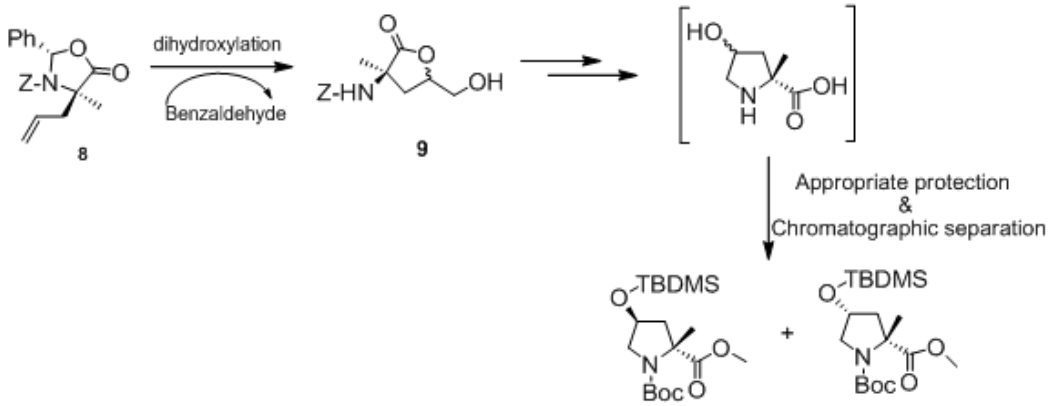

Fig.1. Synthesis of protected diastereomers of 2-methyl-4-hydroxyproline

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P-87

SAC regulates the TNF?-induced muscle wasting by suppressing the Ub-proteosome and apoptosis mechanisms in C2C12 myotubes

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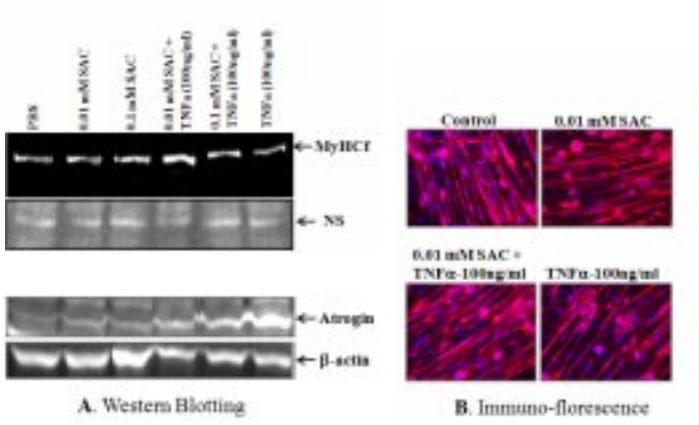
Muscle wasting/loss is a key issue in diverse number of diseases including AIDS, cancer, diabetes, etc [1]. Up to one-third of all cancer patients die due to direct consequences of cachexia and not from cancer itself, while in AIDS, 5% weight loss over a 4-month period is associated with an increased risk of death and opportunistic

infections. Beyond a reduced survival rate, wasting is also related to poor functional status and quality of life. The association of TNF? in impairment of differentiation and muscle loss has been reported very well in these diseases [2]. The present study aimed to investigate the role of S-allyl cysteine (SAC), an active compound with anti-inflammatory properties derived from Allium sativum [3], supplements on pro-inflammatory cytokine (TNF?) induced atrophy in C2C12 myotubes. Real-time PCR, western blot, Immuno-florescence staining and EMSA were used for this analysis. C2C12 cells were treated with TNF? in the presence or absence of SAC. Our data suggest that SAC has tremendous potential to revert the TNF? induced protein loss even at 10 ?M concentration. Data shows that myotube treatment with cytokine (100ng/ml) contributes to reduction in the mean myotube diameter and enhances the degradation of muscle specific proteins i.e. MyHC (fast-type) and creatine kinase while SAC supplementation counteracts TNF? induced protein loss and protects the myotube diameter by suppressing the Atrogin1, MuRF1 and Caspase-3 dependent muscle ubiquitin proteolytic and apoptosis mechanisms. Collectively, our finding suggests that SAC could represent a possible compound to ameliorate the muscle mass under cytokines induced atrophy.



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P-88

Quantitative structure activity relationship based study of pyrrolo-pyrimidinone scaffold for the treatment of chronic pain

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Quantitative structure activity relationship has been performed on a series of thirty two compounds of pyrrolo-pyrimidinone scaffold, using different physiochemical parameters along with appropriate indicator variables.

The physicochemical parameters have been used for the present series of compounds were selected for multiple linear regression analysis (MLRA). Various regression models have been tested and the statitistical data indicate that some of the descriptors provide valuable information to predict activity of these derivatives. The predictive ability of the model was cross-validated by observation of the low residual activity values and appreciable cross-validated R2 values (R2cv) obtained and also by leave one out (LOO) technique.

Keyword: pyrrolo-pyrimidinone scaffold, QSAR, Regression Analysis, MLRA

P-89

QSAR Modeling of HIV-1 Reverse Transcriptase Inhibitor of Aryluracil Derivatives

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Quantitative structure-activity relationship (QSAR) studies has been made on the series of 1-[(2-benzyloxyl/ alkoxyl) methyl]-5-halo-6-aryluracils derivatives that are non-nucleoside reverse transcriptase inhibitors. This study is based on modeling the HIV-1 inhibitors of aryluracils derivatives using Quantum chemical, topological and physicochemical parameters. Various descriptors were calculated empirically and by density functional theory (DFT). Density functional theory-based descriptors were calculated at GGA-PW91 level. Several QSAR equations were formulated through regression analysis and tested with external and internal validation tests and the best equations were selected. The QSAR results revealed that the reverse transcriptase inhibitor activity could be modeled using different DFT- based descriptors such as softness (S), hardness ( ), chemical potential ( ), highest occupied molecular orbital energy, (HOMO) lowest unoccupied molecular orbital energy (LUMO) and empirical parameters such as surface tension (ST), index of refraction (IOR) molecular connectivity (1? to 5?) and Mean Weiner index (WA).Model equations were cross validated by leave one out (LOO) technique.

Keywords: NNRT inhibition; DFT-QSAR; Regression analysis-Molecular descriptor; Frontier electron density

P-90

Hansch Analysis of Catechol Diether Derivatives as Potent Anti-HIV Agents

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Quantitative structure activity relationship (QSAR) study has been made on the Catechol Diether Derivatives. This study is based on modeling of the activity of HIV-1 inhibitors of Catechol Diether derivatives using using

density functional theory based (DFT-based) quantum chemical and empirical parameter (topological and physicochemical).The density functional theory-based (DFT-based) descriptors were calculated at GGA-PW91 level in gas phase. The calculated descriptors were selected for multiple linear regression (MLRA) analysis. Various regression models have been tested and the regression analysis data indicates that some of the descriptors provide helpful information towards designing of new HIV-1 inhibitors with high efficacy. Further, The QSAR models were tested for their statistical significance and reliability by using leaves one out (LOO) cross validation method.

Keywords: HIV-1 inhibitors; Catechol Diether. Derivatives; DFT-QSAR; Regression analysis-Molecular descriptor; Frontier electron density

P-91

Carboxamide-type abcg2 modulators: bioisosteric approaches to improve solubility and stability

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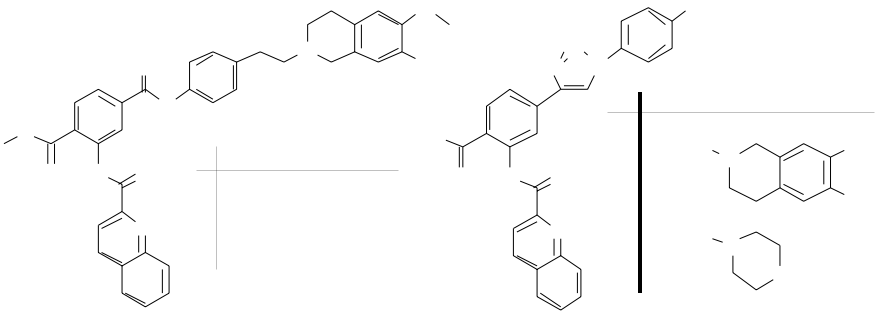
The efflux transporter breast cancer resistance protein (BCRP, ABCG2) is associated with the chemoresistance of malignant tumors. In addition, ABCG2 is highly expressed at the blood-brain barrier, preventing the entry of numerous xenobiotics including drugs into the central nervous system. Recently, UR-ME22-1 (1) and UR-COP-78 (2) were reported as highly potent and selective ABCG2 inhibitors. Unfortunately, these compounds were prone to enzymatic cleavage, preferentially on the central benzamide core [1, 2]. Replacement of the central core with an indole [3] or a triazole (cf. type 3) resulted in compounds, which are resistant against enzymatic cleavage.

Triazole-type modulators (3) showed inhibitory potency in the nanomolar range and retained selectivity for ABCG2 over ABCB1 and ABCC1. Aiming at lower molecular weight and improved solubility, the tetrahydroisoquinoline moiety was replaced (4), as suggested by a fragment regression analysis of data from our laboratory. Regardless of lower AGCG2 selectivity compared to type 3 compounds, this approach resulted in modulators (4) with activities in the three-digit nM range.



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P-92

Putative polyadenylation and cleavage specificity factor RNA14 of fission yeast involve in m-RNA processing

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Posttranscriptional regulation is controlled by splicing machinery and 3' end processing complex. Mutation in the complex subunits leads to abnormal function, producing unusual proteins. Rna14 is predicted to be a component of the cleavage factor IA (CFIA) complex, which is involved in the endonucleolytic cleavage during polyadenylation-dependent pre-mRNA 3'-end formation in s.cerevisiae. Pre-mRNA machinery also coordinates with cell cycle progression although cell cycle is unidirectional irreversible process, regulated by expression level of regulatory proteins. In a synthetic lethal genetic screen we isolated conditional mutants that show mitotic defects in conjunction with checkpoint proteins kinase Chk1. One of such temperature sensitive mutant ts11/ rna14 exhibits reduction in Chk1 protein level and high level of chromosome segregation defects at non permissive temperature. Rna14 protein in budding yeast has been characterized and has been implicated in cleavage and polyadenylation of mRNA in the nucleus. Due to abnormal splicing the introns were retained in the mature transcript which is confirmed by RT- PCR. rna14 mutant was synthetic lethal with bub1? as it creates more lethal chromosome segregation defects. There is a large assembly of pre-mRNA maturation complex ,since we are trying to isolate the protein which is interacted to rna14 and assist the function of polyadenylation and cleavage by tagging of rna14.So rna14 is the suitable target for drug discovery. It involves in polyadenylation and cleavage.If any defect present in rna14 , it demolish the whole pre-mRNA machinery.

Keyword: s.pombe,rna14,bub1

P-93

Design, synthesis and mode of action of some new amide derivatives of 2-(4?-aminophenyl) benzothiazole as potent antimicrobial agents

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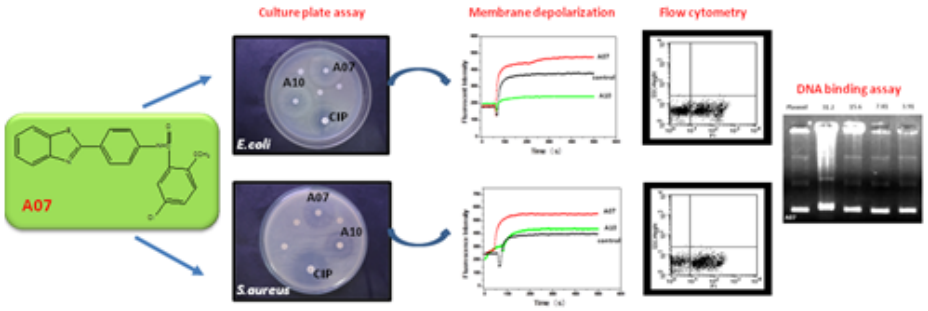
In this study novel benzothiazole derivatives bearing amide moiety were designed, synthesized and evaluated for their antibacterial activity with possible mode of action. Structures of the synthesized compounds were elucidated by 1H NMR, 13C NMR, IR and Mass spectral data. These compounds were screened against four different gram-negative and two different gram-positive bacterial strains by agar disc diffusion method [1]. Among all the synthesised compounds, compound A07 displayed most potent inhibitory activity with minimum inhibitory concentration (MIC) values of 15.6, 7.81, 15.6, 3.91 µg/ml against S. aureus, E. coli, S. typhi and K. pneumoniae respectively. Structure-activity relationship (SAR) studies revealed that electronic and lipophillic factors of phenyl ring had a significant effect on the antimicrobial activity of the designed compounds. The benzothiazole bearing amides exhibited different modes of action based on aryl group substitution as revealed by studies on intact bacterial cells and plasmid DNA. The present study provides us two active compounds (A07 and A10) with membrane perturbing mode of action, elucidated by membrane depolarization, and fluorescent assisted cell cytometry (FACS) and, intracellular mode of action due to binding with DNA.



Schematic outline of most potent compound, benzothiazole bearing amide moeity A07 showing antibacterial activity and its mode of action.

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P-94

Pharmacophore search of the ZINC database and molecular docking: In quest for anti-tubercular lead molecules

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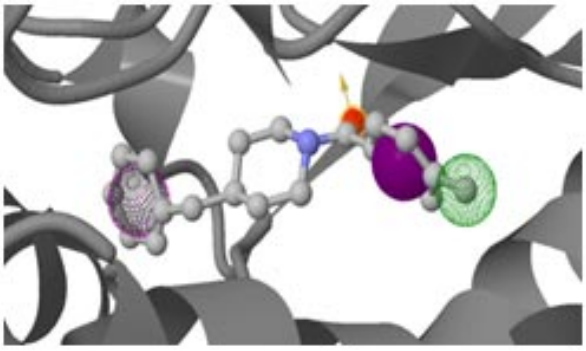
In the present work, a novel molecular operating environment pharmacophore was developed for 5-pentyl-2-phenoxyphenol using the crystal structure of Mycobacterium tuberculosis enoyl reductase target (InhA) inhibited by the ligand 5-pentyl-2-phenoxyphenol (PDB Code: 2B36). The developed pharmacophore contains the features viz. hydrogen donor, hydrogen acceptor, hydrophobic and aromatic pharmacophore class. Later, the ZINC database (last updated 15/10/14) was searched for the molecules corresponding to the developed pharmacophore and retrieved the entire molecules. Here, ZINCPharmer software was used which is a freely available online

pharmacophore search system. A total of 206 hits were found and they were further filtered by limiting the maximum molecular weight as ? 400, rotatable bonds ? 10, RMSD ? 0.9, hit per conformations ? 2 and hit per molecule ? 2. A total of 15 hits were retrieved and they were docked with enoyl reductase target for further validation. Ultimately the binding energy of the docked molecules was found to be in the range of -5 to -9 Kcal/mol through docking with autodock version 4.2 which adds justification to the pharmacophore search. Therefore further research will be continued with the best predicted molecules in the direction of drug development.



Molecular operating environment pharmacophore

Reference

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P-95

Iodine-mediated oxidative annulation for one-pot synthesis of pyrazines and quinoxalines using a multipathway coupled domino strategy

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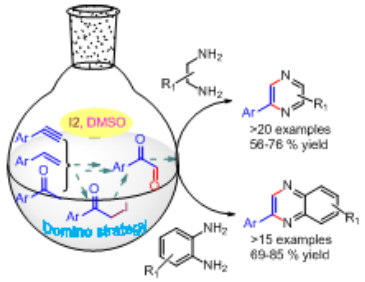
Unlike the conventional 'stop and go' synthesis, the domino strategy explores multiple bond-forming reactions under fixed reaction conditions, reducing the number of reagents or catalysts needed.1 Because of the step economy and reduced purification burden, these reactions are gaining more prominence. To make domino reactions more lucrative, recently, chemists have started coupling two or more domino processes in a one-pot operation.2 herein we report an multi-pathway coupled domino (MPCD) approach for the synthesis of both pyrazines and quinoxalines. An efficient iodine-mediated oxidative annulation of aryl acetylenes-arylethenes-aromatic ketones with 1,2-diamines for the synthesis of pyrazines and regioselective synthesis of quinoxalines is presented. The

overall process involves three different reactions (iodination, Kornblum oxidation, and condensation) that were self-sequentially assembled in a single reactor. In addition, the protocol could exclusively provide singleregioisomer in the case of 3,4-diaminobenzophenone with different aryl acetylenes.



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P-96

Novel Analogues of Lupeol and Their Anti diabetic Activity

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Structural modifications of lupeol at the isopropylene moiety at position C-19 have been described via allylic oxidation using selenium dioxide [Jean et al. (1)]. The antidiabetic efficacy of lupeol analogues were evaluated in vitro as glucose uptake stimulatory effect in L6 skeletal muscle cells. From all seventeen tested compounds, 2, 3, 4b and 6b showed significant stimulation of glucose uptake with respective percent stimulation of 173.1 ($p<0.001$), 114.1 ($p<0.001$), 98.3 ($p<0.001$) and 107.3 ($p<0.001$) at 10 µM concentration. Stimulation of glucose uptake by these compounds is associated with enhanced translocation of glucose transporter 4 (GLUT4) and activation of IRS-1/PI3-K/AKT-dependent signaling pathway in L6 cells [Khan et al. (2)]. Structure-activity relationship analysis of these analogues revealed that ?, ?-unsaturated carbonyl and acetyl moieties were important in the retention of glucose uptake stimulatory effect in L6 skeletal muscles.

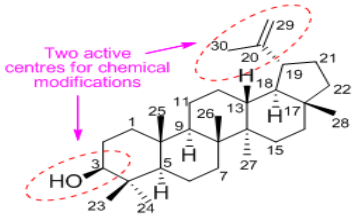

Fig. 1: Basic skeleton of Lupeol, showing the possible chemically active centers.

Keywords: Type 2 diabetes mellitus, Lupeol, Isopropylene moiety, Glucose uptake stimulation

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P-97

A QSAR analysis of Benzothiazole based antimicrobial agents

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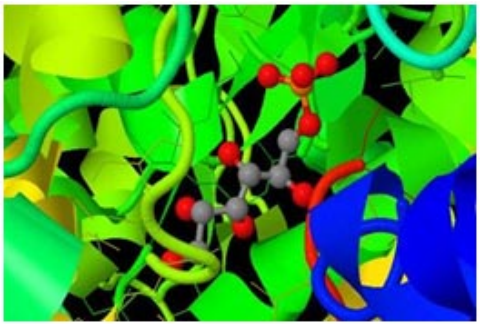
For an accurate prediction of biological activity of a new compound, development of QSAR model is prerequisite. So in this present study QSAR model was developed for the benzothiazole class of compounds that were reported to be effective as an antimicrobial agent. Phase package from Schrodinger software was used to calculate molecular descriptors and the data set containing the descriptors and PMIC values was divided into a training set and a test set where the training set was used to generate pharmacophore model and prediction of the activity of test set was used to validate the proposed model [1]. Further, the developed descriptors were used for the generation of statistically significant model. It has produced r2 value of 0.71, so the obtained model was concluded to be satisfactory. Some of the designed novel benzothiazole molecules were fitted into the QSAR model and predicted their biological activity. Finally the molecules with good predicted biological activity were docked with a microbial target glucosamine 6-phosphate synthase (PDB code: 1JXA) using autodock version 4..2. The binding energy of those docked molecules was found to be in the range of -6 to -9 Kcal/mol. The designed molecules were predicted for good biological activity therefore the process can be continued in the direction of drug development.



Glucosamine 6-phosphate synthase with Glucose 6-phosphate
(PDB code: 1JXA)

Reference

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P-98

Access to Di- and Trisubstituted Oxazoles by NBS-Mediated Oxidative Cyclisation of N-Acyl Amino Acid Derivatives

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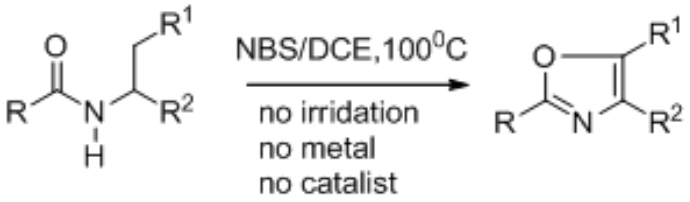
Oxazoles are significant structures found in a large number of biologically active natural products.1A number of research groups have synthesised oxazoles from a variety of starting materials using a range of reagents.2 Very few of these syntheses are general, most of them lead to products with a limited number of substituents, or a limited pattern of substituents (diaryl, triaryl, halomethyl,or aldehyde, etc.), or multiple reagents, or the use of heavy-metal catalysts, or additional oxidants, etc. General approaches to synthesise oxazoles include the cyclisation of amides onto hydroxy groups (serine, threonine derivatives) or onto olefins (from enamides), the cyclisation of diketo compounds, the metal-catalysed electrophilic cyclisation of propargyl amides, etc. Based on recent reports of the synthesis of oxazolidinones from amide derivatives of phenylalanine and of oxazoles from allylic amides. We devised a short reaction cascade for the synthesis of 2,5-disubstituted oxazole- 4-carboxylates from N-acylphenylalanine. A remarkably simple method for the synthesis of di- and trisubstituted functionalised oxazoles under metal- and catalyst-free conditions is described. An iterative bromination and debromination of N-acylated amino acid derivatives with NBS as the sole reagent cleanly led to various substituted oxazoles.



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P-99

Catalytic applications of graphene based nanomaterial for the microwave assisted chemo-selective synthesis of pyrrolo[2,3,4-kl]acridin-1-ones

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Carbon based nanosheets has revealed a new route for their use as two dimensional catalytic supports possessing enormous specific surface area and presence of reactive oxy functional groups. Besides, Ag nanoparticles have become the focus of intensive research because of its catalytic applications for a variety of organic reactions. The hybrid material of Ag NPs and graphene oxide provide excellent surface acidity with good dispersion capability that usually lacks in Ag NPs alone.

Pyrroloacridines are center of interest in medical sciences since they exhibit potential anthelmintic, antibacterial and anticancer activities. These moieties also found as the tetracyclic cores in key metabolites such as plakinidines A-C and alpkinidines. By utilizing a combined concept, a highly stable and recyclable Ag NPs decorated grapheme oxide composites were synthesized by wet chemical method and characterized by TEM, XRD, SEM, EDAX, UV-Vis, Raman and FT-IR spectra. Catalytic applications of the synthesized nanomaterial were scrutinized for the chemo-selective synthesis of pyrrolo[2,3,4-kl] acridin-1-ones by the one pot reaction of dimedone, various anilines and isatins in ethanol under microwave. Used catalyst could be easily recovered simply by filtration and recycled at least 7 times without significant loss in catalytic activity. The synthesized compounds were screened for antibacterial and antitumor activities. Detailed synthetic procedure and pharmacological activities of these compounds will be discussed at the time of presentation in conference.

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P-100

Candidemia induced pediatric sepsis and its association with free radicals, nitric oxide and cytokine level in host

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Candida spp. has become the seventh most frequent causal microorganisms of nosocomial sepsis. Prematurity and low birth weights are strongly associated with the development of neonatal nosocomial bloodstream infections. C. albicans has been the species most often associated with neonatal infections, but recently there has been a changing pattern in the isolates recovered from neonates with invasive candidiasis, which poses resistance to the existing class of azoles like fluconazole, antifungals along with cross resistance to newer triazoles, which results a therapeutic challenge in invasive fungal infections causing high incidence of mortality.

Candida spp. was isolated from blood of neonates and children below 15 years of ages admitted to hospital and susceptible for Candida induced sepsis. Polymerase chain reaction (PCR) based identification and confirmation of individual Candida species was done using DNA sequencing. Antibiotic susceptibility assay and resistance pattern for Fluconazole, Voriconazole and Amphotericin, was done for all the isolates. Further, the change in free radical, cytokine release and nitric oxide synthase expression and nitric oxide release from polymorphonuclear leukocytes isolated from control and pediatric sepsis cases was also performed.

The present study probably for the first time report the change in increasing incidence of non-albicans Candida induced sepsis in neonates and children's admitted to the intensive care unit of hospital and current antibiotics load posing resistance for antifungal treatment strategy and provide serious threats in future treatment. The increase in free radicals in polymorphonuclear leukocytes (PMNs) and increase in expression of nitric oxide synthase expression and nitric oxide release in Candida infected pediatric sepsis cases underlies the role of host factor in dissemination and invasiveness of infection from exogenous sources and pathogenesis of systemic inflammation during sepsis.

Keywords: Candidemia, Nitric Oxide, Interlukin-10, Tumor Necrosis Factor-alpha, Sepsis, Interlukin-1?

P-101

In-situ generated chiral iron complex as efficient catalyst for enantioselectivesulfoxidation using aqueous H2O2 as an oxidant

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Chiral sulfoxides are valuable compounds for their application as chiral auxiliaries,1 ligands,2organo-catalysts and in pharmaceutical industries.A new series of amino alcohol derived Schiff base ligands and their corresponding iron complexes were synthesized in situ to catalyse the asymmetric oxidation of prochiralsulfide using aqueous H2O2 as a terminal oxidant. One of these complexes was found to be very efficient catalyst for the enantioselective oxidation of methyl phenyl sulfide. During the optimization process the electron donating benzoic acid derivative or its Na salt as additive was found to be beneficial to improve both conversion and enantioselectivity. This catalyst was found to very efficient in the enantioselective oxidation of a number of aryl alkyl sulphides with excellent enantioselectivity (75 to 96% ee), very good conversions (up to 92%) and excellent chemo selectivity (up to 98%). Based on the UV-vis. study and ESI-MS analysis we have proposed a catalytic cycle for the oxidation of sulfides.

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P-102

Green synthetic tools for the construction of S-S and C-S bonds

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The amazing phenomena of nature to generate diverse array of molecules always fascinate the chemists to persistently seek new concepts and tools for efficient construction of molecular frameworks. Among the vast array of naturally occurring organic compounds like thorazine, allicin and thienamycin[1]etc, the sulfur containing compounds possessing S-S and C-S bond are on the top because of diverse biological activities associated with them such as antipsychotic, antibacterial, antiprotozol and antileishmanial (Figure 1).

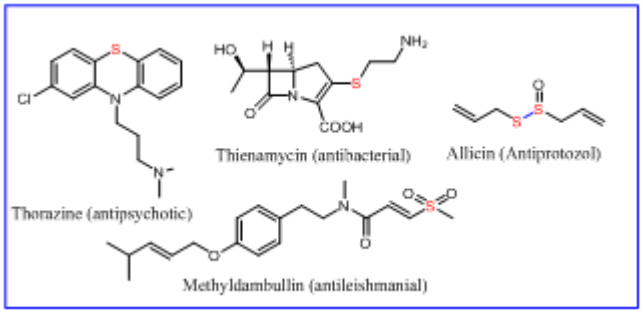

Figure: 1

While many reliable methods have been developed for construction of S-S and C-S bond, harsh reaction conditions are usually required in the traditional methods, hence the fertile ground of green chemistry permeates across various disciplines and puts special emphasis on the sustainable development of methods or tools for S-S/ C-S bonds which avoids the deleterious impact on the environment. Therefore, the synthesis of organosulfur compounds have shifted the attention of scientific community towards "Sustainable or Green Chemistry" [2][3]. In this context, the use of ionic liquids (ILs)[4][5], organocatalyst [6], biocatalyst and water have been exploited as a green tools towards formation of S-S (disulfides), C-S (thioethers and vinyl sulfides) bond formation.

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P-103

One-Pot Facile Synthesis Of [1,2,4]-Triazolyl-Thiazolidinones Using Organocatalysis In Water

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Heterocyclic scaffolds have attracted extensive attention in the design of biologically active molecules. The concept of molecular hybridization, wherein two (or more) structural domains are fused together with the goal of generating a new chemical entity having better biological properties than their precursors, is now being increasingly used by pharmaceutical chemists in their quest for potent new drugs.

[1,2,4]-Triazolyl-thiazolidinones are one such class of heterocyclic hybrids obtained by integrating 1,2,4-triazoles and thiazolidinones, two biologically significant heterocyclic nuclei unto one platform. They have been reported to exhibit interesting medicinal properties. However till date only a few methods for the synthesis of triazolyl-thiazolidinones have been reported. Consequently the development of new synthetic routes to access [1,2,4]-triazolyl-thiazolidinones remains an active research field.

In the last few decades there has been a growing emphasis on the development of green techniques in organic syntheses so as to reduce harm to the environment with particular stress on the use of water as a solvent and organocatalysts for catalyzing the reaction. But the hydrophobicity of most organic substrates is a serious drawback for effecting their reactions in aqueous medium. In this regard surfactants have emerged as an effective tool to overcome this problem.

In this backdrop we have developed a simple one-pot, green strategy for the synthesis of triazole-thiazolidinone hybrids using water as the reaction medium, acetic acid as an organocatalyst and cetyltrimethylammonium bromide (CTAB) as a surfactant. The desired [1,2,4]-triazolyl-thiazolidinones were formed in short reaction times and good to excellent yields.

P-104

Interaction of Mycobacterium avium paratuberculosis, a pathogenic mycobacterium, with murine adipocytes

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Mycobacterium avium subsp. paratuberculosis (MAP) is the causative agent of Johne's disease of ruminants and one of the suspected etiological agents of Crohn's disease (CD), a chronic inflammatory bowel disease of

humans. Many groups have independently isolated MAP from CD tissue using culture and molecular techniques. MAP is able to survive intracellular in macrophages by preventing normal phagosome maturation processes. Adipocytes and endothelial cells are found to have important roles in CD pathogenesis. The "creeping fat" of the mesentery, unique to CD is an ectopic extension of mesenteric adipose tissue (mAT). In the present study we used MAP-K10 strain and found that it is able to infect primary murine adipocytes as well as 3T3L1 adipocyte cell line. MAP persisted inside mature adipocytes without replication and induced pro-inflammatory response by modulating the secretion of TNF- ?, IL-6, MCP-1 and nitrate. We infected Swiss mice orally with MAP and isolated MAP from liver, intestine, spleen and mAT which was confirmed by CFUs and PCR. MAP could not be traced to adipocytes despite the presence in mAT, suggesting the presence of MAP in mesenteric lymph nodes.

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P-105

Effect of hydro-alcohol extract of Cucurbita pepo L. on oxidative stress

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Oxidative stress ensues due to the imbalance between the production and elimination of reactive oxygen species (ROS). [1] This oxidative damage subsequently leads to cell death/apoptosis which in turn aggravates chronic disorders like diabetes and its related complications. [2] This study was designed to evaluate the protective effect of C. pepo against oxidative stress by employing total phenol estimation, total antioxidant capacity, reducing power assay, DPPH, hydrogen peroxide, nitric oxide and superoxide radical scavenging assay along with advanced glycation end products, sorbitol accumulation and aldose reductase (ALR) enzyme inhibition [2, 3]. The results showed that the total phenol content present in hydro-alcohol extract of C. pepo (CHE) was 200 mg/g GAE and total antioxidant capacity was found to be 550 ?M/g ascorbic acid equivalents. In the DPPH radical scavenging activity, hydrogen peroxide scavenging activity, nitric oxide scavenging activity and superoxide radical scavenging activity, CHE had the IC50 values of 4.28 ?g/ml, 164.35 ?g/ml, 116.45 ?g/ml and 31.84 mg/ml, respectively. Reducing power of the extract increases with concentration of 10-320 ?g/ml. Ascorbic acid was used as standard. The formation of AGEs was monitored weekly by measuring fluorescence intensity of the BSA-fructose solutions for 4 weeks. Percentage inhibitions of AGEs formation by CHE (50-500 ?g/ml) was 33.05 to 89.70% respectively. A significant inhibition of AGEs formation (93.37%) was observed in fructose-induced glycated BSA plus aminoguanidine (500 ?g/ml). CHE showed inhibitory effect against sorbitol accumulation with IC50 value 215.70

µg/ml. In aldose reductase inhibition assay, CHE had the IC50 value of 6.205 µg/ml. Quercetin was used as standard. The present study revealed that C. pepo would exert beneficial effects in diabetic complications by virtue of its antioxidants and antiglycation.

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P-106

Effect of Cephalendra indica against oxidative stress in diabetic complications

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Diabetic complications are now a global health problem without effective therapeutic approach. Hyperglycemia and oxidative stress are important components for the development of diabetic complications. Chronic hyperglycemia leads to the formation of advanced glycation end products (AGEs) and sorbitol accumulation which accelerates the development of diabetic complications [1]. Mother tincture, 6C and 30 C of C. indica were procured from Dr. Willmar Schwabe India Pvt. Ltd. Mother tincture, 6C and 30 C of C. indica was assessed for its effect on oxidative stress by employing Advanced Glycation End products, sorbitol accumulation and Aldose reductase (ALR) enzyme inhibition assays [2,3]. The formation of AGEs was monitored weekly by measuring fluorescence intensity of the BSA-fructose solutions for 4 weeks. Percentage inhibitions of AGEs formation by mother tincture of C. indica (0.2-1.0 ml) was found to be 30.39% to 91.77%, respectively; for 6 C (1.0-5.0 ml) 29.98 to 65.71 % respectively and for 30 C (2.0-10.0 ml) 33.05 % to 57.75 % respectively. Mother tincture, 6C and 30 C of C. indica showed inhibitory effect against sorbitol accumulation and IC50 value of mother tincture, 6C and 30 C of C. indica was found to be 0.557, 4.11 and 9.49 ml respectively. In aldose reductase activity, ALR1 was partially purified from kidney of Wistar rat and the activity of ALR1was measured spectrophotometrically by monitoring the oxidation of NADPH at 340 nm and IC50 value of mother tincture, 6 C and 30 C of C. indica was found to be 0.63, 4.44 and 8.54 ml respectively. The present study revealed that C. indica would exert beneficial effects in diabetic complications by ameliorating oxidative stress.

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P-107

Homology modeling of GPR119 receptor for identifying novel leads

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Diabetes is an ever growing metabolic disease affecting a majority of the population around the world. There are many drugs acting on various targets that are in use for the treatment of diabetes, although certainly not without side effects. GPR119 Chu et al.[1] is a receptor belonging to the GPCRs which is expressed in the pancreatic ?-cells and intestinal L-cells and has been investigated as an essential target for diabetes. The GPR119 agonists happen to increase intracellular cAMP levels leading to enhanced glucose-induced insulin release and enhanced incretin hormone glucagon-like peptide 1 (GLP-1) secretion that in turn lower blood glucose level.

The absence of any information on the GPR119 receptor structure enables us to design a homology model of the GPR119 which can help to gain insights into receptor binding of molecules in the anti-diabetes drug design and development process. The homology model of GPR119 is built on the principles of comparative protein modelling. This model was eventually used to study the binding of endogenous ligands to the extracellular loops and the transmembrane region of the receptor using docking and lipid embedded molecular dynamics simulations.

GPR119 homology model was validated based on the DOPE Score and Ramchandran Plot. The free energies of binding energies were calculated for the native ligands to compare with the experimental values and so use them further in drug design process. From the free energies of binding energies of the native ligands, it was observed that the molecule oleoyltyrosinol binds more tightly relative to the other ligands; which is harmonious with the literature data indicating that oleoyltyrosinol is more active than the other fatty acid amides. This asserts that the homology model could be gainfully used to study ligand GPR119 interactions. The GPR119 homology model was also used to study the binding modes and calculate free energies of binding for some of the molecules designed by HQSAR studies Ugarkar et al. [2]

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P-108

Stereoselective Synthesis of (R)-3-Methylthalidomide by Piperidin-2-one Ring Assembly Approach

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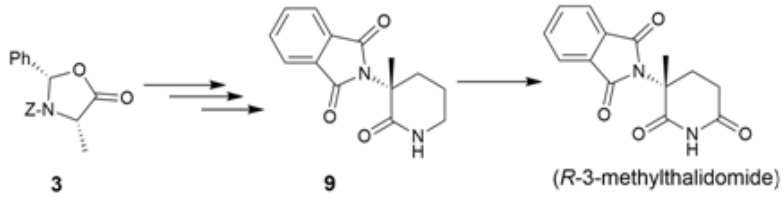
3-Methylthalidomide is a configurationally stable analog of thalidomide Knabe et al. [1] with better TNF-? regulatory activity as compared to thalidomide Chung et al. [2]. Previously reported methods employed for the synthesis of 3-methylthalidomide enantiomers include racemic synthesis followed by chiral resolution Knabe et al. [1], Nishimura et al. [3]. Herein, we described, a simple, straightforward and stereoselective synthesis of (R)-3-methylthalidomide starting from (S)-alanine by piperidin-2-one ring assembly approach in high yield and enantiomeric purity without using chiral auxiliary or chiral reagents. Starting from (R)-alanine corresponding (S)-3-methylthalidomide can be prepared using the same methodology.



3 9 (*R*-3-methylthalidomide)

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P-109

Thermodynamic Interaction of Proteins (hemoglobin and Lysozyme) with aqueous sugar solutions

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In this study we have investigated the volumetric, Ultrasonic and viscometric behavior of two proteins, Hemoglobin and Lysozyme in aqueous solutions of sugars (glucose and maltose) at various temperatures, at 303.15, 308.15 and 313.15 K (close to body temperature).Apparent molar volumes, partial molal volumes, adiabatic compressibility and B-coefficient of these solutions have been computed from density, ultrasonic velocity and viscosity data.The results are interpreted in terms of solute -solvent interactionsand stabilization of these sugars in presence of above proteins.

P-110

An organocatalytic novel C-C bond forming approach for the direct syntheses of highly substituted tetrahydrocarbazoles and Carbazoles

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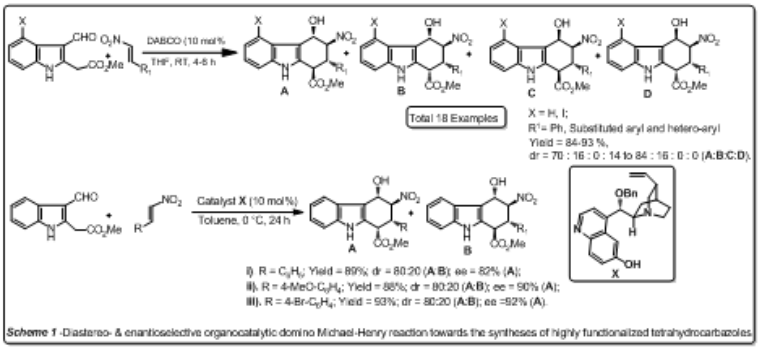
Development of a highly efficient method for the synthesis of functionalized tetrahydrocarbazoles (THCs) and carbazoles is a key research area in drug discovery as well as in medicinal chemistry because these moieties are present in a variety of drug candidates and natural products and many of them synthetic analogues showing potential biological activities. Towards this aim, several transition metal complexes catalyzed syntheses of both racemic and enantioselcetive versions of THCs and Carbazoles have been well documented. However, because of potential environmental concerns about metal catalysts in general, organocatalysis has been paid much attention in the context of green chemistry, as well possibly providing cost effective synthesis of optically active complex molecules from simple raw materials in a highly efficient manner.

In the view of above prospect, for the first time, a very simple, efficient, mild, organocatalytic and one- pot procedure for the synthesis of a series of densely functionalized 1,2,3,4-tetrahydro-9H-carbazole and highly substituted carbazole derivatives have been achieved via a domino Michael-Henry reaction of methyl 3-formyl-1H-indole-2-acetates with b-nitrostyrenes using DABCO as an organocatalyst. Furthermore, the high enantio- (upto 92% ee) and diastereoselective (upto 80:20 dr) synthesis of the title compounds have also been achieved with excellent yields using 9-O-benzylcupreidine (10 mol%) as a catalyst.



Scheme 1 -Diastereo- & enantioselective organocatalytic domino Michael-Henry reaction towards the syntheses of highly functionalized tetrahydrocarbazoles.

We have also extended this optimized protocol for the synthesis of biologically important quinolinone and coumarin fused carbazole derivative along with the synthesis of biologically significant pyrimidocarbazole derivatives (topoisomerase II inhibitors). The detail of the study will be presented.

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P-111

Syntheis and biological evaluation of lupeol analogues as anti-diabetic agents

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A series of naturally occurring lupeol analogues was synthesized by modification of A ring and isopropelene moiety with different carboxylic acids and the anti diabetic activity of lupeol derivatives were evaluated against protein tyrosine phosphatase -1B (PTP-1B) inhibitory activity. Among the tested compounds 9a, 9b, 14a, 14b and 14c showed significant dose dependent activity at 10µm concentration with IC50 values 7.46, 8.01, 8.61, 11.5, 8.78 respectively. Our structure activity relationship revealed that the compounds having unsaturated phenyl ring and substituted aliphatic chain shown significant PTP-1B activity.

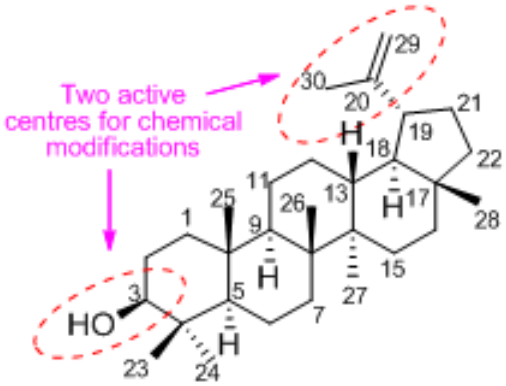

Fig 1: Basic skeleton of lupeol with active centers for modification

Keywords: Type 2 Diabetes, Lupeol, Substituted carboxylic acid, PTP-1B inhibitors

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P-112

Modification McMillan catalyst with ionic liquid as a recoverable catalyst for asymmetric Diels Alder reaction

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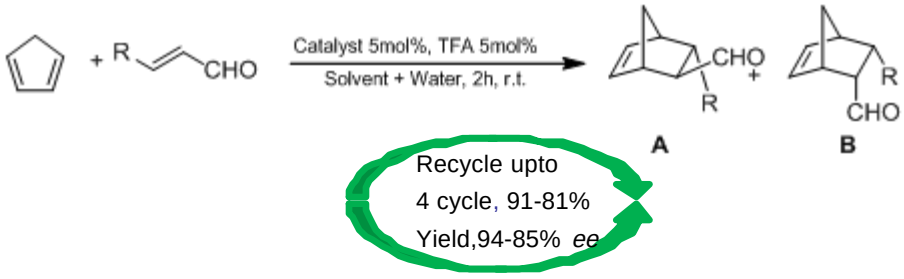
Diels alder reaction is an important tool for the synthesis of enantiomerically enriched cyclohexene moiety and also for carbon-carbon bond formation reaction. It is key a step for the synthesis of many natural products and pharmaceutical compounds. The first enantioslelctive Diels alder reaction was reported by McMillan and coworkers using an organocatalyst, which proceeds by a LUMO-lowering activation mechanism.1-3

We have also synthesized recoverable and reusable ionic liquid tagged McMillan catalyst for enantioslelctiveDiels alder reaction. The Diels alder adduct of cyclopentadiene and crotonaldehydewas obtained with 92% conversion with 94% enantioselectivity. We have recovered and reused ionic liquid tagged McMillan catalyst up to 4 cycles.



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P-113

Click-conceived Pyrrolidotriazoles as Pyrrolizidine Alkaloid Surrogates: conformational constraint as an effective tool for tailoring the selectivity of ?-glucosidase inhibitors

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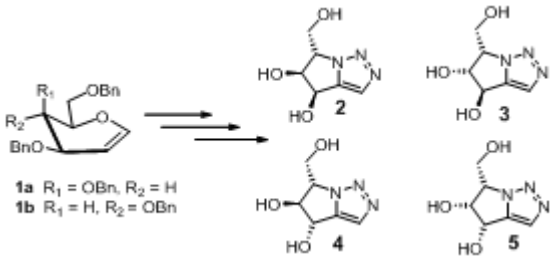
Principle guided design of glycan processing enzyme inhibitors involves embedding aromatic groups onto charge and shape mimics.1,2 Intramolecular azide-alkyne cycloaddition3 was used as a simple and versatile strategy for the synthesis of novel condensed bicyclic triazoles from carbohydrate derived Perlin aldehydes. These newly

synthesised molecules were evaluated for glycosidase inhibition against 11 commercially available enzymes and were found to possess significant affinity (micromolar range) as well as high degree of selectivity for ?-glucosidases. Conformational restriction was identified as an important tool to customize the selectivity of enzyme inhibition by five-membered iminosugars.



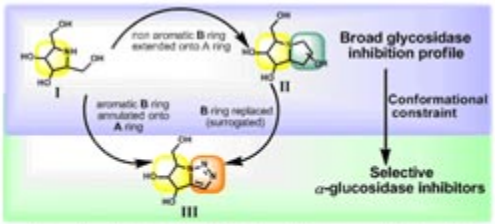


Fig. 2. Structural relationship between polyhydroxylated pyrrolidines **I**, polyhydroxylated pyrrolizidines **II** and proposed triazole surrogates of polyhydroxylated pyrrolizidines **III**. Fusing triazole to **I** results in hydrophobically modified iminosugar **III** showing better activity and selectivity towars α-glucosidases.

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P-114

Anticonvulsant and Neurotoxicity Study of Some Terpenes Incorporated Semicarbazones

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A series of 4- aryl substituted semicarbazones were synthesized by reaction of different 4-aryl substituted semicarbazides with different types of terpenes such as citral (acyclic terpene), menthone (monocyclic terpene) and camphor (bicyclic terpene). The structure of all the synthesized compounds were confirmed by spectral analysis such as I.R., 1HNMR besides the use of elemental analysis. Anticonvulsant activity of hydrazones were evaluated by intraperitoneal (i.p.) maximal electroshock - induced seizure (MES) and subcutaneous pentylene tetrazole (s.c. PTZ) induced convulsion method at 30, 100 and 300 mg/kg dose levels. Neurotoxicity of the compounds were also evaluated at the same dose levels by using Rotorod test. Most of the compounds showed significant anticonvulsant activity. All the compounds exhibited lesser neurotoxicity compared to phenytoin. All the active compounds showed greater protection than sodium valproate. It can be concluded that newly synthesized compounds possessed promising anticonvulsant activity with lesser neurotoxicity compared to conventionally used antiepileptic drugs.

Keywords: Terpenes, Citral, Camphor, Menthone, Semicarbazones

P-115

Highly-Stable Magnetite NanoCo(0)/Al_2O_3-SiO_2 Derived from Co_3O_4-Al_2O_3-SiO_2: An Efficient catalyst for Selective Hydrogenation of Organonitro Compounds to Anilines

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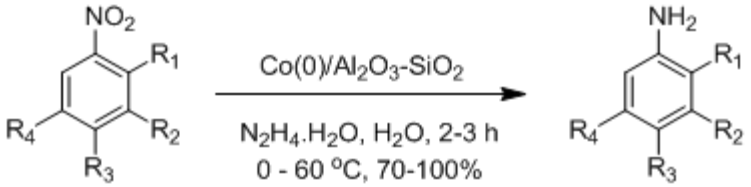
Hydrogenation of aromatic nitro compounds to corresponding aniline derivatives by non-noble metal catalytic system is an interesting research for green and sustainable methodology [1]. Catalysis is a key technology for achieving more benign processes in the chemical, pharmaceutical and material industries. In recent years, nanomaterials have attracted increasing interest in catalysis for their potential use as catalyst and selective drug delivery vehicles. Cobalt is an industrially active metal and having many applications in various organic transformations[2]. Highly stable and magnetic responsive nano Co(0)/Al_2O_3 -SiO_2 was prepared from an inorganic composite precursor cobalt oxide on alumina-silica support [Co_3O_4/Al_2O_3-SiO_2] by calcination and chemical-reduction in a sealed reactor. The characterization of nanoCo(0) on Al_2O_3 -SiO_2 matrix with XPS, electron mictroscopy and vibrating sample magnetometry confirmed that these nanoparticles possessed a mono dispersed spherical morphology, narrow particle size distribution and high magnetic susceptibility. The magnetic property of magnetite Co(0)/Al2O3SiO2 nanoparticles was compared with separately prepared cobalt metal anchored on the alumina and silica and found that Co(0)/Al_2O_3 -SiO_2 nanoparticles acquire unusual hysteretic magnetic susceptibility. The resultant magnetite Co(0)/Al_2O_3-SiO_2 nanoparticles were tested as highly efficient heterogeneous catalyst for selective hydrogenation of a wide range of organonitro componds to corresponding anilines with hydrazine hydrate in water. The cobalt nanoparticles were found to be very stable in water and were easily separated from the reaction mixture by means of external magnetic field.

Keywords: magnetic nanoparticles; hydrogenation; anilines; nitro; hydrazine hydrate; heterogeneous cobalt catalyst.



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P-116

Isolation and identifiation osteogenic constituents from Dalbergia sissoo Roxb. leaves

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For thousands of years, natural products have played an important role throughout the world in treating and preventing human diseases1.Many structural features common to natural products (e.g.chiral centers, aromatic rings, complex ring systems, degree of molecule saturation, and number and ratio of heteroatoms) have been shown to be highly relevant to drug discovery effort 2 .
In our efforts to identify Osteogenic agents from plant sources, we have found Flavonoid rich n-butanol fraction, ethanolic extract and constituents of Dalbergia sissoo leaves for in-vivo anti-osteoporotic activity. Dalbergia sissoo commonly known as "Shisham" or "Sissoo" in India. It is one of the common plants used in traditional medicine and reported to have variety of biological activities.
In our study we have found potential osteogenic activity in ethanolic extract , n-butanol soluble fraction and isolated 2 new (figure-1)and14 known compounds from Dalbergia sissoo leaves and evaluated for osteogenic activity.These compounds were characterized from detailed spectroscopic studies .

Keywords: Dalbergia sissoo, Sissooic acid, Dalsissooside, Osteogenic Osteoblast differentiation.

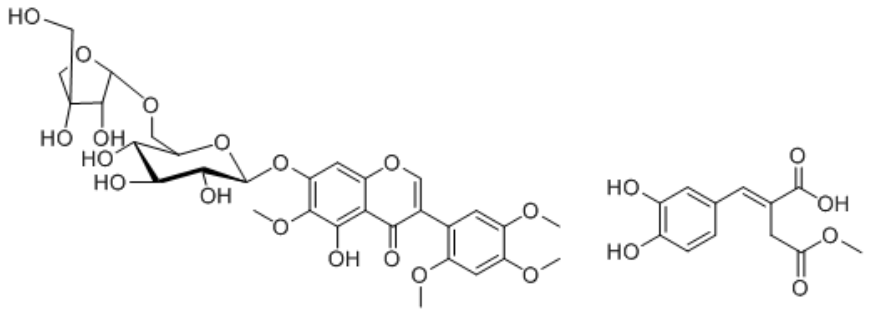

Figure -1,isolated 2 new compounds

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3- † Presenting author

P-117

Osteogenic constituents from Dalbergia sissoo heartwood

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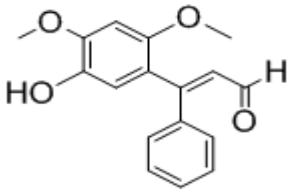
One new neoflavonoid along with seven known compounds were isolated from ethanolic extract of Dalbergia sissoo heartwood and characterised as dalsissooal (1) and cearoin (2),1 dalbergin (3),1 4-methoxy dalbergion (4),2 dalbergiphenol (5),3 dalbergichromene (6),4 methyl dalbergin (7)5 and latinone (8)6. The structures of these compounds were established on the basis of IR, 1H, 13C, DEPT, COSY, HSQC, HMBC and MS data as well as by comparing their spectroscopic data already reported in the literature. All these compounds (1-8) were assessed for osteogenic activity in primary calvarial osteoblast cultures. Compounds 1, 3, 5-8 significantly increased proliferation as assessed by alkaline phosphatase activity and mineralization in calvarial osteoblast cells.



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P-118

Chemical investigations of osteoporotic active plant Ulmus wallichiana and Cissus quadrungularis using DART MS and Q TOF LCMS analysis

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Ulmus wallichiana belongs to the family Ulmaceae, distributed through Himalayas from Afghanistan to W. Nepal. In India this plant is found in Kumaon and Garhwal Himalaya, locally called as Chamarmou, in and around Kumaon traditional healers use this plant for promoting fracture healing. Ulmosides obtained from bark of the plant U. wallichiana has been reported to inhibit osteoblastic resorbtion of bone in vitro. Cissus quadrungularis is an edible plant, commonly known as "bone setter" found in hotter parts of India. C. quadrangularis is well known for the treatment of osteoporosis, gastric disorders in traditional medicine owing to its rich source of carotenoids, triterpenoids and ascorbic acid, and has received considerable attention regarding its role in human nutrition. DART MS and Q TOF LCMS are the advance analytical tool for the chemical investigation of the medicinal plants to check the adulteration and quality control purposes. The reward of medicinal herbs should be better explored with respect to its role in the prevention and treatment of OP. This chemical investigation forms bases to widen the existing scope of the use of medicinal herbs and encourage the development of fingerprinting studies of medicinal plants and promote the modernization of research of Indian system of medicine.

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P-119

Comparative Study and Remidial Aspect on Lung Cancer of the active component(s) of Medicinal Plants in Specific Territories of India

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Cancer is a major health problem in both developed and developing countries, second only to cardiovascular disease. Lung cancer, in particular, is a disease with high morbidity and mortality, and is major cause of death among all type of cancers the world over(˜ 18.2%), causing about 1.38 million deaths per year. The cause of such high mortality rate of lung cancer may be both internal (genetic, mutative, hormonal, poor immune conditions, etc) and external (such as food habits, heavy industrialization, population explosion, life- style, smoking, etc.) Due to high death rate and ill effects of chemotherapy and radiation therapy, many cancer patients seek alternative / complementary medical treatment with milder side effects. Some natural therapies such as direct use of certain medicinal plants or the use of active ingredients extracted from these plants are reported found beneficial in combating cancer. As such there exists a wide scope of deriving potential anticancer agents from these medicinal plants, which need extensive exploration in this area. Till date only a few medicinal plants have attracted the interest of concern therapist. In view of these facts, the objective of present article is to review the medicinal plants with antitumor potential against lung cancer, the status of lung cancer in specific territories of

India and with comparison at Global level, and causes of lung cancer along with their remedial aspects, and mechanism of action.

Keywords: Cancer, Medicinal Plants, Diet, Smoke, Population explosion

P-120

Development and Validation of Ultra High Performance Liquid Chromatography Tandem Mass Spectrometry Method for Simultaneous Determination of Multiple Bioactive Constituents in Fruit Extracts of Myristica beddomeii, M. fragrans and M. malabarica Using Polarity Switch Technique

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Species of genus Myristica viz. M. beddomeii, M. fragrans and M. malabarica are traditionally used for its flavoring and medicinal properties and found as an ingredient in many marketed poly herbal formulations and food products [1, 2]. Among various Myristica species, M. fragrans (Houtt.), commonly known as nutmeg/ Javitri or Jaiphal is a commercially important species, traditionally used as spice and plays a foremost role in the Unani and Ayurvedic system of medicine [3, 4]. Therefore, development of an efficient analytical method for quality assessment of Myristica species is of high importance. In this study, an efficient method using ultra high performance liquid chromatography coupled with electrospray ionization tandem mass spectrometry was developed and validated for the rapid determination of 16 bioactive constituents in different parts of fruit of M. beddomeii, M. fragrans and M. malabarica. Chromatographic separation was achieved on an Aquity UPLC BEH C18 column (50 mm × 2.1 mm id, 1.7 µm) using gradient elution with 0.1% formic acid in water and methanol at a flow rate of 0.4 mL/min in 9.4 min. Quantitative analysis was performed using multiple-reaction monitoring mode with continuous polarity switching in a single analysis. The developed method was validated as per International Conference on Harmonization guidelines. Results indicated that highest total content of 16 bioactive constituents found in mace of M. fragrans. Thus, this new approach based on determination of multiple bioactive constituents provided a promising reference method for the quality control and authenticity establishment of Myristica species and derived herbal formulations/food products.

Keywords: Myristica species, Simultaneous determination, Polarity switch technique

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P-121

Role of Rna Pol Ii Ctd Serine-7 Phosphorylation in Gene Regulation

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The carboxy terminal domain of the largest subunit of RNA polymerase II (CTD) is a repetitive disordered domain that extends from the catalytic core of the enzyme. The CTD is heavily modi?ed by phosphorylation, glycosylation, and proline isomerization. In addition to the enzymes that modify CTD, a number of RNA processing factors and chromatin modi?cation factors interact with this tail domain. Thus, this domain acts as a tether to bring into close proximity the machinery necessary to synthesize and process RNA polymerase II transcripts.

The CTD consists of multiple tandem repeats of the consensus sequence tyrosine-serine-proline-threonine-serine-proline-serine (YSPTSPS) with serine at position 2, 5 and 7. Till date much has been disclosed about the ser2 and ser5 interacting partners of CTD and their role in transcriptional regulation while the third serine at position 7 and its interacting partners and their respective role in mRNA transcription is yet to be known. We have done GAL 4 based yeast two hybrid assay using mutant CTDs (CTD repeats with combinatorial Ser2, Ser5 and Ser7 mutations) as preys and known CTD interacting protein as bait to identify the actual binding of protein with specific phospho CTDs.

Saccharomyces cerevisiae protein Asr1 is a RING finger ubiquitin-ligase that binds directly to RNA polymerase II via the carboxyl-terminal domain (CTD) of the largest subunit of the enzyme we show that interaction of Asr1 with the CTD depends not only on serine-5 phosphorylation but also on seine-7 phosphorylation within the CTD. Ubiquitnylation by Asr1 leads to the dissociation of the Rpb4/Rpb7 heterodimer from the polymerase complex and is associated with inactivation of polymerase function which elucidates the supplementary role of serine-7 phosphorylation in gene regulation.

P-122

Diversity oriented synthesis of lactam fused privileged heterocycles via sequential ugi/coupling reaction

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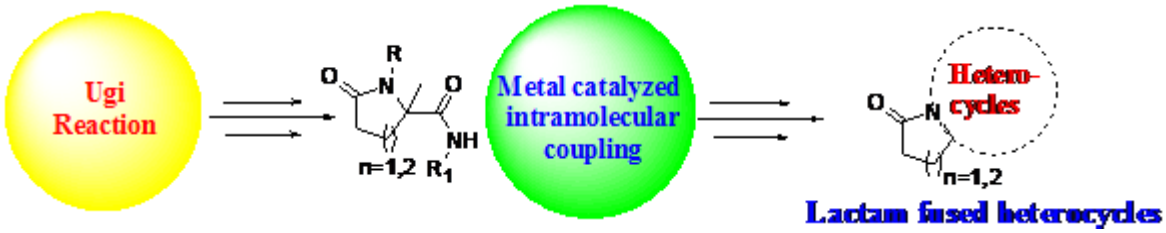
The lactam fused heterocycles [1] are a noteworthy class of compounds with effective muscle relaxant [2], anticonvulsant [3], anti seizure activity [4] and sedative-hypnotic activity. Among the previously documented methods towards the synthesis of lactam fused heterocycles, isocyanide based multicomponent reactions are

mainly important [5]. As part of our program to develop new strategies for the diversity oriented synthesis of biologically important heterocycles [6]. We have developed and reported herein the synthesis of highly diverse lactam fused heterocycles via an efficient method involving Ugi reaction followed by metal catalyzed intramolecular coupling reaction. Microwave irradiation has been successfully applied in green synthasis by our group [7]. Microwave heating was used to accelerate and to improve the efficiency of the Ugi reaction and intramolecular coupling reaction.

General portrait of Ugi/coupling sequence.



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P-123

Protective effects of aqueous and alcoholic extracts of piper longum in experimental rodent models of seizures

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Epilepsy affects 5 to 10 per 1000 of the general population. It is the third most common neurological disorder after stroke and Alzheimer's disease. Available anti-convulsant drugs effectively control epilepsy in about 50% of the patients. Many epileptic seizures are refractory to current anti-epileptic drugs and safety of the anti-

epileptic drugs has always been a concern. Herbal drugs may serve as the alternative for some such patients. Many plants have been used for the treatment of epilepsy in traditional system of medicines have shown useful anti-seizure activity. Herbal remedies have become popular, due in part to the lower risk of adverse reactions. Thousands of plants have been used traditionally to treat various diseases. Among them, species of the genus Piper are important medicinal plants used in various systems of medicine. The Piper longum fruit has been used in traditional medicine, including the Ayurvedic system of medicine.[1] Although there are numerous indications for its use and plant contains many active constituents, controlled trials are needed to determine its anti-epileptic efficacy in small animals.[2-4] The present study was done to evaluate anti-seizure activity of fruits of Piper longum on animal models of seizures and also to find out effectiveness of aqueous and alcoholic extract.

Keywords: anti-oxidant action; anti-seizure activity; fruits; piperine; traditional medicine;

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P-124

Identification and characterization of a putative heptadic sequence of phenylalanine in Lipopolysaccharide neutralizing property of Temporin L and promoting its anti-endotoxin activity

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A 13-residue frog antimicrobial peptide Temporin L (TempL) possesses versatile antimicrobial activities and is considered as a potential lead molecule for the development of new antimicrobial agents. To investigate about the amino acid(s) or amino acid sequences that control the anti-endotoxin property of TempL, a phenylalanine zipper like sequence was identified in it. To evaluate the role of this structural motif, several alanine-substituted analogs and a scrambled peptide having the same composition of TempL were designed. Further, to investigate if leucine residues instead of phenylalanine residues at 'a' and/or 'd' position(s) of the heptad repeat sequence could alter its anti-endotoxin property, several TempL-analogs were designed by substituting these phenylalanine residues with leucine residues. Substitution of phenylalanine residues with alanine residues in the phenylalanine zipper sequence significantly compromised the anti-endotoxin property of TempL as evident by monitoring the TNF-? and IL-6 productions in LPS-stimulated rat bone marrow derived macrophage cells in the absence and presence of TempL and its analogs. However, introduction of leucine residues at the same positions of

phenylalanine zipper sequence significantly augmented the anti-endotoxin property of TempL. The alterations in anti-endotoxin property of TempL following these amino acid substitutions was supported by the change in secondary structures and self-assembly properties of TempL-derived peptides in LPS as well their binding to LPS and peptides-induced dissociation of LPS-aggregates. The results for the first time demonstrate a crucial role of the identified phenylalanine zipper sequence in anti-endotoxin activity of TempL and promoting its anti-endotoxin property by simple amino acid substitutions.

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P-125

Synthesis of Novel fused Ring Pyridine Morpholine Sulphonamide Derivatives

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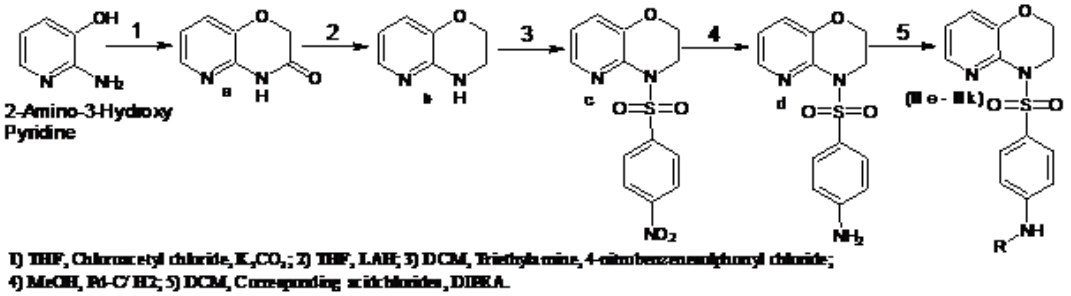
In this study, we have prepared fused ring morpholine. A series of seven novel 4-(2,3-dihydro-4H-pyrido[3,2-b][1,4]oxazin-4-ylsulfonyl)aniline Figure 1 (II e - II k) were synthesized in multistep reaction from commercially available 2-amino-3-Hydroxy pyridine as a starting material. The chemical structures of the synthesized compounds were confirmed by means of 1HNMR and mass spectral data. The High yield and high purity indicates lack of side reaction and by product. Also the synthesized compounds were going to be examining for their antibacterial and antifungal activities in future.

Figure 1: Reaction scheme:



Keywords: Fused Morpholine, pyridine morpholine, Sulphonamide, Sulphonylaniline.

P-126

Synthesis and Biological Evaluation of Flourescent Coumarin-triazoyl Conjugated Glycosides as Potential Antitubercular Agents

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Coumarin derivatives which are widely distributed in the plants have been extensively investigated as anticoagulation, antiviral, anti-inflammatory, antibacterial and anticancer agents.1 Glycosides in which the sugar unit is linked to a coumarin pharmacophore constitute a novel class of glycosides, namely the coumarin glycosides and possess a broad range of biological activities.2 In accord with the intriguing biological profile of coumarins, coumarin glycosides exhibit a broad spectrum of biological activities, such as anti-inflammatory,6 anticoagulant,7 anticancer,8 and antibacterial activities,9 and they are also useful as fluorescent probes for studies on ultrafast DNA dynamics.10Another promising group, 1,2,3-triazole, has emerged as one of the most important heterocycles in current medicinal chemistry and its applications have also been extended to widespread diseases.3

At the same time coumarins and their derivatives show sufficient fluorescence in the visible light range to be used in laser dyes and organic light-emitting diodes. High quantum yields, large extinction co-efficients, and suitable enzymatic and photostability of coumarin dyes make this class of fluorophores excellent candidates for fluorescent labeling of biomolecules and for application as fluorescent probes in different imaging procedures.4The unique photophysical properties of coumarins, their broad distribution in nature and high implication in metabolic and biochemical processes opens the possibility to use these natural products for construction of fluorescent analogs of biomolecular building blocks. 5

While the conjugates of 1,2,3-triazole and coumarin fighting against different diseases have made significant progress, efficient molecules against global tuberculosis control are still urgently needed.
In our study, we concentrate on synthesis of fluorescent coumarin derivatives which are of interest not only because of their antitubercular activities but also because of their application as fluorescent labels in various biological applications. We have synthesized a series of coumarin triazolyzed glycosides and have done their fluorescence and antitubercular activity. The details of scheme and compounds will be presented during poster session. Coumarin was chosen as the profluorophore since it is small in size and also the coumarin and its derivatives represent one of the most active classes of compounds possessing a wide spectrum of biological activity[1-9] Many of these compounds have proved to be active as antitumor[1-2], antibacterial[3,4], antifungal[5-7],anticoagulant[8] and antiinflammatory[9]. In addition, these compounds are used as additives to food and cosmetics [10], dispersed fluorescent and laser [11]. Various analogues of 3-substituted coumarins such as 3-aminocoumarins exhibit antimicrobial activity [12, 13].

In view of this, some novel coumarin-sugar conjugates have been synthesized under the click condition utilizing azido coumarins and sugar propargyl ethers.Azido coumarins were made to react with propargyl ethers of sugars in the presence of CuSO4.5H2O or Cu (OAc) 2, sodium ascorbate in tertiary butanol and water at room temperature to afford regioselectively 1, 4-disubstituted triazole linked coumarin based glycoconjugates. Recently 1, 3-Dipolar cycloadditions (1,3 - dcr) of azides and alkynes (Click Chemistry) has attracted great attention of

many synthetic chemists as the process allows coupling two or more complex molecules resulting into new molecular entity containing triazole ring as linker 'Click chemistry' has been reported to be one of the most frequently used approaches in glycochemistry6 where libraries of compounds can be quickly synthesized. Fluorogenic click chemistry has recently emerged as an ingenious and powerful tool toward numerous biochemical purposes A series of coumarin triazolylglycosides were synthesized in good yields using copper-mediated 1,3-dipolar cycloaddition reactions of carbohydrate azides and 4-alkynyl-substituted coumarins. Tuberculosis (TB) is a global health priority not only due to its morbidity and mortality but also due to its high contagious nature. Thus, it is second largest killer worldwide by a single infectious disease. TB becomes fiercer in combination with HIV or cancer. Therefore, there is an urgent need to explore new antitubercular agents.

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P-127

Microwave Assisted Synthesis of C-4?-Triazolo-spiro-xylonucleosides

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The Huisgen 1,3-dipolar cycloaddition between azide and alkyne leading to 1,2,3-triazole moiety has gained considerable attention due to its vast applications. With the novel structural features and physiochemical properties, triazole is recognized as a privileged structure in drug design and discovery. Presence of a spirocarbon in nucleosides may restrict the flipping of sugar ring that have a profound impact on the properties of the compound and can modulate the biological activity of nucleosides. Since the synthesis of sugar-modified nucleosides is an arduous task, especially with all natural nucleobases, we have synthesised our designed C-4?-triazolo-spiro-xylonucleosides (I-IV, Figure 1) under microwave irradiation. The detailed synthetic scheme will be presented during the poster session.

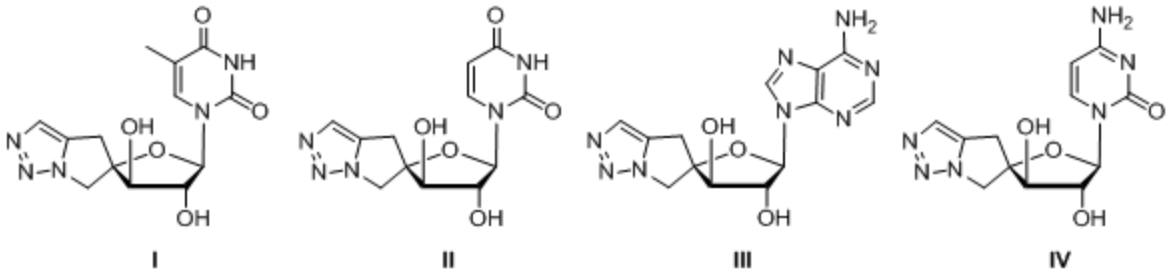

Figure 1. Structures of targeted C-4?-triazolo-spiro-xylonucleosides (I-IV).

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P-128

In vitro activities of root juice of musa balbisiana relevant to treatment of diabetes

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Diabetes mellitus (DM) is known to cause hyperlipidemia through various metabolic derangements. Among several metabolic derangements, insulin deficiency has been considered to stimulate lipolysis in the adipose tissue and give rise to hyperlipidemia and fatty liver. Thus in diabetes hypercholesterolemia and hypertriglyceridemia often occurs, leading to oxidative stress and increase free radical generation, which are hypothesized to play a significant role in the pathogenesis of DM. Folklore studies have revealed that root juice (RJ) of Musa balbisiana (MB) is used for the treatment of diabetes. In the present investigation the antioxidant, antihyperglycemic and antihyperlipidemic activity of RJ of MB was evaluated in STZ induced diabetic rat. In in vitro antidiabetic assay RJ inhibit the glucose movement in the dialysis bag as compared to the control (no extract). RJ was feed orally for 15 days to the STZ induced rat. Hypoglycemic effect, change in body weight, water intake and lipid profile of diabetic mice treated with RJ was assessed and compared with normal, diabetic control and standard drug (glibenclamide) treated rat. Significant differences were observed in fasting blood glucose ($p<0.05$), water intake, body weight and serum lipid profile ($p<0.01$) of RJ treated diabetic rat, when compared with diabetic rat. It can be concluded that RJ possesses antihyperglycemic properties. In addition this extract can prevent some diabetic related complications.

Keywords: Antioxidant, hyperglycemic, hyperlipidemia, hypertriglyceridemia,Musa balbisiana.

P-129

(S)-PyrrolidineContaining Chiral Mn(III) Salalen and Salan complexes as Catalysts for the Asymmetric Nitro-Aldol Reaction

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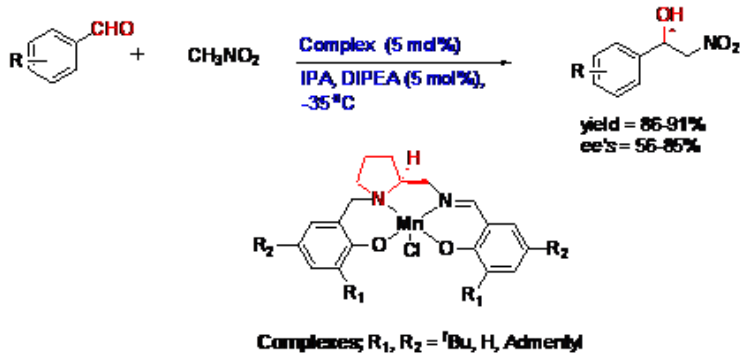
Chiral salen ligands are one of the privilege ligands in asymmetric catalysis and it's Mn(III) complexes were found to be very efficient catalysts for the asymmetric epoxidation reaction[1] and resolution of secondary alcohols [2], it's Copper complexes also efficiently catalyzed asymmetric henry reaction [3]. Herein, Chiral Mn(III) salalen and salan complexes synthesized from the (S)-proline were used as catalysts for the asymmetric nitro-aldol reaction. Recently we have also reported catalytic activity of these ligands in asymmetric Strecker reaction [4]. The 5 mol% of complex catalyzed the asymmetric nitro-aldol reaction gave yields upto 91%and ee's(85%).



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P-130

In vitro evaluation of carboxymethylated bael fruit gum as excipient for F4 fimbriae oral formulation

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In the present study, carboxymethylated bael fruit gum (CBFG) was investigated as a novel excipient for oral tablet formulation of F4 fimbriae vaccine to ensure its protection in the stomach and permit its consequent release in the intestinal fluid. Carboxymethylation of Bael fruit gum was achieved by reacting it with monochloroacetic acid under alkaline conditions. F4 fimbriae, thus formulated with CBFG as tablets showed a higher stability in gastric fluid containing pepsin after 2 h of incubation than the free, F4 fimbriae in solution which in these conditions digested completely. In simulated intestinal medium containing pancreatin, the F4 fimbriae were liberated from CBFG tablets over a period of 6 h based on the fast swelling during its passage from gastric acidity to alkaline intestinal medium, enzymatic hydrolysis triggering their rapid, almost total dissolution. Thus, F4 fimbriae formulated with CBFG showed higher survival rates in acidic gastric conditions and for extended periods than the free F4 fimbriae in solution.

P-131

A Metal-Free Tandem Approach To Prepare Structurally Diverse N-Heterocycles: Synthesis of 1,2,4-Oxadiazoles and Pyrimidinones

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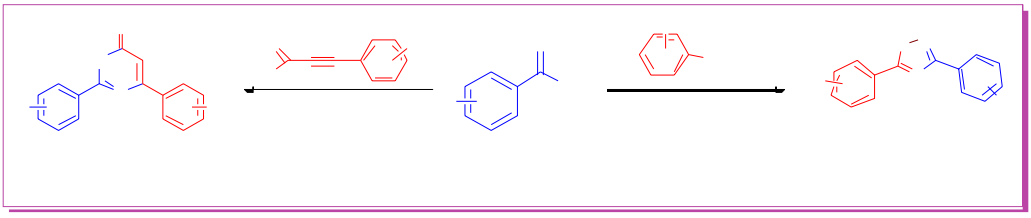
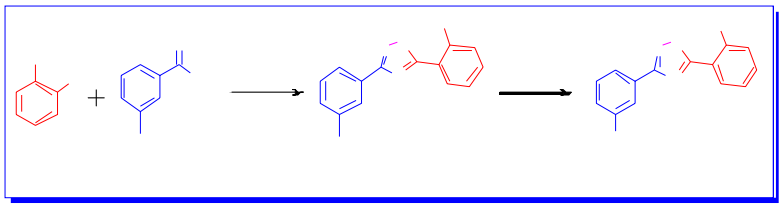
Abstract: Nitrogen-containing heterocycles are ubiquitous in many natural and synthetic bioactive molecules.[1] Within drug discovery and development, the 1,2,4-oxadiazole ring system is a privileged scaffold forming an essential part of several drugs and drug lead molecules.[2] Pyrimidinones are also of wide occurrence and display significant biological activities.[3] In this perspective, we report an innovative metal-free one-pot approach to the diversity oriented synthesis of N-heterocycles, 1,2,4-oxadiazoles and 2,6 disubstituted pyrimidin-4-ones via carboxamidation of amidines with aryl carboxylic acids and aryl propargylic acids.[4] The reactions occur at room temperature forming N-acylamidines which undergo tandem nucleophilic addition-deamination-intramolecular cyclisation to give the corresponding heterocyclic compounds in good to excellent yields. This one pot approach has led to the successful synthesis of the drug lead molecule, ataluren, 3-(5-(2-fluorophenyl)-1,2,4-oxadiazol-3-yl) benzoic acid[5] in two steps.





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P-132

In situ generated hydrochloric acid catalyzed synthesis of 14-substituted-14H-dibenzo [a, j] xanthenes at room temperature

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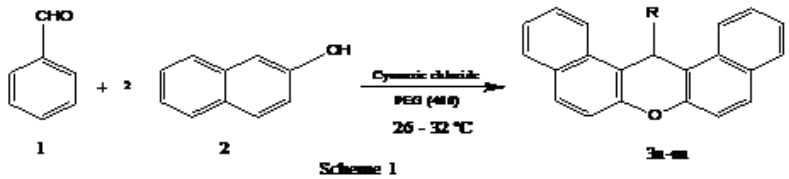
In recent years, the synthesis and pharmacology of xanthenes have been extensively investigated due to their wide range of biological activities. They display many activities such as antiviral Seyyedhamzeh et al [1], antibacterial Hideo et al [2] and anti-inflammatory activities Karimi-Jaberi et al [3], finds use in biodegradable agrochemicals Abdel Gali et al [4], cosmetics and pigments Ellis et al [5], fluorescent materials Callan et al [6], luminescent sensors Poupelin et al [7], and in laser technologies Banerjee et al [8]. Literature survey indicated a large number of reports on the synthesis of xanthenes. However, these reported methods have one or the other disadvantages such as tedious experimental procedure, use of hazardous reagent and high loading of catalyst. Consequently, there is scope for further renovation of such synthetic methods, which avoids both harsh reaction conditions and high loading of catalyst. Herein, we report a new, simple and efficient method for the synthesis of xanthenes using PEG-400 as solvent medium in presence of cyanuric chloride at room temperature (Scheme 1).



Scheme 1

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P-133

Synthesis of Novel fused Ring Morpholine Monofluoroaniline Derivatives

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Nitrogen and oxygen containing heterocyclic compounds like morpholine[1] and fused ring morphlines[2-3] are very important building blocks in medicinal chemistry[4] field. So the morpoline derivatives are extensively very essential in the drug discovery research, which stimulate research activity in the field of the broad spectrum of biological activity [5] study. After the literature survey that many morpholine derivative molecule are shows very good biological activity in different therapeutic area such as antibacterial[6], antiviral, anticancer, antimicrobial, antidiabetic, anti-Inflammatory, antimalarial, antifungal[7], Antiemetic etc.

It is well known that the introduction of fluorine[8-9] atom into organic molecule causes dramatic changes in its biological profile, mainly due to high electro negativity of fluorine causes increase lipid solubility. Hence, in the present study, some new derivatives of pyridinemorpholine-3-fluroaniline have been synthesized. Their characterization was done by spectroscopic methods like 1HNMR and mass spectral data. Also were the synthesized compounds were going to be examining their antibacterial and antifungal activities in future.

In this study, we prepared fused ring morpholine, a series of seven novel 4-(2,3-dihydro-4H-pyrido[3,2-b][1,4]oxazin-4-yl)-3-fluoroaniline (I e - I k) were synthesized in multistep reaction from commercially available 2-amino-3-Hydroxy pyridine as a starting material. The chemical structures of the synthesized compounds were confirmed by means of 1HNMR and mass spectral data. The High yield and high purity indicates lack of side reaction and by product. Also were the synthesized compounds were going to be examining their antibacterial and antifungal activities in future.

Keywords: Fused Morpholine, pyridine morpholine, Fluorophenyl, Fluroaniline.

P-134

C1-Symmetric Symmetricin situ generated Cu(II) Salalen and Salan complexes: Efficient Catalysts for Asymmetric Henry Reaction

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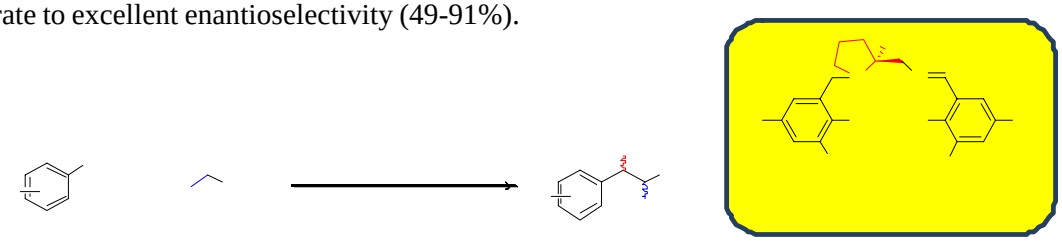
In situ generated Cu(II) salalen and salan complexes were used as catalysts for the asymmetric Henry reaction between aromatic aldehydes and nitromethane/nitroethane. The C1 symmetric Chiral salalen and salan ligands were synthesized from (S)-proline [1, 2]. These ligands are the analogous of Salen ligand, which are found to be very privileged lgands for the asymmetric Henry reaction [3]. Recently we have reported asymmetric strecker reaction with these (S)-proline derived chiral salalen ligands [2]. The 10 mol% ofin situ generated Cu(II) complex of ligand 2 was found efficient catalysts for the asymmetric Henry reaction in isopropanol by using 4-methoxyphenol (10 mol%) as an additive at room temperature, afforded the ?-nitro alcohols in good to excellent yield (62-93%) and moderate to excellent enantioselectivity (49-91%).



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P-135

Study on in vitro controlled release of L-Arginine encapsulated into unmodified MCM-41

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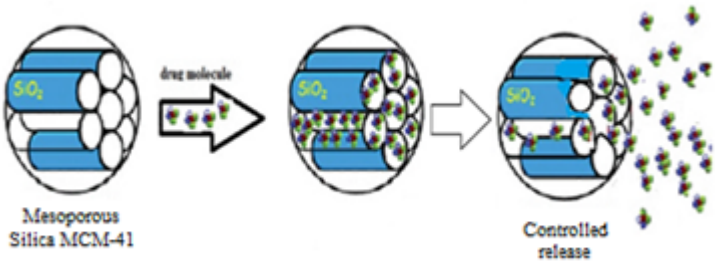
L-arginine is a semi essential amino acid and is also substrate for the synthesis of nitric oxide (NO) which is involve in maintenance of glomerular filtration rate, regional vascular tone, and renal blood flow, polyamines

which is involve in tissue repair and wound and agmatine and influence hormonal release and the synthesis of pyrimidine bases. It was found that in case of oral administration, the bioavailability of L-arginine decreases as it is utilized by arginase for the production of urea and ornithine and thus competes with NO synthase for substrate availability [1]. So, oral administration does not show any vasodilatory effect. Therefore oral administration of L-arginine using drug delivery system is expected to overcome the mention problems and provide sufficient amount of L-arginine for NO production. MCM-41 has emerged as a new generation of matrix for controlled drug delivery system [2].

The present paper consist synthesis of MCM-41, impregnation of L-arginine on MCM-41 and their characterization using various physicochemical techniques.



The controlled release study was carried with different amount of L-arginine loaded sample in simulated body fluid (SBF) at room temperature and under stirring condition. It was found that MCM-41was able to release L-arginine in a controlled manner. 55 % L-arginine release was observed for initial 10 h and then slow and delayed release was observed which was reached to 80% up to 32 h. We have also investigated the release mechanism and kinetics using first ordered release kinetic model as well as Higuchi model.

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P-136

Silicosis- An incurable lung disease

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Silica is the second most common element on the surface of the earth. It is found in sand, many rocks such as granite, sandstone, flint and slate, and in some coal and metallic ores. The cutting, breaking, crushing, drilling, grinding, or abrasive blasting of these materials may produce fine silica dust. Silicosis is a form of occupational lung disease caused by inhalation of crystalline silica dust, and is marked by inflammation and scarring in forms of nodular lesions in the upper lobes of the lungs. Silicosis is due to deposition of fine dust (less than 1µm in diameter) containing crystalline silicon dioxide in the form of alpha-quartz, cristobalite, or tridymite. Silicosis is

characterized by shortness of breath, fever, and cyanosis. It may often be misdiagnosed as pulmonary edema (fluid in the lungs), pneumonia, or tuberculosis. Treatment options currently focus on alleviating the symptoms and preventing complication. So here an attempt has been made to attract the attention of doctors, researchers, NGO's to develop a proper medication and vaccine kit for the complete treatment of this disease.

Keywords: Silica, Lung disease, Doctor

P-137

Synthesis and biological evaluation of novel curcumin like compounds as spermicides

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Sexually transmitted infections (STIs) are a group of communicable infections which are primarily transmitted through sexual contact. STIs may cause by different origins depending upon the causal organism (for ex. bacterial, fungal, viral or parasitic) Bacterial vaginosis, herpes, Chlamydia, trichomoniasis, gonorrhoea, Hepatitis B virus, HIV and syphilis are some of the common sexually transmitted diseases. Spermicides are contraceptive substances, when inserted in vagina prior to sexual intercourse, immobilize/kill the spermatozoa. Ideal spermicide should prevent the penetration of spermatozoa into the endo cervical canal of uterus along with microbicidal effects on the organisms responsible for STIs such as Trichomonas vaginalis, N. gonorrhea, T. pallidum, Candida albicans and other species. Moreover spermicides should be nonirritating to vaginal and penile mucosa, and also the organisms such as Lactobacillus.

Curcumin (diferuloyl methane), a yellow compound present in the rhizomes of Curcuma longa(Turmeric, a well-known Indian spice) possesses array of biological activities namely anti-tumor, anti-inflammatory and anti-infective activities along with activity against HIV. When curcumin is used in the concentrations of 300 ?g/mL, 100% immobilisation of spermatozoa was achieved.

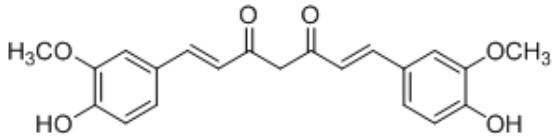

Fig: Structure of curcumin

In this present investigation we have targeted to synthesize a series of compounds which have resemblance with curcumin structure and their spermicidal activity was observed. Details of these compounds and their activity will be discussed during the presentation.

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P-138

Design, synthesis and mode of action of some new amide derivatives of 2-(4?-aminophenyl) benzothiazole as potent antimicrobial agents

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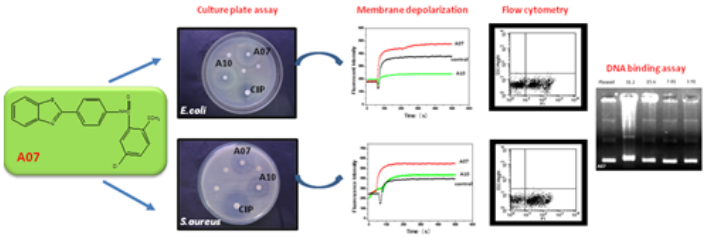
In this study novel benzothiazole derivatives bearing amide moiety were designed, synthesized and evaluated for their antibacterial activity with possible mode of action. Structures of the synthesized compounds were elucidated by 1H NMR, 13C NMR, IR and Mass spectral data. These compounds were screened against four different gram-negative and two different gram-positive bacterial strains by agar disc diffusion method [1]. Among all the synthesised compounds, compound A07 displayed most potent inhibitory activity with minimum inhibitory concentration (MIC) values of 15.6, 7.81, 15.6, 3.91 µg/ml against S. aureus, E. coli, S. typhi and K. pneumoniae respectively. Structure-activity relationship (SAR) studies revealed that electronic and lipophillic factors of phenyl ring had a significant effect on the antimicrobial activity of the designed compounds. The benzothiazole bearing amides exhibited different modes of action based on aryl group substitution as revealed by studies on intact bacterial cells and plasmid DNA. The present study provides us two active compounds (A07 and A10) with membrane perturbing mode of action, elucidated by membrane depolarization, and fluorescent assisted cell cytometry (FACS) and, intracellular mode of action due to binding with DNA.



Schematic outline of most potent compound, benzothiazole bearing amide moeity A07 showing antibacterial activity and its mode of action.

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P-139

Validated HPLC method for estimation of chiral purity of a new antimalarial compound CDRI- S011-1793 and its isomer S012-0585

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The difference in chirality and enantioselectivity not only affects the pharmacodynamics but also largely alters pharmacokinetics (ADME), which consequently leads to the variation in effects and biological activities. Adopting enantiomer selective analytical methods and specification of enantiomeric purity of the optically active compounds prior to marketing of a new drug is a pre-requisite according to USFDA guidelines. With this aim a new validated HPLC method for chiral separation of CDRI compound No S011-1793 and S012-0585 has been developed. Compound S011-1793 is a 4-aminoquinoline derivative with potential antimalarial activity. Final separation was achieved on a Phenomenex-LUX cellulose-1 chiral column with the mobile phase comprising of hexane, isopropanol, methanol (95:4.5:0.5) and incorporation of triethylamine (0.8%) with flow rate being 2.0 mL/min and detection wavelength being 254nm. The percentage optical purity was found to be 98.89% and 99.43% on area normalization basis and retention times were about 5.50 min and 7.70 min for S011-1793 and S012-0585 respectively. The method was validated on parameters of LOD, LOQ, linearity, inter and intra-assay variations, robustness and recovery as per ICH guidelines.

P-140

Protective effect of a Di-Herbal Formulation of Clerodendron colebrookianum and Allium sativum on lipid peroxidation and antioxidant status in Hypercholesterolemic rats

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Hypercholesterolemia, the most common cause of atherosclerosis, is treated in the North-east Indian traditional phytotherapies with a decoction of Clerodendron colebrookianum (CC) and Allium sativum (AS). The present study evaluates the protective effects of a di-herbal formulation (HF) of CC and AS in high cholesterol diet induced hypercholesterolemia in rats. Five groups of six Wistar albino rats each viz. Control, Hypercholesterolemia (HC), HC plus HF (100 mg/kg bodyweight of rat), HC plus HF (200 mg/kg bodyweight of rat) and HC plus standard drug (Finofibrate) were studied in a chronic model of hypercholesterolemia conducted for duration of 28 days. The serum lipid profile, Thiobarbituric acid reactive substances (TBARS) level as indicator of lipid peroxidation and level of antioxidant enzymes were estimated. Treatment with HF showed significant ($P<0.01$) reduction in serum lipid profile (Total Cholesterol, Triglycerides, LDL-cholesterol), TBARS and increase in

antioxidant enzymes in a dose dependent manner when compared to the hypercholesterolemic group. The results of the study clearly indicate that aqueous extract of HF has significant effect on hypercholesterolemia associated lipid peroxidation and antioxidant status. Hence, it can be explored as a potentially promising remedy for prevention of hypercholesterolemia.

Keywords: Herbal formulation, Hypercholesterolemia, Clerodendron colebrookianum, Allium sativum, Lipid peroxidation, Antioxidant enzymes

P-141

Clinical Evaluation of Antidiabetic Activity of Herbal Formulation (Mehagni)

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Diabetes mellitus is a heterogeneous metabolic disease characterized by altered carbohydrate, lipid and protein metabolism. So many traditional herbs are being used by diabetic patients to control the disease. But very few studies are performed to investigate the efficacy of these herbs clinically. In the present study, an attempt has been made to investigate clinically the antidiabetic activity of herbal formulation which is contained Haridra, Amalaki, Madhunasini, Ekanayakam, in non-insulin dependent diabetes mellitus (NIDDM) patients. Literature survey reveals their antidiabetic activity in animals, but no such studies were performed clinically. The study was performed in two different groups for a period of 3 months. Each group was having 20 NIDDM patients, whereas five patients were kept as control subjects. Inclusion and exclusion criteria were formed for the study. Written consent was taken from the patients. Initial fasting blood glucose level, postprandial blood glucose level (PPBGL), glycosylated hemoglobin (HbA1c) and urine glucose level was estimated at the time of registration in the study and then after each week during the entire period of the study. At the end of the study, the initial and final readings were compared. There were significant changes in FBGL, PPBGL and HbA1c of patients who were receiving these herbal formulation. Collectively as compared to the other patients who were on their standard oral hypoglycemic (glibenclamide) therapy.

Keywords: Antidiabetic activity, Mehagni, Glibenclamide.

P-142

Enantioselective Quantification of Carbinoxamine Maleate In Human Plasma Using A Polysacharide Based Chiral Column

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A chiral ultra fast liquid chromatographic method was developed and validated for separation of carbinoxamine maleate enantiomers in human plasma. The bioanalytical procedure involves extraction of carbinoxamine maleate enantiomers and pargeverine hydrochloride (internal standard) from human plasma with a simple liquid-liquid extraction process. No endogenous substances were found to interfere with the peaks of drug and internal standard. Resolution was obtained in a normal phase mode on a Lux amylose-2 (250 x 4.0mm, 5?m) column with mobile phase composed of n-heaxane : isoproponol :ethanol :diethylamine (85:7.5:7.5:0.1v/v), at a flow rate of 1.0ml/min. The enantiomers and internal standard were detected at 220 nm wavelength using a photodiode array detector. The internal standard and both the enantiomers were detected at 4.9, 5.8min and 6.7 min, respectively. Method validation was performed as per US Food and Drug Administration guidelines and the results met the acceptance criteria. The correlation coefficient for linear regression curves of enantiomer 1 and enantiomer 2 were ?0.997. The inter-day precision and intra-day precision coefficient of variations was 4.26% or less for all the selected concentrations. The accuracy determined by average recovery of enantiomer1 and enantiomer 2 were within the acceptable limits. The method was useful for the monitoring the enantiomers kinetic behaviour in the human plasma.

P-143

Validated Bio-Analytical Method Development for Simultaneous Estimation of Clopidogrel and Aspirin in Human Plasma by Rp-Ultra Fast Liquid Chromatography

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A simple, sensitive, rapid and precise Ultra fast liquid chromatographic (UFLC) method for the simultaneous determination Clopidogrel and Aspirin in human plasma according to USFDA draft guidelines was developed and validated.

In the current study, the analysis was performed on phenomenex C8 (250 × 4.6mm, 5?m) column using phosphate buffer (pH-2.5) and acetonitrile (35: 65 v/v) as mobile phase at flow rate of 1.5 mL/min. In this developed method Clopidogrel and Aspirin eluted at a retention time of 2.697 and 5.337 min respectively. The proposed method is having linearity in the concentration range from 10 to 50?g/mL of Clopidogrel and Aspirin. The current method was validated with respect to linearity; precision, lowest limit of detection (LOD), accuracy and recovery according to the USFDA guidelines.

The system consisted of a pump (Shimadzu, prominence, UFLC), with 20µl sample injector, along with a PDA detector at a wavelength of 230 nm and 252 nm for Aspirin and Clopidogrel respectively. Data was compiled using Shimadzu LC Solution software.

A good linear relationship over the concentration range of 10-50µg/ml was shown. Validation of the method was carried out as per the USFDA draft guidelines. The method developed was found to be precise, accurate, specific, linear and selective.

Statistical analysis shows that the method is reproducible and selective for the estimation of Clopidogrel and Aspirin in dosage form.

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P-144

Ligand free Pd-Catalyzed Isocyanide Insertion using Ugi-MCR Precursers: Synthesis of Pyrido[1, 2-a]imidazole-isoquinoline polycycles

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Isocyanides based multi component reactions have emerged as powerful tool in the construction of small heterocycles of biologically important scaffolds.1 The unique property of the isocyano group, which enables isocyanides to react with electrophiles, nucleophiles, and radicals has made these synthons versatile for its application in organic synthesis.2 Recently discovered isocyanide insertion reactions are continuously exploring for its application in heterocyclic synthesis.3 Following our work on isocyanide insertion, we have developed a library of pyrido[1, 2-a]imidazole-isoquinoline polycycles using Ugi-MCR adduct via Pd(OAc)2 mediated insertion cyclisation approach.4

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P-145

Synthesis of Novel Betacarboline-Tetrazole Hybrid as Antileishmanial agents

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Leishmanaisis affects almost 88 countries of which 72 are classified as developing countries, including 13 of the least developed countries in the world with a population of 350 million at risk.1 Among these visceral leishmaniasis (VL) is most severe form, called Kala-azar or black fever that are transmitted between hosts by the bite of female phlebotomine sand flies. Current remedies is mainly depends on heavy matals based drugs which are toxic enough for long time treatment.2 Tetrazoles are resistant to biological degradation thus they could be isosteric substituents of various functional groups in the development of pharmaceutical products.3 As part of our continuing research which approaches pharmacophore hybridization to develop novel chemotherapeutic agents against L. donovani, we developed a series of tetrazole containing cyclic betacarboline backbone and evaluated their antileishmanial activity as well as their cytotoxicity.4

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P-146

Design and synthesis of the natural product inspired tetrahydroquinoline- tetrazole hybrid as antileishmanial agents

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Chemotherapy against leishmaniasis is inadequate because it is mainly based on antimony agents like sodium stibogluconate and meglumine antimoniate, amphotericin B, miltefosine, and paromomycin and the mode of action of these compounds are poorly understood [1]. Leishmaniasis is a disease caused by infection with human protozoan parasites belonging to the Leishmania [2]. Recently, the emergence of drug resistantance has led to

treatment failures for many infectious diseases, including malaria and leishmania. Small nitrogen heterocycles such as quinolines [3], pyrimidines [4] and other classes of compounds have been reported as antileishmanial agents. Isoquinoline analogues, berberine, an active leishmanisidal constituent of many plant families (e.g. Annonaceae, Menispermaceae, Berberifaceae) showed highest leishmanisidal activity [5]. In our journey against anti-infectious diseases, our group has identified some synthetic analogues of Isoquinoline as potent antileishmanial agents [6]. Herein, we have synthesized a series of natural product based tetrahydroquinoline-tetrazole hybrids with our delight some of derivatives showed significant antileishmanial activity (IC50 range 1.67 to 5.91 μM) against extracellular promastigote stage which are further tested for intracellular amastigote activity.

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P-147

Biophysical Characterization of Saccharomyces cerevisiaeRegulator of Transcription Protein 'Rtr1'

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Rtr1 is the enzyme responsible for the transition of RNApolymerase II (RNAPII) into the elongation and termination phases of transcription by removing the phosphoserine 5 mark present on highly conserved carboxy terminal domain (CTD) of RNAPII which comprises of multiple heptapeptide repeats with the consensus sequence Y1S2P3T4S5P6S7.Activity of Rtr1 resides in its N-terminus (NTD,highly conserved)and auto inhibited by C-terminus (CTR, less conserved). NMR analysis on S. cerevisiae Rtr1 yields well dispersed peaks from the NTD, suggesting for a domain with a well-defined fold, while peaks originating from the CTR cluster within a narrow spectral region are more intense, suggesting the partially structured protein.In our study we have cloned, overexpressed and purified full length Rtr1 as well as NTD and CTR. We have performed the activity analysis of these three proteins with para nitro phenyl phosphate (pNPP) as a substrate. We have also analyzed the oligomeric assembly and denaturation profiles of these proteins.To find out the position of interaction of Rtr1 with RNAPII CTD we have used a GAL4 based yeast two hybrid assay using mutant CTDs (CTD repeats with combinatorial Ser2, Ser5 and Ser7 mutations) as prey and full length Rtr1 as bait.

P-148

Recognition and Evaluation of Mycobacterial Triacylglycerol Synthase Promoter Activity under Diverse Environmental Stress Conditions Using True-Red Reporter

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Mycobacterium tuberculosis (M.tb) stores fatty acids in the form of triacylglycerol (TAG) for use as a source of carbon and energy during dormancy. M.tb genome encodes 15 genes related to TAG metabolism among which only triacylglycerol synthase 1(tgs1) is characterised. For instance a truncated tgs1 does not completely stop TAG accumulation by M.tb which means that other tgs enzymes can take over the job at least partially.Here we report about one such tgs gene (conserved hypothetical protein) which is least characterised and shows significant amino acid sequence identity to diacylglycerol acyltransferase family of A. calcoaceticus. In our study we identified the native promoter of the gene and assayed promoter activity under different environmental stress conditions using true-red reporter Turbo-602 RFP. Reporter expression helps to comprehend the role of tgs in adverse environmental cues and contributes towards understanding the dormant bacilli. Consequently triacylglycerol synthase induction can be a prospective anti-TB drug target.

P-149

A reversed-phase liquid chromatography method development and validation for S007-1235, a potent anti-leukemic compound, in rat serum and application to serum protein binding studies

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In quest of search for new, safe and potent anti-leukemic agent, Central Drug Research Institute has developed S007-1235, a thioaryl naphthylmethanone oxime ether analog. The compound displayed robust cancer cell-specific cytotoxicity and promising anti-proliferative activity with good safety index [1]. To develop it as a potential candidate drug the pharmacokinetic profiling of the compound is essential, for which a validated bioanalytical method in suitable biomatrix is a prerequisite. With this rationale a simple and robust reversed-phase high performance liquid chromatography (RP HPLC) method was developed and validated for quantitative determination of S007-1235 in rat serum. Chromatographic separation was achieved on a Supelco Discovery HS C18 (5 µm, 100 × 4.6 mm) column using acetonitrile, methanol and phosphate buffer (PB, 0.01 M, pH 3.5) (30:35:35, % v/v) as mobile phase at a flow rate of 1.0 mL/min. Detection was performed at wavelength 290 nm.

Serum samples were processed by employing simple liquid-liquid extraction technique using n-hexane and isopropyl alcohol (98:3, % v/v). The method was validated in terms of selectivity, accuracy, precision, sensitivity, reproducibility and stability as per the US FDA guidelines [2]. The linearity was established in the range 10 to 2000 ng/mL (R2 ? 0.999). Recovery of the compound from spiked control serum was more than 95% with the variations (accuracy and precision) within acceptable limits. The method was successfully applied for determination of serum protein binding of S007-1235 in rat serum using charcoal absorption assay [3].

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P-150

Identification of novel phenyl butenonyl C-glycosides with ureidyl and sulfonamidyl moieties as antimalarial agents

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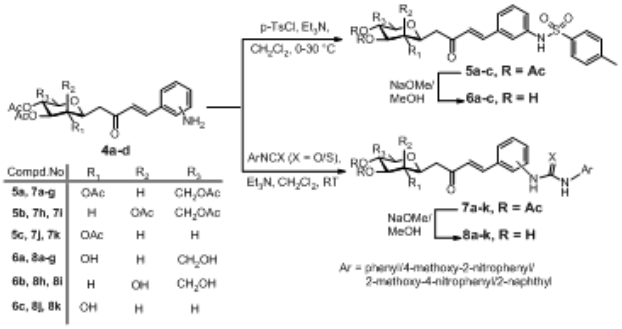
Malaria, the most severe parasitic disease, infects more than 500 million people and continues to kill around one million children each year. Mostof the malarial infections and deaths are due to Plasmodium falciparum and Plasmodium vivax species. The recent emergence of resistance necessitates the search for new antimalarial drugs which overcome the resistance and acting through novel mechanisms. The dihydropteroate synthase (DHPS), hemoglobin degradation enzymes, and shikimate pathway enzymes have been identified for the novel potential targets for new antimalarial drugs in the last decade Roberts etal.[1] Very recently a class of hemoglobin degradation enzymes,plasmepsins has been discovered as a validated drug target and diphenylureas are known to inhibit this enzyme and display antimalarial activityJiang etal.[2]Diphenylpropenones (chalcones)also exhibit antimalrial activity and malaria trophozoite cysteine protease has been proposed as possible target for this class of compound Dominguez etal. [3]

Inspired by the above facts we thought to design and synthesize compounds based on sugars having C-linked phenyl propenone moiety and diphenyl urea units together to get hitherto unreported antimalarial agentsTripathi etal. [4] In order to further analyze the feature requirement of these molecules in 3D space, we analyzed the common features through HipHop algorithm.



Compd.No	R_1	R_2	R_3
5a, 7a-g	OAc	H	CH_2OAc
5b, 7h, 7i	H	OAc	CH_2OAc
5c, 7j, 7k	OAc	H	H
6a, 8a-g	OH	H	CH_2OH
6b, 8h, 8i	H	OH	CH_2OH
6c, 8j, 8k	OH	H	H

Scheme: Synthesis of the N-sulfonylaminophenyl, ureido and thioureido glycopyranosides

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P-151

Copper Catalyzed Highly Efficient Oxidative Amidation of Aldehydes with 2-Aminopyridines in Water

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The amides are important building blocks in organic chemistry and ubiquitous in natural products and pharmaceuticals. Transition metal catalyzed oxidative amidation is gaining more attention for synthesis of diversified amides. Oxidative amidation of aldehydes with amines is more atoms economic and there is more substrate scope. However, these reactions required high temperature, high catalyst loading, strong bases, ligands and anhydrous organic solvents. Thus, there is an emergent need of oxidative amidation methodologies in aqueous media under mild conditions. N-(pyridine-2-yl) amides are biologically active scaffolds such as some glucokinase activators are in second phase of clinical trials, Matschinsky et al. [1]. Previously, Huang et al. [2] reported the synthesis of N-(pyridine-2-yl) benzamide derivatives using CuI in DMF at 80º C for 24 hr. We have developed an efficient amide synthesis from aldehydes with 2-amino pyridines by using Cu salts as catalyst and molecular iodine as an oxidant under mild condition in water (Scheme 1). Further biological studies of these compounds are under progress.

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P-152

Synthesis and Characterizations of Some Novel Pyrimidothiazenes for their Biological Activity

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Pyrimidines play an important and unique role in medicinal chemistry because it is an important constituent of nucleic acids. Furthermore, these pyrimidine derivatives are found to have wide range pharmacological activities as phosphodiesterase inhibitor [1], antiviral [2], antileishmanial [3], antibacterial [4], diuretics [5] and antihypertensive [6]. Due to development of drug resistance in parasitic area as the existing drugs have limited in their pharmacological efficacy, designing of new potent, selective and less toxic pharmacologically active heterocycles remains a major challenge for medicinal chemists. Keeping in view importance of pyrimidines in antiparasitic area, we have presently synthesized the a series of some novel substituted pyrimidothiazenes for their antiviral potency. Some of the synthesized molecules displayed significant antiviral activity. In this presentation, the detailed synthetic procedure, mechanism of reactions characterizations by their spectral data (1H NMR, 13C NMR, IR, EIMS and UV) analysis and antiviral activity of the synthesized compounds will be discussed.

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P-153

Tungstic acid as an efficient catalyst for the synthesis of benzimidazoles

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Benzimidazole derivatives are of wide interest because of their diverse biological activity. The compound which contains benzimidazole nucleus shows activities like antitumor, antiviral, atimalarial, anti-inflammatory etc. Lansoprazole, Omeprazole, Pentaprozole, Thiobendazole are already used as drug candidates. In addition, benzimidazoles are very impotent intermediates in synthetic routes and serve as ligands for asymmetric catalysts.

Due to the numerous biological and synthetic applications of the benzimidazole compounds has prompted organic chemist to study their syntheses. In this context, numerous efforts have been made to synthesize benzimidazole derivatives.

One of the most common methods for the preparation of benzimidazole derivatives involves the condensation of an o-phenylenediamine and carbonyl compounds such as aldehydes and acid derivatives. The condensation of o-phenylenediamine with carboxylic acid often requires strong acidic conditions and high temperatures, this is the most popular approach in general for the synthesis of benzimidazole derivatives. Literature survey revealed that the condensation of o-phenylenediamine with different substituted aldehydes in the presence of various catalysts viz. SC(OTf)3 or Yb(OTf)3, sulphamic acid, H2O2-HCl, FeBr3, DDQ, PhI(OAc)2, KHSO4,HfCl4 BF3.OEt2, ceric ammonium nitrate, iodine, Silica sulphuric acid etc to yield the 2-substityetd benzimidazoles.

Unfortunately, many of these methods suffer from one or other kind of drawbacks such as drastic reaction conditions, low yields, tedious workup procedures, and co-occurrence of several side reactions. Therefore the development of new efficient method to overcome these drawbacks is needed.

As part of our research activity in developing various synthetic methodologies, we have developed facile method for the synthesis of benzimidazoles using tungustic acid as an efficient catalyst by the cyclocondensation of aldehydes with o-phenylenediamines. The reaction completed within short time with high yields of the products and catalyst is recoverable from reaction and reusable.
The details of the work will be presented.

P-154

Aminoquinoline-Pyrimidine Hybrids: Synthesis, Antimalarial Activity and SAR studies

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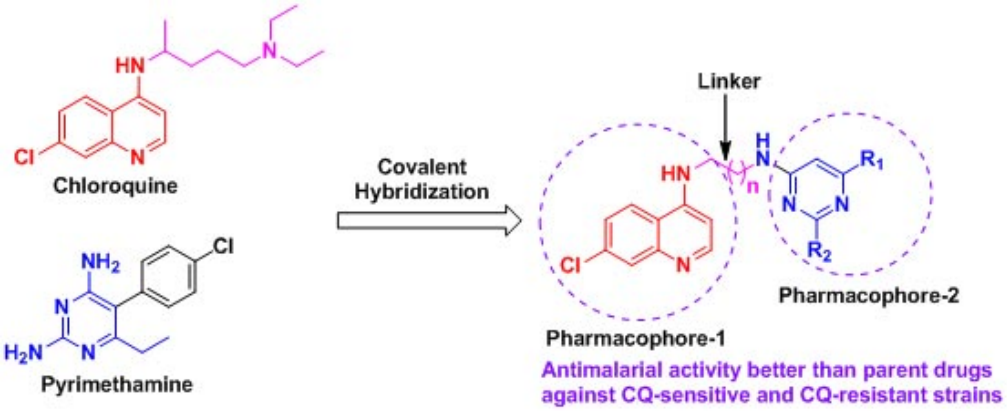
Malaria, transmitted in humans through the bite of female Anopheles mosquito and caused by the infection with any of the five species of Plasmodium viz. P. vivax, P. malariae, P. ovale, P. knowlesi and P. falciparum, of which the latter one is the most lethal, is still epidemic in large parts of the world, especially in sub-Saharan Africa, South America and Southeast Asia with approximately 207 million cases of malaria in 2012 and an estimated 627 000 deaths. Currently, WHO recommends artemisinin-based combination therapy with a conventional antimalarial due to the fear of development of parasite resistance and persistence in the body of the host [1]. Several approaches have been made towards the development of new antimalarial agents to address the problem of drug-resistance, and the concept of molecular hybrids has shown promising results. In hybrid antimalarials, two (or more) discrete antimalarial scaffolds are linked covalently, usually through a spacer, in an anticipation that these compounds may act by inhibiting simultaneously two (or more) different conventional targets [2]. Towards this end, we had synthesised 4-aminoquinoline-pyrimidine based hybrids [3-6] in an anticipation that these may act by simultaneously disrupting the heme-detoxification pathway (by 4-aminoquinoline core) and halting the tetrahydrofolate synthesis (DHFR inhibition by pyrimidine nucleus) in the malarial parasite. The synthesized hybrids have shown promising in vitro and in vivo antimalarial activities against CQ-sensitive and CQ-resistant P. falciparum strains. Further modifications on these hybrids have revealed interesting structure-activity relationships which will help in improved design of these hybrids with better antimalarial potential [7].



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P-155

Novel 3,5-bis(arylidiene)-4-piperidone based monocarbonyl analogues of curcumin: Anticancer activity evaluation and mode of action study

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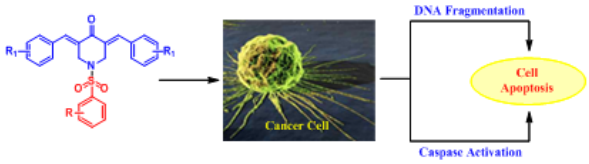
Diversity of biological functions depends upon the interactions that protein undergoes. Such interactions are critical for practically all cellular, signalling and regulatory pathways. The dysfunction of these pathways is the cause of many diseases including cancer and neurological diseases. Therefore, controlling the damages and alterations due to these protein interactions that causes or accelerate human diseases is a prime target for drug discovery [1]. Target specific therapeutics generally cannot combat multi-genic diseases such as cancer, or diseases that affect multiple tissues. Therefore, to combat this issue, combination therapy and multi-targeted hybrids offer a better approach in curtaining these diseases [2]. Curcumin remains one of the most widely studied bioactive agent which is attributed to its diverse health benefits such as antioxidant, antibacterial, anti-inflammatory, anticarcinogenic, analgesic, wound healing, and eupeptic properties. But poor pharmacodynamics and pharmacokinetic profile have halted its journey to become a successful drug. In order to improve its bioavailability and ADMET properties, 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]. Sulphonamide moiety connected to aromatic/hetrocyclic/aliphatic ring is an important pharmacophore for the generation of new drugs [4]. Therefore keeping in mind the concept of hybrid molecules and in continuation of our on-going efforts in this area [5-8], 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.



Mode of action studies of piperidone-sulphonamide curcumin conjugates

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P-156

Coupling of Phenylhydrazines in Water to access Biaryls and biologically active molecules

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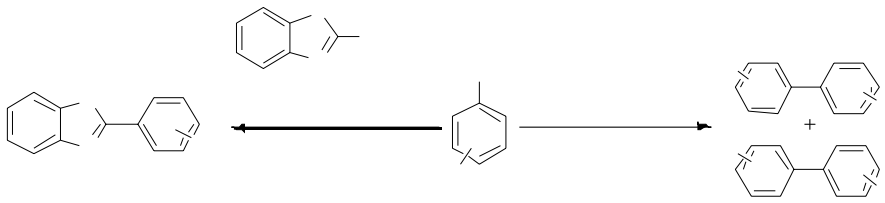
An efficient protocol has been developed for the synthesis of biaryls via Pd/Cu catalyzed coupling of phenylhydrazines in water. Homo and cross couplings were successfully achieved in a ligand-free catalytic system, at room temperature and water as sole reaction medium. The present method also afforded unique 4,4'-biquinoline and anticancer pharmacophore 2-arylbenzothiazole efficiently.



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P-157

Synthesis of oxadiazole and pyrimidine fused 1,4-benzodiazepine analogues of medicinal interest through phenylamino spacer

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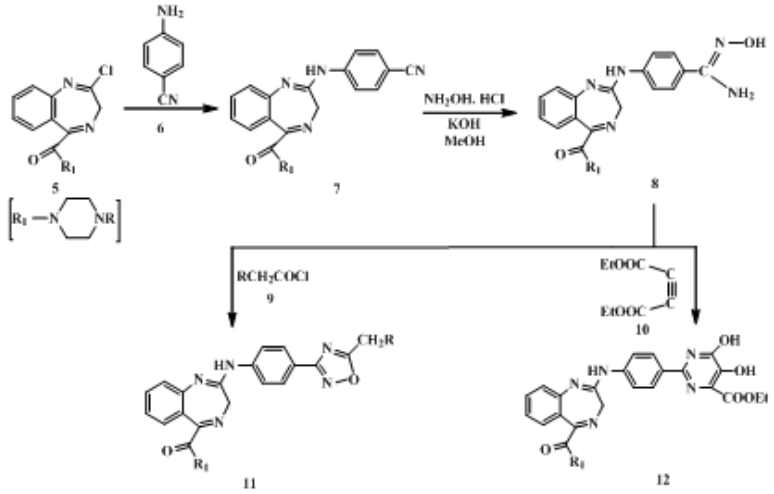
We report in this communication, the preliminary results of our study focused in the direction of developing possible substitute to 'HAART' in the anti-HIV chemotherapy in which we used the potential of anti-HIV prone

privileged template of 1,4-benzodiazepin-2-one-5-methylcarboxylate nucleus, as a building block and incorporated on to it, at its 2-position the vital fragments of pyrimidine and oxadiazole through a phenylamino spacer.

An examination of the structure of 1,4-benzodiazepin-2-one-5-methylcarboxylate (3) (which was obtained readily from the ring expansion of 1-chloroacetylisatin (2) under the influence of methanolic solution of hexamine) revealed that C5 methyl of carboxylate and C2 carbonyl function (which existed as a part of NH-C=O group) in the molecule were the only two sites in its seven membered ring which provided scope for its further funtionalization and elaboration to produce the structural analogues of medicinal utility.

For the sake of brevity, in this communication we report only the first phase of study carried out during this investigation. It consisted of the conversion of the methylcarboxylate derivative (3) to its amide by its reaction with N-methylpiperazine. Subsequently, the C2 (NH-C=O) group was converted to its 2-chloro analogue on treatment with POCl3 and DMA. The 2-Cl atom (an imino chloride/ imidoyl chloride) is a highly reactive species known to be activated for nucleophillic attack. Its nucleophillic displacement with p-aminobenzonitrile (6) yielded 7. The key intermediate amidine (8) was formed from 7 its reaction with H2N-OH.HCl + KOH (in MeOH) following the procedure reported in the literature for such reactions on other substrates containing the nitrile group. Established protocols on amidine derivative (8) was applied, which consisted of employing the reaction of acetylchloride (9) and dimethylacetylene dicarboxylate (10) (DMAD) to on it to form the compounds (11) (bearing oxadiazole ring) and (12) (bearing pyrimidine ring) on benzodiazepine nucleus respectively through an aminophenyl spacer. The structures of the compounds were established on the basis of their spectral data. Exploration of the chemistry and biological activity of the compounds are under study.



P-158

Modeling of Inhibitory activity of Dihydro-Pyrazolyl-Thiazolinone Derivatives as Potential COX-2 Inhibitors through QSAR analysis

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Quantitative structure activity relationship (QSAR) study has been made on the dihydro-pyrazolyl-thiazolinone derivatives. This study is based on modeling of COX-2 inhibitors of dihydro-pyrazolyl-thiazolinone derivatives using topological and physicochemical parameters. It has been demonstrated that steric, electronic and topological parameters along with indicator variables are significantly correlated with activity. The multiple regression analysis reveals that the four-parametric model containing Xeq, Mv, I1, I2 as correlating parameters is the best for modeling the activity of the compounds under present study which was able to explain 89.7% of the variance in the data. The QSAR models were tested for their statistical significance and reliability by using leave one out cross validation method.

Keywords: COX-2 inhibitors; QSAR; Dihydro-Pyrazolyl-Thiazolinone Derivatives; Physicochemical Parameters.

P-159

Synthesis of novel quinazoline-4(3H)-one Compund as anticancer agent

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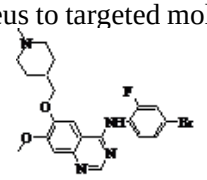
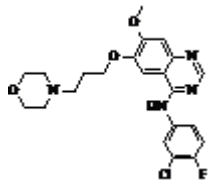
Many of the quinazolinones derivatives shows antibacterial, antifungal, antiviral, antitumor, anticonvulsant activities as well as the inhibitory effects for thymidylate synthase and poly- (ADP-ribose) polymerase [1-7].On the other hand, heterocyclic containing substituted aromatic amines nucleolus also exhibit various pharmacological activities and because of the established biological activities, our own interest to synthesize 2-substituted aryl quinazoline-4(3H) one and 2-substituted aryl quinazoline-4(3H)-thione derivatives. In this work, an efficient synthesis for the preparation of some novel quinazolinones by 2 steps.In the step-I, various 2-substituted benzoazin-4-ones are formed by the reaction of cheap anthranilic acid and benzoyl chloride /acetic anhydride/propanoic anhydride. In step II, 2-substituted benzoxazine 4-ones, which are formed in step I are coupled with various substituted aromatic amine compounds. The resulting novel aryl quinazolinone derivatives were characterized by 1H NMR spectra analysis. The resulting quinazolinone further converted in to thio quinazolinone derivatives using phosphorous pentasulfide as sulfonation agent reagent.

Anthranilic acid used as cheap raw material for preparation of 2-alkyllquinazolin-4(3H)-one and 2-aryllquinazolin-4(3H)-one which was further coupled with substituted aromatic amine to prepare target molecule followed by substitution in aromatic ring to prepare series of compounds.

Following anticancer molecules possesses 3H-quanzolinone ring system with aromatic amines are having similar nucleus to targeted molecules

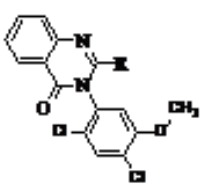
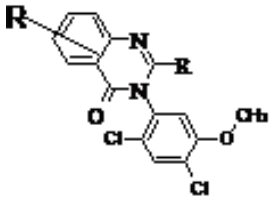
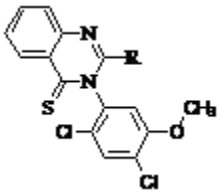


Vandetanib (Anticancer)



Gefitinib (Anticancer)

Following targeted compounds have been prepared for our further development and for biological activity.

R = -CH3, -CH2-CH , X= -Cl,-Br,-I,-O-CH3

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P-160

Pharmacokinetic studies of a novel anti-leishmanial compound, S013-0244, in rats

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The compound S013-0244, a novel indole-2-carboxamide derivative, developed by CSIR-CDRI, has shown potent anti-leishmanial activity. To develop it as a potential candidate drug, its absolute bio-availability was estimated following per oral and intravenous administrations in young and healthy male Sprague-Dawley rats. Pharmacokinetic parameters were calculated by noncompartmental analysis using WinNonlin program.

A rapid, sensitive and simple liquid chromatography-tandem mass spectrometry method was developed and validated for the quantification of S013-0244 in rat serum. The method requires low serum volume (10 ?L) with a shot run time of 3 min. Excellent linear relationships (r2 ?0.99) were obtained between the measured and added concentration over a range of 1-250 ng/mL. Validation parameters (accuracy, specificity, precision, recovery, matrix-effect and stability) were assessed as per US FDA guidelines [1]. The precision and accuracy were acceptable as indicated by relative standard deviation ranging from -11.76 to 2.10% and bias values ranging from 3.29 to 9.8%.

Its absorption was rapid with maximum concentration (Cmax) at 1 h and could be monitored up to 24 h after oral dosing. Volume of distribution (Vss, 6.04 ± 1.99 L/kg) was greater than the total blood volume of rat (0.054 L/kg; Davies et al. [2]) indicating high extra-vascular distribution of the compound. Moreover, the systemic clearance (1.80 ± 0.36 L/h/kg) was lower than the hepatic blood flow of rat (2.9 L/h/kg; Davies et al. [2]) suggesting an insignificant amount of extrahepatic elimination of this compound. The compound exhibited high absolute bioavailability (98%). The details will be presented.

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P-161

Aminoquinoline-Pyrimidine Hybrids: Synthesis, Antimalarial Activity and SAR studies

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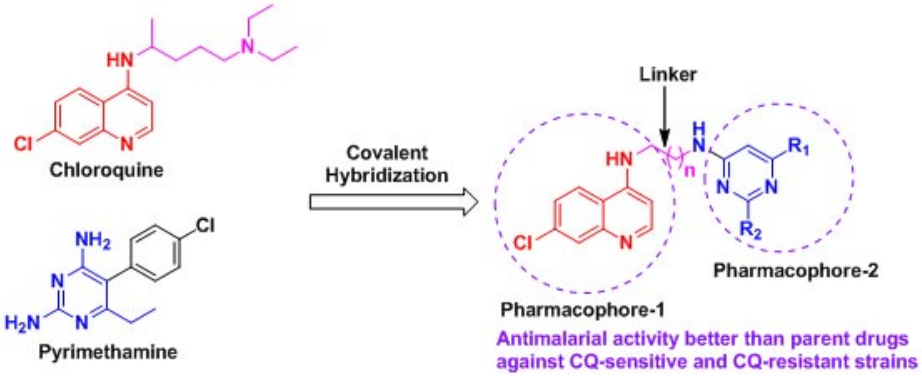
Malaria, transmitted in humans through the bite of female *Anopheles* mosquito and caused by the infection with any of the five species of *Plasmodium* viz. *P. vivax*, *P. malariae*, *P. ovale*, *P. knowlesi* and *P. falciparum*, of which the latter one is the most lethal, is still epidemic in large parts of the world, especially in sub-Saharan Africa, South America and Southeast Asia with approximately 207 million cases of malaria in 2012 and an



estimated 627 000 deaths. Currently, WHO recommends artemisinin-based combination therapy with a conventional antimalarial due to the fear of development of parasite resistance and persistence in the body of the host [1]. Several approaches have been made towards the development of new antimalarial agents to address the problem of drug-resistance, and the concept of molecular hybrids has shown promising results. In hybrid antimalarials, two (or more) discrete antimalarial scaffolds are linked covalently, usually through a spacer, in an anticipation that these compounds may act by inhibiting simultaneously two (or more) different conventional targets [2].

Towards this end, we had synthesised 4-aminoquinoline-pyrimidine based hybrids [3-6] in an anticipation that these may act by simultaneously disrupting the heme-detoxification pathway (by 4-aminoquinoline core) and halting the tetrahydrofolate synthesis (DHFR inhibition by pyrimidine nucleus) in the malarial parasite. The synthesized hybrids have shown promising *in vitro* and *in vivo* antimalarial activities against CQ-sensitive and CQ-resistant *P. falciparum* strains. Further modifications on these hybrids have revealed interesting structure-activity relationships which will help in improved design of these hybrids with better antimalarial potential [7].

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P-162

Synthesis, characterization and antibacterial activity of 4-(7-(1H-pyrazol-4-yl)-5H-pyrrolo[2,3-b]pyrazin-2-yl)-N-isopropylpyrimidin-2-amine derivatives

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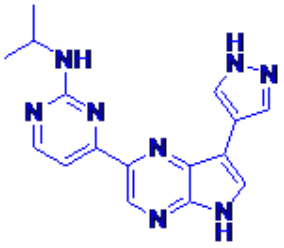
The new substituted 5H-pyrrolo[2,3-b]pyrazine derivatives exhibiting an antibacterial activity have been synthesized. The various substituted pyrimidine and pyrazine derivatives have shown significant activity against Gram-positive pathogens including super bugs such as methicillin-resistant staphylococcus aureus and some fastidious Gram-negative bacteria. 4-(7-(1H-pyrazol-4-yl)-5H-pyrrolo[2,3-b]pyrazin-2-yl)-N-isopropylpyrimidin-2-amine (1a) shows the antibacterial activity with satisfactory results.

The Key intermediate N-isopropyl-4-(5-tosyl-5H-pyrrolo[2,3-b]pyrazin-2-yl)pyrimidin-2-amine was prepared by the sonagashiro reaction of N-(3,5-dibromopyrazin-2-yl)acetamide using trimethyl silyl acetylene, PdCl2(PPh3)2, K2CO3, DMF in microwave at 150 o C for 30 min. followed by the cyclization using cesium carbonate and



1a

protection with tosyl chloride to afford 2-bromo-5-tosyl-5H-pyrrolo[2,3-b]pyrazine and then it was treated with ethoxy vinyl tributyl tin, PdCl2(dppf).DCM in DMF followed by the acidic hydrolysis using 6N HCl to afford 1-(5-tosyl-5H-pyrrolo[2,3-b]pyrazin-2-yl)ethanone which was then treated with DMA-DMF followed by the cyclization with isopropyl guanidine to afford key intermediate N-isopropyl-4-(5-tosyl-5H-pyrrolo[2,3-b]pyrazin-2-yl)pyrimidin-2-amine. Iodination of N-isopropyl-4-(5-tosyl-5H-pyrrolo[2,3-b]pyrazin-2-yl)pyrimidin-2-amine in sodium iodide, DMF followed by the Suzuki coupling using 4-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan -2-yl)-1H-pyrazole in Pd(PPh3)4, Potassium acetate in Toluene/Ethanol/Water (1:1:1 ratio) in microwave at 120 o C for 15 min. Detosylation using potassium carbonate in methanol to afford 4-(7-(1H-pyrazol-4-yl)-5H-pyrrolo[2,3-b]pyrazin-2-yl)-N-isopropylpyrimidin-2-amine (1a). The structures of all the compounds were established using the analytical techniques includes IR, LCMS and NMR spectroscopy.

P-163

Synthesis of Some Bio-Active Thieno[2,3-D]Pyrimidine Derivatives

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Various substituted thieno[2,3-d]pyrimidine derivatives were synthesized from 2-amino thiophene derivative. The structures of synthesized compounds were elucidated by IR, NMR spectroscopy and elemental analysis. Additionally, the compounds were screened against a variety of other microbial targets and as a result, selective activity against several fungi was also observed. Some of the tested compounds showed promising activity. Detailed syntheses, spectroscopic and biological data are reported.

Keywords: Thieno[2,3-d]pyrimidine; Antimicrobial activity.

P-164

Studies on Synthesis and Antimicrobial Screening of Some Thienopyrimidines

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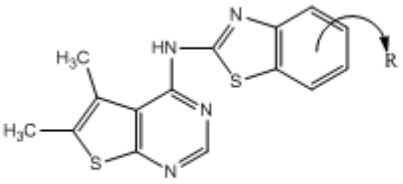
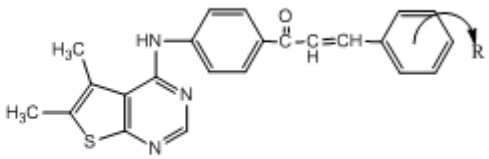
Various substituted thienopyrimidine derivatives were synthesized from 2-amino thiophene derivative. The structures of synthesized compounds were elucidated by IR, NMR spectroscopy and by elemental analysis. Additionally, the compounds were screened against a variety of other microbial targets and as a result, selective activity against several fungi was also observed. Some of the tested compounds showed promising activity. Detailed syntheses, spectroscopic and biological data are reported.

Keywords: Synthesis, Characterization, Antimicrobial activity.



N-(substituted benzo[*d*]thiazol-2-yl)-5,6-dimethylthieno[2,3-*d*] pyrimidin-4-amine



3-(substituted phenyl)-1-(4-(5,6-dimethylthieno[2,3-*d*]pyrimidin-4-yl amino)phenyl)prop-2-en-1-one

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P-165

Simple Molecular Engineering of Glycol Nucleic Acid: Progression from Self-pairing to Cross-Pairing with cDNA and RNA

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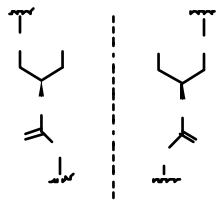

Introduction: Key inputs from Eschenmoser's group in solving the mystery of chemical etiology of nucleic acid structure has established that Watson-Crick base pairing can be supported by sugars in the backbone that differ from the naturally selected ribose/ deoxyribose RNA or DNA[1] among which Tetrose Nucleic acid(TNA) proved to be the best[2].Eric Meggers structurally simplified TNA to an atom economic novel nucleic acid analogue known as Glycol Nucleic Acid (GNA)[3].A chiral carbamate analogue of PNA, namely, the Polycarbamate Nucleic Acid (PCNA) was synthesized in our laboratory[4]. Here, our approach is to make shorter, atom-edited PCNA which is structurally closely related to GNA/TNA, namely, Glycol Carbamate Nucleic Acid (GCNA) to study binding preferences with RNA/DNA.

Result and Discussion: Enantiomeric monomer units (R,S)-GCNA were synthesized by simple organic transformations from L-Serine. Solid phase synthesis of oligocarbamates was achieved by using L-lysine derivatized MBHA resin. We synthesized the thyminyl-octamer sequence of both the enantiomeric (R,S)-GCNA-1 initially to test their binding to cDNA and RNA. Further, we chose a mixed pu/py sequences, (R,S)-GCNA-2, to study their parallel/antiparallel mode of binding to DNA, mismatch discrimination, RNA binding, and if the sequences also exhibit self pairing with complementary (R,S)-GCNA-3 oligomers. CD studies of the monomers, single strand (R,S)-GCNA, complex with DNA and complementary (R,S)- GCNA of one of the sequences were also done

Sequences and melting temperatures (UV-Tm values in ºC) of cross-paired and homoduplexes

Sequences	UV-Tm values º C					
	cDNA-4	p-cDNA-5	mmDNA-6	cRNA-4	R-GCNA-3	S-GCNA-3
R-GCNA-2: atattattaatt-Lys	40.8	26.1	26.4	29.6	>80.0	20.1
S-GCNA-2: atattattaatt-Lys	27.5	nt	16.5	26.5	21.6	>81.0
DNA-2: 5'-ATATTATTAATT	22.8	nt	nt	20.7	nd	nd

Capital letters denote DNA/RNA sequences, small letters denote R/S-GCNA, cDNA-4: 5'-AATTAATAATAT, p-cDNA-5: 5'-TATAATAATTAA mmDNA-6: 5'-AATTATTAATAT, cRNA-4: 5'-UAUAAUAAUUAA. (R,S)-GCNA- 3: aattaataatat-Lys, Nd: not determined, nt: no sigmoidal transition.

In conclusion, these studies describe the synthesis of chirally homogeneous (R)- and (S)- Glycol Carbamate Nucleic Acids (GCNA) from naturally occurring L-serine. The formation of highly stable self-paired and moderately stable cross-paired complexes with natural nucleic acids is the unique feature of this backbone.

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P-166

Synthesis of new N-aryl-2-(5-arylisoxazol-3-yl)acetamide analogs and anti-HCV activity evaluation

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Hepatitis C virus (HCV) belongs to the Flaviviridae family predominantly infecting hepatocytes. The infection is silent and in long-term may lead to serious liver disease, including fibrosis, cirrhosis followed by hepatocellular carcinoma which continues to be an important cause of morbidity and mortality. The prophylactic treatment has been of very limited success and so far no vaccine is available. The medicinal chemistry approaches with breakthrough exploration in HCV biology were translated recently into first generation DAAs, boceprevir and telaprevir (protease inhibitors) approved by US FDA. The current standard of care (SoC) for HCV treatment includes one of the approved protease inhibitors combined with pegylated interferon-? (PegIFN) and ribavirin (RBV). The new regimen improves sustained viral response (SVR) rates to approx 75%, however it also adds side effect burden to patients and in many cases treatment discontinuation. Overall, drug-resistance, drug-drug interactions, and side effects are major concerns and demands discovery of new drugs with better therapeutic potential. In our continuous effort to discover new potent anti-HCV agents, we had synthesized fourteen new N-aryl-2-(5-arylisoxazol-3-yl)acetamide analogs and evaluated for anti-HCV activity. However, none were found significantly active and further screening against other viruses are under process.

P-167

One pot hydrophosphonylation reaction of isatins and its derivatives using magnetic particle supported catalyst

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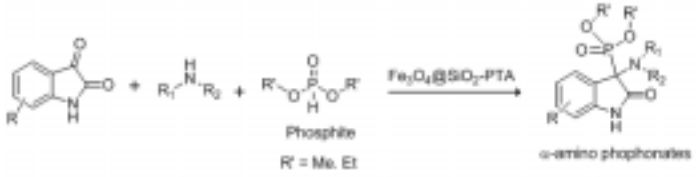
Magnetic recoverable Fe3O4@SiO2-PTA catalyst has efficiently catalyzed one pot hydrophosphonylation reaction of isatins and isatin imines using different phosphonates. In this reaction the addition of hydrogen-phosphonates to electrophilic centers like carbonyl or imine is considered to be one of the most interesting topic in synthetic organic chemistry, the resulted products ?-hydroxy phosphonates and ?-amino phosphonates have much attention due to their important biological activities. It is an active synthon for various pharmaceuticals like antibiotics, anti-virals and antitumor agents. Allen et al. [1] Several attempts have been made for the development of efficient catalytic systems for this versatile reaction like Yadav et al. [2]. Hosseini et al.[3]. However, most of the reported catalytic protocols are non-recyclable and makes the process industrially non-viable. With our on growing interest on developing recyclable catalysts for organic transformation herein we are reporting the supported heteropoly acid (phosphotungstic acid) as a recyclable catalyst for hydrophosphonylation reaction.The catalyst was efficient for the hydrophosphonylation reaction of less reactive substrates like isatin and its derivatives (Scheme 1). The catalytic protocol is simple, efficient and solvent-free for the synthesis of ?-hydroxy and ?-amino phosphonates using Fe3O4@SiO2-PTA as a catalyst and resulted in good to excellent yields (upto 98%) under neat condition. To the advantage, this catalyst was recyclable upto five times with retention of its activity.



Scheme 1: Synthesis of ?-hydroxy and ?-amino phosphonates

Reference

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P-168

Asymmetric Friedel - Crafts Addition of Indoles to N-Sulfonyl Aldimines Catalyzed by Cu(II) Chiral Amino Alcohols Based Schiff base Complexes

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Friedel-Crafts alkylation of arenes is an important C-C bond forming reaction in organic chemistry. Asymmetric version of this reaction[1] can provide a useful strategy for the synthesis of enantioenriched alkylated arene products, which are potential starting materials for various biologically active compounds. Although excellent results in term of yield and enantioselectivity have been reported in Friedel-Crafts alkylation of indoles with imines; the synthetic protocol for the reported catalysts are multi-steps and silent on catalyst recyclability, which is an important aspect for the acceptability of these catalysts in industries. We have synthesized the recyclable copper(II) chiral amino alcohol based Schiff base complexes which smoothly catalysed the Friedel-Crafts alkylation of indole with aryl aldimine with good yields (up to 98%) and enantioselectivities up to 97%. To understand the mechanism of the catalytic Friedel-Crafts addition reaction, the kinetic investigation was carried out with different concentrations of the catalyst Cu(II)-Schiff base complex, indole and N-(3-nitrobenzylidene)-4-methylbenzene sulphonamide as a model substrate. An appropriate mechanism of the Friedel - Crafts alkylation reaction is proposed [2].

Table1. Chiral Cu (II)-Schiff base catalysed enantioselective F-C reaction of sulfonyl imines.

Entry	N-sulphonylimines	R1/ R2	Yield %	Ee %
1	p-NO2C6H4	p-NO2C6H4/Me(2a)	3a (96)	97
2	m-NO2C6H4	m-NO2C6H4/Me(2b)	3b (98)	92
3	p-ClC6H4	p-ClC6H4 /Me(2c)	3c (89)	96
4	m-ClC6H4	m-ClC6H4 / Me(2d)	3d (85)	97
5	o-ClC6H4	o-ClC6H4 /Me(2e)	3e (75)	72
6	p-MeC6H4	p-MeC6H4/ Me(2f)	3f (70)	75
7	m-MeC6H4	m-MeC6H4 /Me(2g)	3g (68)	70

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P-169

Phosphotungstic acid as an efficient catalyst for allylation of isatins and N-Boc amido sulfones under solvent free condition

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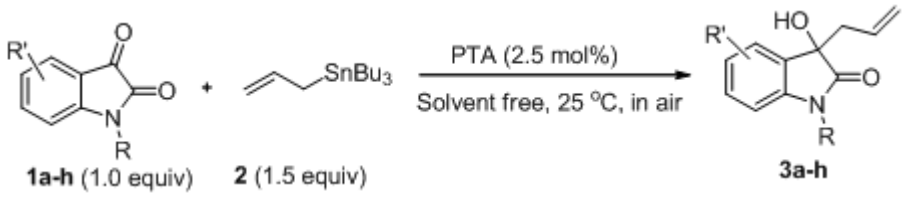
The present work demonstrated the use of phosphotungstic acid (H3PW12O40.H2O) as an efficient catalyst for the allylation of isatin derivatives as well as N-Boc ?--amido sulfones with allyltributyltin as an allylating agent under solvent free condition at room temperature. Excellent allylation product yields (up to 99%) for the isatins substrates and good to excellent yields (up to 98%) for the N-Boc ?--amido sulfones were observed. Diverse biological activity of allylation products of isatins and its derivatives are major driver for exploring newer and effective catalytic allylation protocols. [1] In addition, alkene functionality in 3-allyl-3-hydroxy-oxindole can be judiciously utilized to synthesize desired organic molecule. [2] We have used PTA as a catalyst for the allylation of isatins with allyltributyltin and indeed got excellent yields (up to 99%) of allylation products under solvent free condition at RT.

In conclusion, we have developed a simple, convenient and efficient protocol for allylation of less reactive isatins and N-Boc amido sulfones by using catalytic amount of phosphotungstic acid. This catalytic protocol has several advantages in terms of mild reaction condition, green catalyst, solvent free condition, low catalyst loading (2.5-5 mol%) and good to excellent yields. Based on 1H, 13C and 31P NMR studies the probable mechanism was proposed for the allylation reaction using PTA as a catalyst.

Keywords: Allylation, Isatin, amidosulfones

Table 3. Allylation of isatins 1 with allyltributyltin 2



1a-h (1.0 equiv) **2** (1.5 equiv) **3a-h**

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P-170

Synthesis and characterization of chiral Cu(II)complex and their application in the asymmetric aza-Henry reaction

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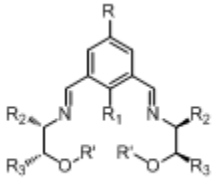
The recent growth in application of enantio pure bio-active agents has increased the quest for the development of asymmetric synthetic methodologies that provide remarkable stereocontrol in end products. In this regard, organic compounds bearing two vicinal nitrogen functionalities[1]are of interest and considered to be one of the key area of synthetic organic chemistry. In this concern, reactions that utilize the addition of active C?H nucleophiles to C=X (X= N or O) bonds represent some of the most fundamental C?C bond formation reactions. We are interested inaza-Henry reaction[2] due to the commercial importance of the reaction and the end product is a versatile synthon for various valuable biological active compounds such as vicinal chiral diamines and ?-amino acids.[3]With our ongoing interest on developing simple catalytic systems with affordable reaction conditions, we have developed insitu generated chiral Cu(II) catalyst for the asymmetric aza-Henry reaction of N-tosyl derived imines using nitromethane. The chiral ligand can be easily synthesized in just one step from the commercially available starting materials. The chiral catalyst was efficient and the desired products were obtained with good yield (upto 80%) and excellent enantioselecitivity (upto 99%) in wide range of substrates.



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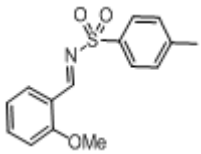
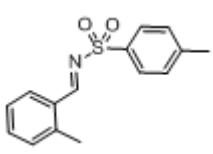
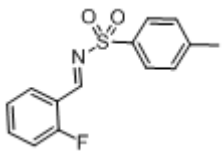
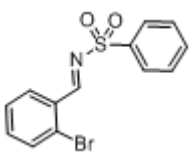
Scheme:-Optimization reaction condition for asymmetric aza-Henry reaction

Table-1

											
Entry	Yield(%)	ee(%)	Entry	Yield(%)	ee(%)	Entry	Yield(%)	ee(%)	Entry	Yield(%)	ee(%)
1	82	99	2	76	96	3	80	90	4	70	92

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P-171

Asymmetric Allylation of Sulfonyl Imines Catalyzed by in situ Generated Cu(II) Complexes of Chiral Amino Alcohol Based Schiff Bases

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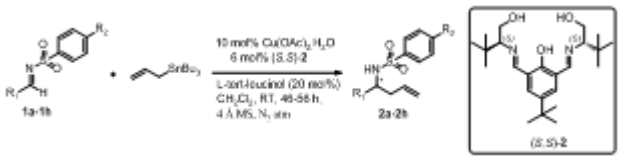
A catalytic route for enantioselective synthesis of homoallyl amines through Cu(II)-Schiff base catalyzed reaction of allyltin with various N-sulfonylimines is described. The allylation reaction is promoted by simple in situ generated Cu(II)-amino alcohol based Schiff base complex. The addition of allyltin to aldimines delivers the desire products up to 90% yield and 99:1 enantiomeric ratio.

The asymmetric allylation reaction of imines is a well-known synthetic tool for the production of chirally enriched homoallyl amines. Enantiomerically pure homoallyl amines are important building blocks for the construction of biologically active compounds [1]. In this present work we have reported the catalytic efficacy of the in situ generated Cu(II)-chiral Schiff base type complex for enantioselective allylation of sulfonyl imines.

Chiral Schiff base ligands were prepared by the condensation of aromatic bis-aldehyde with different chiral amino alcohols by following literature procedure [2]. After getting optimum ligand ((S,S)-2) we have optimized all the reaction parameters e.g. solvent, temperature, catalyst loading and additives and its amount. Then we have applied this optimum reaction condition for various aromatic sulfonyl imines substrates (Table 1).

Table 1. Chiral Cu (II)-Schiff base catalysed enantioselective allylation of sulfonyl imines.



Entry	N-sulphonylimines	R1/ R2	Yield %	Ee %
1	Ph	C6H5/Me (1a)	2a (60)	90:10
2	p-ClC6H4	p-ClC6H4/Me (1b)	2b (66)	97:3
3	p-FC6H4	p-FC6H4/Me (1c)	2c (69)	95:5
4	p-NO2C6H4	p-NO2C6H4/Me (1d)	2d (67)	90:10
5	m-ClC6H4	m-ClC6H4/Me (1e)	2e (64)	91:9
6	o-ClC6H4	o-ClC6H4/Me (1f)	2f (70)	83:17
7	2-naphthyl	2-naphthyl/Me (1g)	2g (84)	97:3
8	trans-cinnamyl	(E)-C6H5CH=CH/Me (1h)	2h (76)	93:7

aIsolated yields after column chromatography. ber determined by chiral HPLC using OD-H, AD-H, IA chiral column.

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P-172

Desymmetrization of meso-epoxides with anilines by Binol based Iron catalysts

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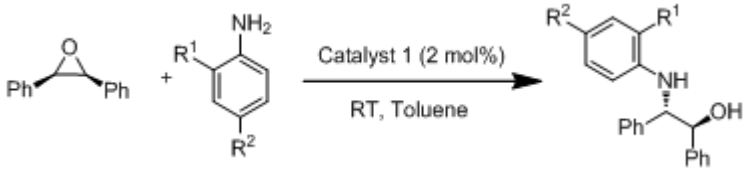
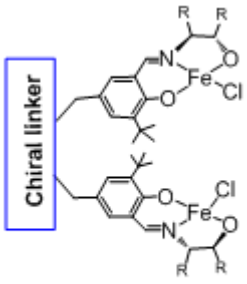
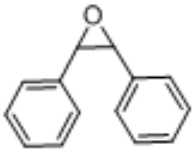
Chiral ?-amino alcohols are the class of compounds which finds its use in broad spectrum of applications in pharmaceuticals, agrochemicals, flavours, fragrances [1] and also as chiral auxilaries for asymmetric synthesis [2]. In literature diverse catalytic methods were reported for the synthesis of chiral ?-amino alcohols among them the catalytic asymmetric ring opening (ARO) reaction of an epoxide with an amine is one of the best method [3], because it allows the formation of enantiopure ?-amino alcohols in a single step with an atom efficiency. A number of efficient catalytic methods have been reported for the ARO of meso-epoxides with alkyl/aryl amines using catalysts based on chiral ligands with different metal ions viz., titanium, niobium, copper, lanthanides, chromium, iron, scandium, indium and bismuth to provide ?-amino alcohols in excellent yield and enantioselectivity[4-5]. But the recyclability of the chiral catalyst and enviromental issues with the reported catalyst motivated us to develop a efficient catalytic system for the ARO reaction. By keeping these issues in mind we have designed and synthesized a new chiral dinuclear iron based catalyst which works efficiently in ARO reaction of meso-epoxide with aniline and it gives excellent yield (upto 95%) and enantioselectivity (upto 99%) of the chiral ?-amino alcohols.

Key Words: Meso epoxides, Amino-Alcohols, ring opening





Catalyst-1

Entry	Epoxides	Anilines	Time	Yield (%)	ee (%)
1	 Stilbene oxide	Aniline	20	95	99
2		2-OMe	18	92	96
3		4-OMe	18	90	94
4		2-Cl	24	75	96
5		2-Me	22	86	89

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P-173

Chiral V(V) dinuclear salen complex catalyzed enantioselective hydrocyanation reaction of aldimines

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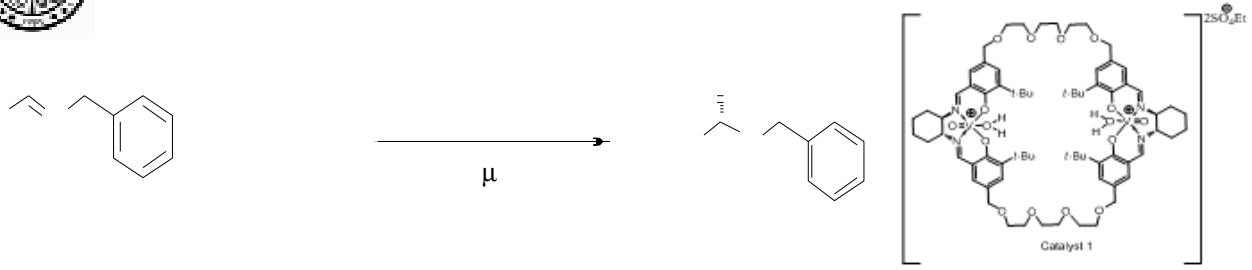
The catalytic asymmetric hydrocyanation (Strecker) reaction represents one of the simplest and atom economic, multi-component, carbon-carbon bond formation reaction to afford ?-amino nitrile, which on subsequent hydrolysis gives natural and unnatural amino acids. [1,2] In this context, various chiral metal complexes [3] and organocatalysts [4] were reported for this versatile reaction. As chiral ligands are expensive, the recycling of chiral catalyst is highly desirable to offset the catalyst cost. Our group has been involved in developing recyclable chiral catalysts for various asymmetric organic transformations, by fine tuning the solubility of the catalyst by increasing its molecular weight so that the catalyst can be easily precipitated out by non-polar solvents like hexane in post work up. [5] Herein we have explored the catalytic activity of chiral dinuclear vanadium based salen complex in asymmetric hydrocyanation reaction of various aldimines using trimethylsilyl cyanide as a source of cyanide at -20 oC. The catalyst 1 was found to be efficient and the desired product - aminonitrile was achieved in excellent yield (upto 92%) with high chiral induction (ee up to 94%) in 10 h. The catalytic system worked well up to four cycles with retention of its activity and enantioselectivity.



Scheme 1. Enantioselective addition of TMSCN to various *N*-benzyl aldimines catalyzed by dinuclear V(V) salen complex **1**

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P-174

Anti-malarial drug discovery usingAutodockVina forplasmepsin protein of Plasmodium falciparum

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Malaria is still one of the most widespread and lethal diseases in the world, affecting the tropical parts of the globe. Every year there are more than 500 million clinical cases of malaria and several millions of them are children. Emerging drug resistance and the lack of a functioning vaccine are twomain reasons behind the failure to control and eradicate the disease. ThePlasmepsins are aspartic proteases involved in the degradation of the host cell hemoglobin that is used as a food source by the malaria parasite. Plasmepsins are highly promising as drug targets, especially when combined with the inhibition of falcipains that are also involved in hemoglobin catabolism. In the present study, we have focused on virtual screening approach against in-house Heterocyclic Compound library: Heterobase for Plasmepsin Protein of Plasmpodium falciparum 3D7. Amongst various available docking softwares, we have used AutodockVina tool for docking of total 3000 compounds against Plasmepsin target with PDB ID 1J8J. The comparison with 27 well-knowndrugs were also carried out as a control drugs for this target. The Scoring of best molecule was depended upon the binding energy of compounds. Total 20 best compounds were analyzed for manual curation to identify binding pattern using LIGPLOT and iGemdock Software. The results indicate Compound 3001 show better binding affinity than Quinone, Chloroquine andartemisinine. The presence of plasmepsin in food vacuole of parasite directly affected by solubility of the drug. So, the lead compound 3001 was further optimized for improvement of solubility using DSA Calculator (Drug Solubility & Absorption Predictor) followed by re-docking of improved compounds for binding patterns with receptor molecule. The resulting best lead Compound 3001 may exhibit significant inhibition of plasmepsin protein in Plasmodium falciparum.

P-175

Synthesis, Characterization and biological evaluation of some metal chalcone complexes

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Chalcone skeleton represents an essential group in natural as well as synthetic products and some of them possess wide range of pharmacological properties which includes germicidal, bactericidal, fungicidal, anti-inflammatory, carcinogenic and antioxidant effects,A S Albogami, et.al [1]. In our study, we have used metals to complex with chalcone and to evaluate biological potential of chalcone metal complex, Rafique et.al [2]. In our present work we report synthesis of chalcone metal complexes and its biological evaluation. The research work includes synthesis of chalcones by Claisen-Schmidt condensation of 2-hydroxy acetophenone and aromatic aldehydes, P. Venkatesan, et.al [3]. Further, these chalcones were complexed with Co(II) and Fe(II) metals, Irudayasamy[4] and their structures were elucidated by analytical (FTIR,1H NMR and Mass) Methods. The identity of compounds were elucidated by IR, NMR and mass spectrometry. The potential analogues were screened for their anti-bacterial and antifungal activity against Staphylococcus aureus and Candida albicaus strains and found to possess antibacterial and antifungal activity. Complexed molecules were also examined for their invitro anticancer activity[5] against HCT 15 and MCF 7 cell line. The analogues showed promising findings for the same.

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P-176

Synthesis, Anti-Tb Activity and Docking Studies of 2, 5 -Diaryl 1, 3, 4-Oxadiazole

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Tuberculosis is the leading cause of death worldwide. One third of the world's population is infected with tuberculosis and TB has also been associated with immune-compromising diseases, J Smithy et al (1). With the emergence of powerful strains of causative bacteria Mycobacterium tuberculosis, there is a need to proactively

discover and develop new leads on existing or newer targets, K Mdluli et al (2). Nitrogen containing heterocycles have been explored widely in search of new drug molecules. The 1,3,4- Oxadiazole ring system is toxophoric in nature due to its N-C-O moiety and bioactive potential associated with the ring, Nagaraj et al (3). In this work, we present the newer 2,5-diaryl-1,3,4-Oxadiazole analogues which can be considered as a promising lead, R Somani et al (4). Targeted molecules were synthesized using reported methods, then purified and characterized using spectroscopic techniques, S El Khawas et al (5). The molecules were further docked on shikimate kinase (PDB code 2YIQ), J Pereira et al (6). The docking studies revealed that these compounds interacted with shikimate kinase (PDB code 2YIQ) enzyme with the residues, through hydrogen bonding of Arg 58A, Arg 117A, hydrophobic interaction of Gly80A, Gly81A, Arg117A, Asp34 and pi-stacking interaction of Phe49 and Phe57 determined at resolution of 1.8 Å . These interactions were on the lines similar to that of co- crystal ligand, shikimic acid (shikimate). The compounds were also evaluated for their anti TB activity against Mtb at Tubeculosis Antimicrobial Acquisition Coordination Facility, USA. Herein the correlation between docking studies and anti TB activity is explained.

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P-177

Synthesis of chiral ?-nitronitriles

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The asymmetric hydrocyanation ofnitroolefins give bifunctional?-nitronitrile whichplay a key role in the synthesis of chiral building blocks such as b-amino acids,[1] 1,3-amino alcohols,[2] and 1,3-diamines and have a wider application in the pharmaceutical industry. Till date only very few organocatalyst [3,4] and transition metal (Ti and V) [1,5] based catalytic system have been successfully developed for this reaction but with moderate enantioselectivity. In our quest to develop more efficient catalytic system, initially we have screened different

metal sources withJacobsen'ssalen ligand and selected Al as preferred metal. Thereafter the reactivity of different Al-complexeswere tested and reaction parameters like catalyst loading, additives, temperature and solvent were optimized. After the successful optimization, catalyst 1 (5 mol%), 4-phenylpyridine-N-oxide as an additive using toluene as a solvent at -15 oC and this protocol(Scheme 1) was extended for its applicability in various aliphatic nitroalkenes. In all the cases the present protocol gave desired product with good yield (upto 90%) and enantioinduction (upto 90%). Based on the NMR and IR studies we have proposed a plausible catalytic cycle showing the dual role of4-phenyl pyridine-N-oxide as an axial ligand as well as activating the cyanide source TMSCN.

Scheme:1 Asymmetric hyrocyanation of nitroolefins

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P-178

Tungstic acid as an efficient catalyst for the synthesis of benzimidazoles

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Benzimidazole derivatives are of wide interest because of their diverse biological activity. The compound which contains benzimidazole nucleus shows activities like antitumor, antiviral, atimalarial, anti-inflammatory etc. Lansoprazole, Omeprazole, Pentaprozole, Thiobendazole are already used as drug candidates. In addition, benzimidazoles are very impotent intermediates in synthetic routes and serve as ligands for asymmetric catalysts.

Due to the numerous biological and synthetic applications of the benzimidazole compounds has prompted organic chemist to study their syntheses. In this context, numerous efforts have been made to synthesize benzimidazole derivatives.

One of the most common methods for the preparation of benzimidazole derivatives involves the condensation of an o-phenylenediamine and carbonyl compounds such as aldehydes and acid derivatives. The condensation of o-phenylenediamine with carboxylic acid often requires strong acidic conditions and high temperatures, this is the

most popular approach in general for the synthesis of benzimidazole derivatives. Literature survey revealed that the condensation of o-phenylenediamine with different substituted aldehydes in the presence of various catalysts viz. SC(OTf)3 or Yb(OTf)3, sulphamic acid, H2O2-HCl, FeBr3, DDQ, PhI(OAc)2, KHSO4,HfCl4 BF3.OEt2, ceric ammonium nitrate, iodine, Silica sulphuric acid etc to yield the 2-substityetd benzimidazoles.

Unfortunately, many of these methods suffer from one or other kind of drawbacks such as drastic reaction conditions, low yields, tedious workup procedures, and co-occurrence of several side reactions. Therefore the development of new efficient method to overcome these drawbacks is needed.

As part of our research activity in developing various synthetic methodologies, we have developed facile method for the synthesis of benzimidazoles using tungustic acid as an efficient catalyst by the cyclocondensation of aldehydes with o-phenylenediamines. The reaction completed within short time with high yields of the products and catalyst is recoverable from reaction and reusable.

The details of the work will be presented.

P-179

Lornoxicam loaded solid lipid nanoparticles for topical delivery: ex vivo assessment and pharmacodynamics activity

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The gastric irritant effects of peroral lornoxicam can be attenuated using skin as the route of administration. The present work was focused on the development, characterization, ex vivo skin permeation and skin targeting behaviors of lornoxicam-loaded solid lipid nanoparticles (SLNs). Lornoxicam loaded SLNs were prepared by emulsification solvent evaporation technique. The particle size and polydispersity index were measured by dynamic light scattering technique and was found to be at 180.7±4.4 nm, 0.223±0.006, respectively. The shape and surface topography of SLNs were observed by transmission electron microscopy (TEM). Lornoxicam loaded SLN gel and lornoxicam gels were prepared and the gels were evaluated with respect to in vitro occlusivity, skin irritation and ex vivo skin permeation studies. Lesser skin irritancy and good oclusivity was observed with SLN gel as compared to the lornoxicam gel formulation. The ex vivo permeation data showed that SLN gel could significantly increase the extent of lornoxicam in skin and it showed skin targeting effect significantly. The anti-inflammatory activity of lornoxicam loaded SLN gel was stronger than that of lornoxicam gel and marketed formulation in carrageenan persuaded rat paw edema. These results suggest the SLN gel as the promising carrier for topical delivery of lornoxicam with skin targeting potential.

Keywords: Lornoxicam, SLNs, Topical delivery, Anti-inflammatory, Skin targeting.

P-180

Anticancer activity of novel 2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene)-N-phenylacetamides

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A novel 2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene)-N-phenylacetamide and 2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene)-N-tolylacetamide were synthesized. Monica donghi et al,(1) and Olaf Kinzel et al,(2) reported 3-hydroxy-4-oxo-4H pyrido[1,2-a] pyrimidine-2-carboxylates as potent inhibitor for HIV-1 virus. Pyridino[1,2-a]pyrimidinyl compounds had been patented as anticancer agentby Weibo Wang et al,(3). Hence the biological properties and drug likeliness properties of the synthesized compounds were predicted using the software's OSIRIS, Chemdraw and Molinspiration. The compounds exhibited a positive value for drug likeliness as calculated from OSIRIS molecular property explorer. The compounds also showed low risk against mutagenicity and low values for logP indicating the greater ability to penetrate through the membrane. Docking studies were also carried out using schrodinger software to study the binding properties of the compounds. The compounds were tested for their cyto toxic effect on the human cervical cancer cell line (HeLa) Both the compounds showed cytotoxic effect on the cancer cells. Docking studies were also carried out using schrodinger software to prove the anticancer activities of the compound.

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P-181

New modulated design, docking and synthesis of metallic cluster containg SnIV and their potential topoisomerase II inhibition activity: In vitro DNA binding and cleavage studies

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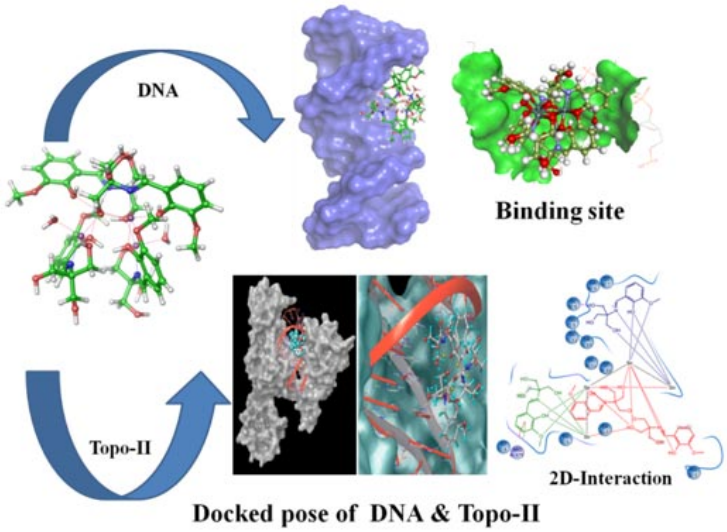
New metallic cluster (1) was synthesized and characterized by single X-Ray crystallography and other spectrometric methods. In vitro DNA binding studies of the cluster with CT DNA were carried out by employing various biophysical and molecular docking techniques which revealed that cluster strongly binds to DNA and cleaves pBR322 DNA via hydrolytic pathway (confirmed by T4 DNA ligase assay) and inhibited Topo-II activity in a dose-dependent manner. Furthermore, cluster was docked into the domain of human-Topo-II in order to probe the possible mechanism of inhibition.



Docked pose of DNA & Topo-II

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P-182

Role of Cationic Charge on Antimicrobial Activity of ?-Melanocyte Stimulating Hormone against Staphylococcus aureus

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?-Melanocyte Stimulating Hormone (?-MSH) an endogenous neuropeptide well known for its anti-inflammatory and anti-pyretic activity. -MSH and its C-terminal fragments like other antimicrobial peptides possess a rapid and potent antimicrobial activity against Staphlococcus aureus irrespective of its resistance to methicillin (Singh and Mukhopadhyay) [1]. In the present study our aim was to increase the antibacterial efficacy of ?-MSH by increasing the net cationic charge (Q). The analogues of ?-MSH (Q=+1) were custom synthesized varying net

charge from Q=+2 to +5. An increase in net cationic charge monotonically increased the killing efficacy of ?-MSH against Staphylococcus aureus (ATCC 29213). It was found that the analogues having charges +4 and +5 analogues showed 16.4% and 17.6% higher killing efficacy as compared to that of ?-MSH respectively. Flow cytomeric analysis also showed 88.3% increase in propidium iodide uptake of ?-MSH analogue (Q=+5) indicating more membrane damage in staphylococcal cells as compared to ?-MSH. -MSH and its analogues showed less than 25% hemolytic effect even at higher concentrations than the dose required for their antibacterial effect. Thus the increase in cationic charge of ?-MSH improved staphylocidal activity and membrane damaging efficacy of the peptides without compromising their toxic effect. It also indicated that electrostatic interaction may be crucial for ?-MSH to selectively disrupt microbial membrane leading to bacterial cell death without harming host cell membrane.

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P-183

Docking Studies of Substituted Chroman amides

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Based on rationale on chroman amides, in particular, the six-substituted ones, Computer Aided Drug Design was carried out. The virtual studies were carried out on antiepilectic receptor. The docking scores of selected best compounds (amongst 20 perspectives) were comparative to that of the standard values for antiepilectic drugs. Prior to docking of the generated dataset, a workup program was carried out on literature dataset including QSAR methods like LOO (Leave One Out) and based on the IC50 value. Thence a new dataset was envisaged for our study. The conclusive result of docking program on Glide (vs 5.0) module of Schrodinger LLC of envisaged dataset gave perspective for synthesis. A synthetic scheme was prepared based on laboratory feasibility. Successful synthesis was carried out and compounds characterized by physical, chemical and spectral methods.

P-184

Bio-catalytic anomeric separation and fluorescent study of coumarin-4-yl-triazolyl-2?-deoxy-ribofuranosides

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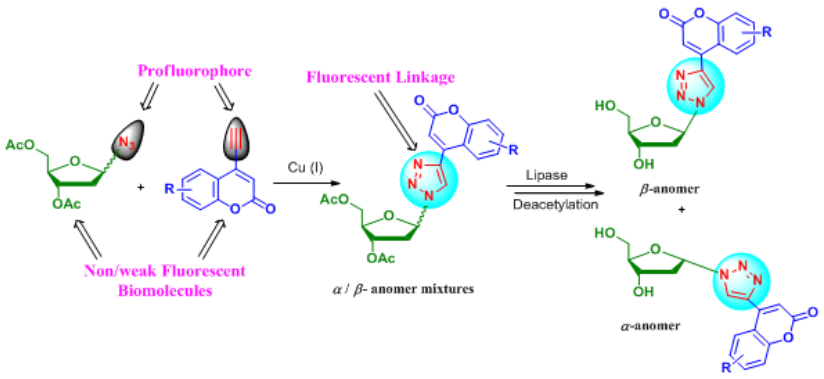
Fluorescent unnatural nucleosides are widely used in fluorescent labelling of DNA/RNA in bioorganic and medicinal chemistry. Over the last few years, different research groups have reported the synthesis of fluorescent coumarin triazolylglycosides using copper (I) catalysed azide alkyne cycloaddition (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 anomers of nucleosides has always been a challenging task for synthetic chemists.2-4 Our attempt to separate ?- and ?- anomers from anomeric mixtures of coumarin-4-yl-triazolyl-2?-deoxy-ribofuranosides by column chromatography also failed. Herein, we report successful separation of both ?- and ?- anomers of 1-(3?, 5?- di -O-acetyl- 1?,2?-dideoxy-?,?-D-ribofuranos-1?-yl)-4-(coumarin-4??-yl)-1,2,3-triazole derivatives using Novozyme®-435 catalysed deacetylation reaction (Scheme1). All synthesised compounds have shown fluorescence in blue or green region with moderate quantum yields (? = 0.1-0.3).



Scheme 1

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P-185

Convenient route to ?-C-glycosides: Synthesis of sugar-PEGamphiphilicco-polymer for encapsulation of non-polar drugs

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The C-glycosides are important stable class of carbohydrate derivative that possess interesting biological properties. They are used as synthetic intermediates to prepare amino acids, C-linked disaccharides, heterocycles of biological importance1and as models in enzymatic and metabolic studies because of the fact that the conformations of glucose, mannose and their C-linked analogs has little difference.2 Few synthetic approaches have been developed over the years for the preparation of ?-C-glycosyl aldehydes. In most of the synthesis of ? -C-glycosyl aldehydes either the ?-anomer has to be isomerized or the ?-isomer has to be separated from the anomeric mixture formed during the synthesis.3 We herein report a convenient and straightforward method for diastereoselective synthesis of ?-C-glycosyl aldehydes and carbinols from D-glucose and D-mannaose, and use of these glycosylcarbinols for co-polymerization with PEG-1000 diethyl ester to afford amphiphilic sugar-PEG co-polymer, which has been found to be a potential encapsulating system for nonpolar drugs/model drugs.4

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P-186

Molecular Modelling and Dynamics Studies for TrypanothioneSynthetase of trypanosomatids

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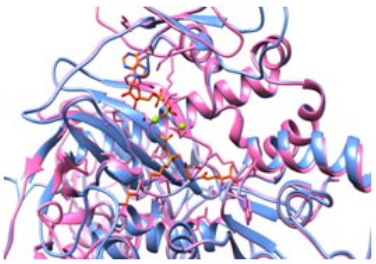
The protozoan parasites Trypanosoma and Leishmaniacause neglected diseases such as Chagas' disease,African sleeping sickness and various forms of Leishmaniasis and still possess challenge to mankind. In the present era of structure based drug discovery trypanothionesynthetase has emerged as new drug target and is genetically as well as chemically validated[1]. It is bifunctional enzyme possessing synthetase and amidase domain and catalyzes biosynthesis and hydrolysis of glutathione-spermidine adduct trypanothione which is main intracellular thiol-redox metabolite in parasitic trypanosomatids[2] .This contribution describes the homology modelling of Leishmaniadonovani and Trypanosomabruceiand molecular dynamics simulations shed light to trypanothione biosynthesis and explains the binding sites for substrates viz glutathione, spermidine and ADP. This computational analysis will provide better insight in structural and substrate binding mechanism and hence will serve in rational identification and design of specific inhibitors of T (SH)2 biosynthesis.



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P-187

Synthesis, characterization and antimicrobial activities of hydroxytriazenes

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The present paper describes synthesis of flouro chloro substituted hydroxytriazenes[1-4]. Further these compounds have been duly characterized by CHN, IR, 1H NMR and Mass spectral analysis. The compounds have been used for biological activity studies against 4 bacteria and 6 fungal strains. The MIC (Minimum inhibitory concentration) values varied between 25 µg/mL to 50 µg/mL.

Keywords: Hydroxytriazene, Antimicrobial activity

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P-188

Effect of Grewia asiatica (Phalsa) on scopolamine induced memory deficit and behaviour mediated by monoamines

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Aim : To study effect of Grewia asiatica (Phalsa) on scopolamine induced memory deficit and behaviour mediated by monoamines.

Introduction: Management of cognitive disorders has been challenging since long. Grewia asiatica also known as phalsa contains anthocyanins and posesss high antioxidant, radioprotective and anti diabetic activity. Nootropic drugs like Piracetam and cholinesterase inhibitors like Donepezil are associated with several side effects. So nootropic activity of different extracts ie. Petroleum ether, chloroform and methanolic of Grewia asiatica fruit is assessed in scopolamine induced amnesia in wistar rats.

Method : Elevated plus maze is used as exteroceptive model. Scopolamine (1mg/kg) is used to induce amnesia and piracetam (120mg/kg) as standard drug. At the end of the experimental protocol biochemical parameters like Acetylcholinesterase, Lipid peroxidase and Superoxide dismutase are measured in brain homogenate. Effect of extract on monoamine mediated behaviour is studied using Haloperidol induced catalepsy and lithium induced head twitches.

Result: Methanolic extract at a dose of 200mg/kg among all three extracts causes highest significant reduction in TL time on elevated maze as measured on 7th and 14th day (parameter for acquisition memory) and on 8th and 15th day (parameter for retention memory) significantly compared to scopolamine group ($p<0.001$). It further decreases acetylcholinestrase and Lipid peroxidase content and an increase in SOD level compared to scopolamine group significantly. Methanolic extract also decreases haloperidol induced catalepsy duration and number of lithium induced head twitches at 200 and 400 mg/kg significantly ($p<0.001$) compared to vehicle group.

Conclusion: Thus the study shows promising effect of Grewia asiatica fruit extract in enhancing learning and memory due to presence of certain bioconstituents and modifies dopamine and serotonin mediated behaviour.

P-189

Simultaneous spectrophotometric determination of cobalt and nickel using 3-hydroxy-3-phenyl-1-(4-trifluoromethyl phenyl)triazene

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Simultaneous spectrophotometric determination of cobalt and nickel by H-point standard addition method (HPSAM) is described. The method was based on different colour reactions of 3-hydroxy-3-phenyl-1-(4-trifluoromethyl phenyl)triazene (HPTPT) with cobalt and nickel in aqueous medium at pH 7.5-9.0 in the presence of surfactant triton X-100 at two wavelength 410 and 445 nm. Experimental conditions such as colour development, reagent concentration, pH of the medium were optimized. The developed method has also been successfully applied to spectrophotometric determination of Co^{2+} and Ni^{2+} in synthetic samples with RSD of 0.55 and 0.10%, respectively.

Keywords: Hydroxytriazenes, Simultaneous Spectrophotometry, Cobalt, Nickel

P-190

Nature-inspired Synthetic and Natural Pterocarpans and Their Therapeutic Potential

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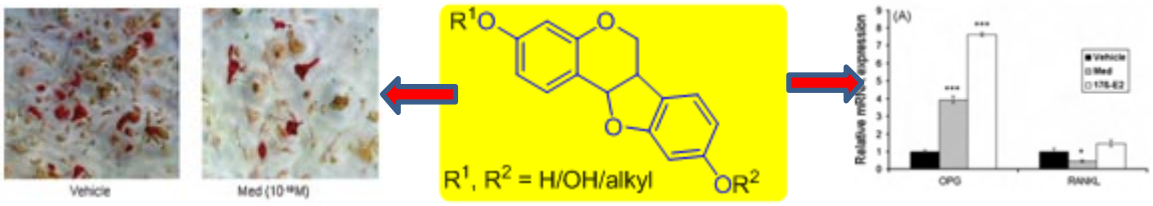
Osteoporosis, is characterized by low bone mass and microarchitectural deterioration of bone tissue resulting in the bone fragility and a consequent increment in fracture risks as the life expectancy going to increase.1 Natural products play a crucial role in the area of drug discovery. During drug development program in CDRI it was observed that crude extract of Butea monosperma exhibited in vitro bone forming (osteoblast mineralization) activity.2 Medicarpin, a pterocarpan class of naturally occurring benzopyran furanobenzene compound was synthesized in gram scale to investigate its effects on murine bone cells and in ovariectomized (OVx) mice. Medicarpin, at as low as 10?10M suppressed osteoclastogenesis in bone marrow cells (BMCs). In co-cultures consisting of calvarial osteoblasts and BMCs, presence of medicarpin increased osteoprotegerin (OPG)/receptor activator of NF-?B ligand (RANKL) ratio and reduced mRNA levels of osteoclast markers including tartrate-resistant acid phosphatase and receptor activator of NF-?B (RANK).3



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P-191

Rational-Based Design and Synthesis of Novel Functionalized Biphenyls and Pyranones as Potent Antihyperglycemic Agents

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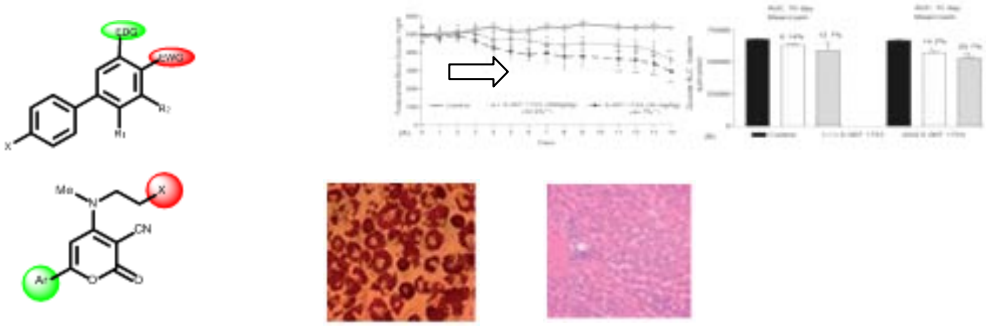
Type 2 diabetes mellitus (DM) is a chronic metabolic disorder which has global impact. Its scourge has affected around 382 million people of the world's population in 2013 and by 2035, this will rise to 471 million.1 Despite the availability of several classes of anti-diabetic drugs, maintenance of sufficiently long-term glycaemic control remains a common challenge, and side effects have also become an increasingly important issue.2

For the last few years, in our laboratory we are involved in the design and synthesis of new antihyperglycemic agents for the treatment of diabetes.3 We reported the synthesis and antihyperglycemic activity of novel dihydronapthofurans and dibenzofurans.4 In continuation, the biphenyl and pyranone skeleton was chosen for further antihyperglycemic studies and showed exceptional PTP-1B inhibitory and insulin sensitizing cum hepatoprotectant activity respectively.5,6 In this presentation, synthesis, in vitro and in vivo antihyperglycemic activity of these compounds will be discussed.



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P-192

Donor-Acceptor Based Arenes and Heteroarenes for Cell Imaging and Metal sensing Applications

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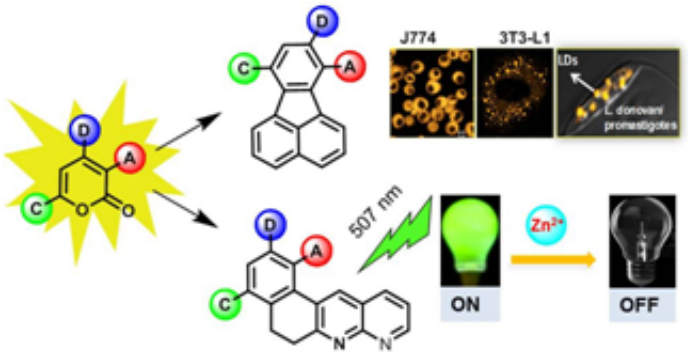
Fluorescent organic molecules play an important role in chemical and biological sciences. In biological point of view, these fluorescent molecules are being used as fluorescent probes for live cell imaging of specific intracellular target proteins to understand intracellular events and elucidating various biological phenomena in cell biology and drug discovery.1 In our laboratory we are engaged in design and synthesis of new donor-acceptor based ?-conjugated fluorescent organic molecules with variety of excitation and emission wavelength and their application in biological (as bio-marker for live cell imaging),2 chemo-sensing3 and material sciences.4-6

In this poster well designed and rapid synthesis of a new series of arenes and heteroarenes and their exciting applications in selective fluorescence staining in live cell and heavy metal detection will be discussed in detail.



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P-193

Synthesis, Characterization, Pass & in Vivo Anti-Inflammatory Activity of Sulfacetamide Based Hydroxytriazenes

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In the present paper seven hydroxytriazenes synthesized from diazotized sulfacetamide have been screened for theoretical biological activities using PASS (prediction of activity spectra for substances). Further all the seven compounds have been characterized on the basis of IR, 1H NMR, 13C NMR & Mass spectra along with m.p. determination. Theoretical prediction for all these compounds indicated good anti-inflammatory activities (Pa> 88-97%), on the basis of which these activities have been validated experimentally by in-vivo studies on Male or female Wistar albino rats. The value ranges from 89-98.80%. Thus the present paper deals with computer aided drug design (CADD) and experimental validation of the predicted activities.

P-194

Formulated natural plant extracts from nutmeg and pepper show antifungal activity against clinical isolates of Candida albicans and affects cellular morphology and ergosterol

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Candida is an opportunistic fungal pathogen accounting for high rates of mortality and morbidity in immunocompromised individuals. Of all Candida spp, Candida albicans is the fourth most common cause of nosocomial infections globally. Emergence of multidrug resistance and limitations in availability of broad spectrum drugs with minimum host side effects have been hindering the control and treatment of fungal infections.

In the recent times, natural products have gained impetus in their use as antimicrobials owing to their broad spectrum, multiple targets in the microbial cells and negligible host toxicity. For this study we prepared formulations of two plant products, nutmeg and pepper. The formulations were prepared by extracting the active components using isopropanol followed by subsequent distillation and emulsification by ethylacetate. Anti-Candidal activity of the formulations of these two extracts were confirmed by both microdilution assay and spot assays. The growth inhibition was found to be more in pepper than nutmeg. Formulations of nutmeg and pepper revealed more than 80% growth inhibition at respective concentrations of 50µl/ml and 25µl/ml (v/v). Treated cells showed reduced ergosterol content, altered cell morphology, cell wall thickening, membrane aberrations and cytoplasm displacement. The antimicrobial effects observed may be due to the phenol, polyphenols, terpenoids, flavanoids, alkaloids and quinones present in the plant extracts. Further investigations are underway. This study has the potential to

contribute to the development of new therapeutic strategies for further clinical applications in the treatment of Candidiasis.

Keywords: Candida albicans; antifungal agents; natural plant products; ergosterol; pepper; nutmeg

P-195

Determination of Famotidine: A Novel Inhibitory Kinetic Spectrophotometric Method

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A kinetic spectrophotometric method for the determination of famotidine, based on its inhibitory effect on Hg(II) catalyzed substitution of cyanide ion, by 4-cyanopyridine in hexacyanoferrate(II) is described. Famotidine ions form strong complexes with Hg(II) catalyst which is used as the basis for its determination at trace level. The progress of reaction was monitored, spectrophotometrically, at 477nm (?max of [Fe(CN)5CNpy]3?, complex) under the optimum reaction conditions at: [Fe(CN)64-] = 5 × 10-3 M, [4-CNpy] = 2.5 × 10-4 M, [Hg2+] = 2 × 10-5 M, pH = 2.8 ± 0.02, I = 0.02 M (KNO3) and temperature = 25±0.1°C. A linear relationship obtained between absorbance (measured at 477nm at different times) and inhibitor concentration, under specified conditions, has been used for the determination of [famotidine] in the range of 0.2 - 2.0 × 10?5M with a detection limit of 5.2 × 10?7 M. The standard deviation and percentage relative standard deviation have been calculated and reported with each datum. A most plausible mechanistic scheme has been proposed for the reaction. The values of equilibrium constants for complex formation between catalyst-inhibitor (KCI), catalyst-substrate (Ks) and Michaelis-Menten constant (Km) have been computed from the kinetic data. The influence of possible interference by major cations and anions on the determination of famotidine and their limits has been investigated.

P-196

Novel 3-aminopyrazine 2-carbohydrazides as an anti-tubercular agent

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The novel series of twenty six 3-amino-N'-benzylidenepyrazin-2-carbohydrazide derivatives (3a-z) were synthesized by microwave irradiation method [1,2]. The major intermediate 3-aminopyrazine 2-carbohydrazide was isolated by lyophilization. All the compounds were screened for anti-tubercular activity against Mycobacterium tuberculosis H37Ra by using XRMA protocol [3]. Out of 26 synthesized compounds, four 3-amino-N'-

benzylidenepyrazine-2-carbohydrazide derivatives, 3i, 3j 3v and 3z were found significantly active against M. tuberculosis H37Ra at a concentration of 100 µg/ml.

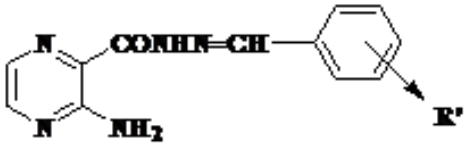

Fig. 1. 3-amino-N'-benzylidenepyrazin-2-carbohydrazide derivatives (3a-z)

The compounds 3i, 3j, 3v and 3z showed % inhibition of 99, 98, 92 and 87 % of the mycobacterium, respectively. This was found to be comparable to that by the standard drug rifampicin (94.21%). The MIC and IC50 values for these compounds were found in the range of 24-110 and 5.9-11.1 µg/ml, respectively.

To prove the structural characteristics influencing the antimycobacterial activity of these compounds, an SAR classification model was derived based on a binary QSAR approach termed as "Recursive Partitioning Analysis (RPA) [4]. The structural features highlighted by the RP model can serve as a guide to design new lead compounds.

Fig. 2. RP Model

Table 1. Statistical results of recursive partitioning

Class	No. of molecules	Activity	% of molecules	Class % as Obs Correct	Overall % Pred Correct	as Enrichment Ratio
1	20	0	76.92	100	100	1.30
2	6	1	23.08	100	100	4.33

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P-197

Synthesis and Characterization of Some Promising Fluoro Group Containing Antimicrobial Agents: A New Class of Pyrazole Barring Pyrimidine Motifs

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In view of eternally swelling demand for novel antimicrobial agents, the supreme significant goal for chemists is to confirm that the next era of synthetic approach for medicinal drugs and fine chemical synthesis is more sustainable than the current generation. Fluoro group heterocycles showed some promising results against bacterial and fungal strains. In continuation to this, the present work deals with the synthesis and antimicrobial activity of novel series of 5-(4-arylidene-3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carbonyl)-4-(2-fluorophenyl)-6-methyl-3,4-dihydro pyrimidin-2(1H)-ones. The structures of the newly compounds were elucidated by IR, 1H-NMR, 13C-NMR, and Mass spectra. Newly synthesized compounds were screened for in vitro antimicrobial activity against Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyogenes, Candida albicans, Aspergillus niger and Aspergillus clavatus by using serial broth dilution method.

P-198

Baeyer-Villiger Oxidation of Cyclohexanone Using Zeolite-Y Based Nanoporous Materials

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Zeolite-Y based nanoporous materials were prepared by Flexible ligand method. Prepared materials were characterized by powder X-ray diffraction (XRD), spectral studies (UV-Vis and FTIR), ICP-OES, elemental analysis, SEMs, BET and thermogravimetric (TG) analysis. Oxidation of cyclohexanone was carried out over neat complexes as well as zeolite-Y based nanoporous materials using t-butyl hydroperoxide as an oxidant. The effect of experimental variables (solvents, reaction temperature, the amount of catalyst used and the reaction time) were examined in order to get suitable reaction conditions.

Keywords: Baeyer-Villiger oxidation, cyclohexanone oxidation, nanoporous materials.

P-199

Anti-Infective Assay of Newly Synthesized 4-Oxo-Thiazolidine Derivatives

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A new series of 4-oxo-thiazolidine was synthesized by condensation reaction. These synthesized compounds (AJP5a-j) were identified and characterized by various techniques like FT-IR, 1H-NMR, 13C-NMR and mass spectroscopy. In- vitro antimicrobial activities were evaluated against four bacterial strains: Staphylococcus aureus (MTCC-96), Streptococcus pyogenus (MTCC-442), Escherichia coli (MTCC-443), Pseudomonas aeruginosa (MTCC-1688) and two fungal pathogens: Candida albicans (MTCC 227) and Aspergillus clavatus (MTCC 1323). The results were expressed as minimal inhibition concentration (MIC g/mL) in comparison with standard drugs. Compounds AJP5a, AJP5c, AJP5d, AJP5e, and AJP5i were showed moderate to good activity against selected bacterial strains (MIC= 62.5 g/mL to 125 g/mL). In vitro antitubercular activity of compounds AJP5a-j was carried out against Mycobacterium tuberculosis H37Rv. Two compounds AJP5c and AJP5j showed good antituberculosis activity in comparison with standard drugs.

Keywords: 4-oxo-quinazoline; 4-oxo-thiazolidine; Antibacterial activity; Antifungal activity; Antitubercular activity

P-200

Microwave-Assisted Facile Synthesis of Some Novel Indole and Pyridine Based 1,3,4-Oxadiazole Derivatives As Potential Antitubercular Agents

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Microorganisms resistant to multiple antimicrobial agents pose a serious threat to mankind, increasing morbidity and mortality and henceforth the overall healthcare cost [1]. Treatment of mycobacterial infections is often difficult because these bacteria are intrinsically resistant to most common antibiotics and chemotherapeutic agents [2]. In continuation to this [3-4], a rational approach was adopted for the synthesis of some novel indole and pyridine based 1,3,4-oxadiazole derivatives under conventional heating as well as microwave irradiation technique and characterized by IR, 1H NMR, 13C NMR spectroscopy and mass spectrometry. Entitled compounds 5a-t were tested for their in vitro antitubercular activity again H37Ra and mycobacterium bovis BCG. Details of reaction conditions and activity results will be presented in poster presentation.

P-201

Oxidation of Cyclohexene Catalyzed By "Ship In Bottle" Complexes

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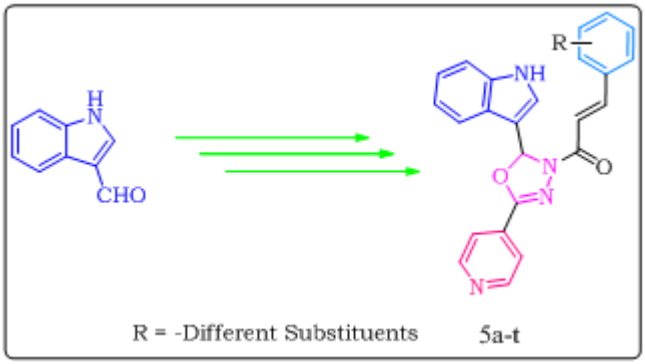
Transition metal [M = Mn(II), VO(IV)] complexes with Schiff base ligand of 2-hydroxyacetophenone and ethylenediamine (H2hacen) have been entrapped within nanopores of zeolite-Y by flexible ligand method. These materials have been characterized by various physico-chemical techniques such as ICP-OES, FT-IR, 1H- and 13C-NMR, Elemental analyses, and UV-Vis electronic spectral studies, BET, TGA, mass spectrometry, scanning electron micrographs (SEMs), X-ray diffraction patterns (XRD), conductivity as well as atomic absorption spectroscopy (AAS). These materials have been utilized as heterogeneous catalysts for liquid phase oxidation of cyclohexene using TBHP and/or H2O2 as an oxidant. The results showed high activity and selectivity of all catalysts toward the formation of cyclohexenone, cyclohexenol, and cyclohexene peroxide from cyclohexene. The reaction parameters have been optimized for the maximum oxidation of cyclohexene. These catalysts can be recovered and reused without remarkable loss of activity

Keywords: Zeolite-Y entrapped complexes, Schiff base ligand, and oxidation of cyclohexene



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P-202

Catalytic Oxidation of Limonene Over Zeolite-Y Entrapped Oxovanadium (Iv) Complexes As Heterogeneous Catalysts

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A series of VO(IV) complexes with Schiff base ligands derived from vanillin thiophene-2-carboxylic hydrazone (VTCH), vanillin furoic-2-carboxylic hydrazone (VFCH), salicylaldehyde thiophene-2-carboxylic hydrazone (H2STCH) and/or salicylaldehyde furoic-2-carboxylic hydrazone (H2SFCH) have been synthesized as neat and their entrapped complexes into the nanopores of zeolite-Y. These compounds were characterized by several techniques like chemical analysis (ICP-OES and elemental analysis) and spectroscopic methods (FT-IR, electronic, XRD, SEMs and BET). All the prepared catalysts were tested over the liquid phase limonene oxidation reaction, using t-butyl hydroperoxide (TBHP) and/or 30% H2O2as oxidants. Limonene glycol, carveol and carvone were the main products obtained during chemical reaction. It was observed that zeolite-Y based entrapped complexes exhibited higher catalytic activity than neat VO(IV) complexes. These zeolite-Y based entrapped complexes are quite stable and recyclable under current reaction conditions. Amongst them, [VO(VTCH)2]-Y showed higher catalytic activity (97.7%) with limonene glycol (45.1%) selectivity.

Keywords: Zeolite-Y VO(IV) complexes, Heterogeneous catalysts, Limonene oxidation

P-203

In-Vitro Antimicrobial Assay of Extracts Of Aerial Parts Of Cassia Species

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Total eight solvents were used to extract various secondary metabolites from aerial parts of C siamea, and C javanica. Antibacterial assay of eight extracts was done against bacteria Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli and Pseudomonas aeruginosa. The results were compared against standard antibiotics. Antifungal assay of eight extracts was done against fungi strains Candida albicans, Aspergillus niger and Aspergillus clavatus and results were compared against standard antifungal agents. The overall results provided evidence that the leaf extract of C. siamea in acetone might be a potential source of new antimicrobial drug against gram positive and gram-negative bacteria studied in present work. It is concluded from the results that phytochemicals are responsible for such inhibition of multi resistance microorganisms and four major families of phytochemicals were identified by GC-EI-MS method.

Keywords: Cassia siamea; Cassia javanica; antibacterial assay; antifungal assay; Disc dilution method; Phytochemicals

P-204

Microwave Assisted Synthesis of Novel 1,3,4-Oxadiazole Analogues As Potential Antitubercular Agents

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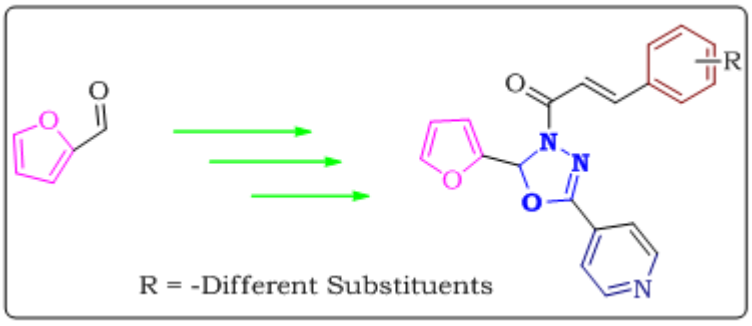
Tuberculosis (TB) is a global epidemic caused by the pathogenic bacterium Mycobacterium tuberculosis [1]. Emergence of new virulent forms of TB such as multi drug resistant (MDR-TB) and extremely drug resistant (XDR-TB), and its synergy with human immunodeficiency virus (HIV) has become a major threat to mankind [2-3]. All the above facts necessitated an urgent need to develop newer potent and fast acting antitubercular agents with improved biological properties. Keeping this in view and in continuation of our previous work [4-5] we synthesized 1-(2-(furan-2-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-3-(aryl)-prop-2-en-1-ones by conventional as well as microwave method in order to better yield. Details of reaction conditions and activity results will be presented in poster presentation.



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P-205

A New Synthetic Methodology and In Vitro Antimicrobial Evolution of Pyrimidine Clubbed Imidazole Derivatives

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The emergence of microbial strains resistant to the recent antibiotics highlights the need for search of novel antimicrobial agents. In continuation to this, the present work deals with the synthesis and antimicrobial activity of novel series of N-(4-arylidene-2-mercapto-5-oxo-4,5-dihydro-1H-imidazol-1-yl)-4-(4-fluorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides. The structures of the compounds were elucidated by IR, 1H-NMR, 13C-NMR, and Mass spectra. All the newly synthesized compounds were screened for in vitro antibacterial and antifungal activity on against E. coli (MTCC-443), P. aeruginosa (MTCC-1688), S. aureus (MTCC-96), S. pyogenes (MTCC-442), C. albicans (MTCC-227), A. niger (MTCC-282) and A. clavatus (MTCC-1323) by using serial broth dilution method.

P-206

Simultaneous Rp-Hplc-Pda Determination of Salicylamide, Salicylic Acid and Deferasirox in The Bulk Api Pharmaceutical Dosages Forms

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The reverse phase high performance liquid chromatographic (RP-HPLC) method has been developed for simultaneous estimation of starting material, impurities and final product in bulk API forms. The proposed method utilizes waters symmetry C18 (250 cm × 4.6 mm, 5 ?m) column, mobile phase consisting of buffer and acetonitrile in the proportion of 40: 60 (v/v) with apparent pH adjusted to 3.2, and UV detection at 245 nm. The described method was linear (r2 ? 0.99) over a range of 1-50 ?g/ml and relative standard deviation values for intra-day and inter-day precision studies were less than 1.0% for all ingredients. The analytical mean recoveries of salicylic acid, salicylamide and deferasirox by the developed RP-HPLC method were 99.74%, 99.52% and 99.40 % respectively. This method was validated by evaluation of different parameters like specificity, accuracy, precision, system suitability, linearity, LOD and LOQ according to ICH guidelines. The method has been successfully applied for the analysis of drugs in pharmaceutical dosages forms.

P-207

Synthesis, Characterization and Antimicrobial Studies of Novel Quinoline Based Pyrazoline Heterocycles

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The bio-active properties of heterocycles in general make them more interesting in the area of drug discovery program and pharmaceutical industries. A series of compounds 2-[5-(2-chloro-6-fluoro(3-quinolyl))-3-(aryl)-2-pyrazolinyl]-1,3-thiazolin-4-ones (4a-l) were synthesized and structures of these compounds were elucidated by spectral IR, 1H NMR, 13C NMR, and mass spectra analysis. Newly synthesized compounds were screened for their antibacterial and antifungal activities on E. coli, S. aureus, P. aeruginosa, S. pyogenes, C. albicans, A. niger and A. clavatus. Evaluation of antimicrobial activity showed that several compounds exhibited greater activity than reference drugs and thus could be promising new lead molecules.

P-208

Synthesis and antimicrobial assessment of some quinoline clubbed 1,3,4-oxadiazole derivatives

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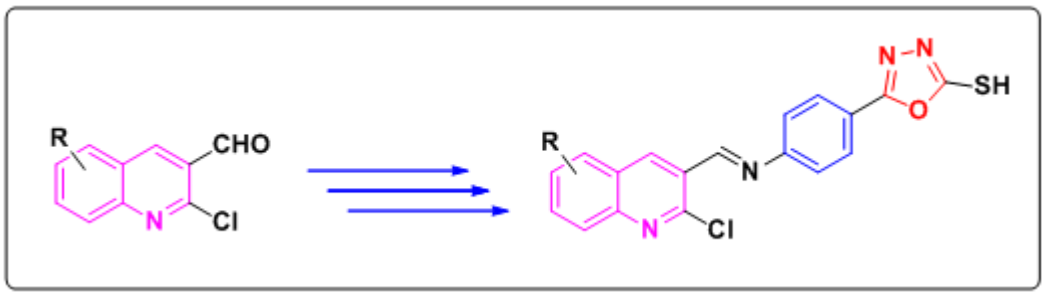
The emergence of microbial strains resistant to the present antibiotics highlights the need for search of newer antimicrobial agents. In continuation to this,1-4 the present paper deals with the synthesis and antimicrobial activity of a novel series of 5-(4-(((2-chloroquinolin-3-yl)methylene)amino)phenyl)-1,3,4-oxadiazole-2-thiol. The newly synthesized compounds 6a-j were proficiently synthesized and characterized by IR, 1H NMR, 13C NMR



spectroscopy and mass spectrometry and were in full agreement with the proposed structures and evaluated for their in vitro antibacterial activity against four bacterial and three fungal human pathogenic strains using conventional broth microdilution method. Details of reaction conditions and activity results will be presented in poster presentation.

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P-209

Metabolomics as a tool to investigate bio-prospection of plants

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Metabolite profiling provides information about a plethora of metabolites and thus is an efficient tool to screen plants for novel bioactive compounds from phyto-resources. It is important to figure out entire range of metabolites of medicinal plants so as to identify bioactive molecules. Lack of complete information of the phytoconstituents limits its application for therapeutical role. Commiphora wightii (Arnott) Bhandari (syn. Commiphora mukul) commonly known as guggul, is one of the most revered taxa in traditional medicinal system for its unique pharmaceutical applications. The medicinal importance of guggul is attributed to the presence of two-ketosteroids, guggulsterone-E and guggulsterone-Z, which are present in stem as well as in gum resin of the plant. The NMR and GC-MS based non-targeted metabolite profiling identified 118 chemically diverse metabolites including amino acids, fatty acids, organic acids, phenolic acids, pregnane-derivatives, steroids, sterols, sugars, sugar alcohol, terpenoids, and tocopherol from aqueous and non-aqueous extracts of leaves, stem, roots, latex and fruits of C. wightii. Very high concentrations of quinic acid and myo-inositol in aqueous extracts of leaves and fruits; a substantial quantity of a-tocopherol, N-methylpyrrolidone and, trans-farnesol in non-aqueous extracts of leaves and fruits, makes the taxa distinct, since these metabolites with medicinal properties find immense applications as dietary supplements and nutraceuticals.

P-210

Photocatalytic Oxidative Heterocyclization of Semicarbazones: An Efficient Green Approach for the Synthesis of 1,3,4-Oxadiazoles

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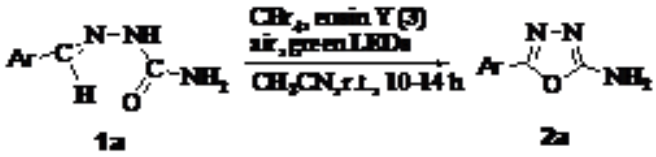
The development of green methods for the formation of C-C and C-N bonds is of great importance and remains a pre-eminent goal in current synthetic chemistry.1 In this venture, photocatalysis using visible light represents a unique strategy because of its inherent green chemistry features.2. In requisite of a cheap, ecofriendly and metal-free catalyst, an organic dye eosin Y has pledged to be indispensable for high photocatalytic performances.3

Among five-membered heterocyclic compounds, 2,5-disubstituted 1,3,4-oxadiazoles have become an important construction motif for the development of new drugs. Several methods are reported in the literature utilized reagent require special care for handling and are not eco-compatible.4 The work-up procedure for each synthetic step to yield desired products requires great precautions. Hence, the development of simple, efficient and ecofreindly methods for the rapid and concise synthesis and modification of oxadiazole motif need to be developed.5

Therefore, we have developed an efficient, metal free and direct pathway for a one-pot synthesis of 2-amino-5-aryl-1,3,4-oxadiazoles under mild conditions. The protocol involves the visible light mediated intramolecular, aerobic oxidative heterocyclization of substituted semicarbazones to 1,3,4-oxadiazoles using CBr4 as an oxidant and eosin Y as the photoredox catalyst. This protocol is a superior alternative to the existing syntheses of 1,3,4-oxadiazoles with the advantage of employing visible light and atmospheric oxygen as the greenest and sustainable reagents.



Scheme 1. Photooxidative heterocyclization of semicarbazones

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P-211

New osteogenic phytoceramides and acylated phytosterol glucosides from Pterospermum acerifolium Willd. seed coat

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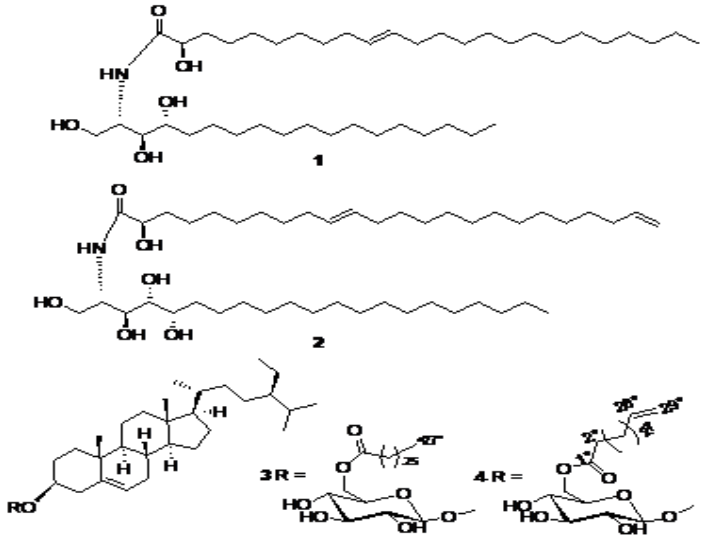
The Pterospermum acerifolium (Linn.) Willd. belongs to the family Sterculiaceae is distributed through Southeast Asia, from India to Burma. The plant is locally known as Kanak Champa. P. acerifolium has a wide application in traditional system of Indian medicine. The plant has been reported to inhibit the growth of cancer cells,1 and treatment of smallpox.2 A number of flavonoids and their glucosides, lignans, terpenes and amino acidshave been isolated from this plant in the search of chemical constituents.3-6 We isolated four new compounds including phytoceramides (1, 2) and acylated phytosterol glucosides (3, 4) (Fig. 1) along with five known compounds



from the seed coat of P. acerifolium. New compounds (1, 2, 3 and 4) were evaluated for their osteogenic activity using neonatal (1-3 days old) rat calvaria derived primary osteoblast cultures. Compound 1 and 2 showed a significant stimulative effect on differentiation of cultured osteoblast cells.7

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P-212

A Glycal Approach to the Synthesis of Macrolide (-)-A26771B

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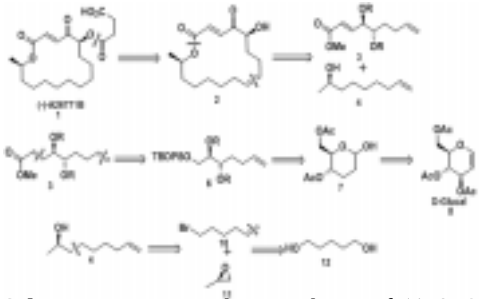
Macrolide antibiotics are a safe and effective class of drugs for the treatment of respiratory tract infections since most of which target the bacterial ribosome by reversibly binding the 50S subunit in the peptidyl traseferase center, which ultimately blocks protein synthesis. (-)-A26771B, a white solid 16 membered macrocyclic lactone, shows moderate activity against gram-positive bacteria, mycoplasma and fungi was first isolated from the fungus pencillium turbatum by K. H. Michel *et al.* in 1977[1] and later its absolute configuration was established by Kuniaki Tatsuta and his group in 1980.[2] Structurally it possesses *ã*-oxo-*ä*-acyloxy-*á,â*-unsaturated carboxyl functionality and two asymmetric centers at 5*S* and 15*R* stereochemistry. Because of these interesting structural feature as well as biological activity, synthetic community was attracted to total synthesis of this macrolide.[3] Up to date more than ten different strategies have been developed of which only few are based on chiron. Our attention in carbohydrate based chemistry towards the synthesis of macrolides encouraged us to synthesis of (-)-A26771B**.**



Scheme 1: Retro synthetic pathway of (-)-A26771B

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P-213

Organocatalytic Asymmetric Mannich Cyclization of Hydroxylactams with Acetals: Total Syntheses of (-)-Epilupinine, (-)-Tashiromine, and (-)-Trachelanthamidine

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Naturally occurring izidine alkaloids (pyrrolizidine, indolizidine,and quinolizidine) and their synthetic variants are of considerable importance because of their diverse biological activities [1]. The syntheses of izidine alkaloids have been described using chiral-pool [2], chiral auxiliary [3] and catalytic approaches. But these approaches are defined and specific to syntheses of izidine alkaloids. Prompted by the biosynthetic pathway of pyrrolizidine alkaloids [4], here we report an asymmetric, organocatalytic, one-pot Mannich cyclisation between a hydroxylactam and Acetal with a Macmillan catalyst to offer fuse, bicyclic alkaloids bearing a bridgehead N atom. Both aliphatic and aromatic substrates were used in this transformation to furnish chiral pyrrolizidinone, indolizidinone, and quinolizidinone derivatives in up to 89% yield and 97% ee. The total syntheses of (-)-epilupinine, (-)-tashiromine, and (-)-trachelanthamidine also achieved to demonstrate the generality of the process.

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P-214

Study of free radicals in mediating carcinogenesis through occupational exposure

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The purpose of the proposed study is to identify the mechanisms contributing to metal-induced cancer. Particularly, the role of free radicals/reactive oxygen species and the underlying signaling pathways in the regulation of apoptosis/cell proliferation will be studied. This study will elucidate the molecular mechanisms by which workers exposed to metals (occupationally) such as arsenic and chromium, develop cancer in the later stages. The working hypothesis is that free radical reactions play an important role in cell signaling; and an alteration in the cell cycle process leads to the abnormal/uncontrolled cell proliferation. Molecular biology, cell biology and biochemical techniques will be carried out in the proposed study.

P-215

Characterization of Indian Himalayan Medicinal Mushrooms

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Indian medicinal mushroom,*Ophiocordyceps sinensis* is popularly known as Yarsagumba (winter worm summer grass) in India, Nepal and Bhutan. It is one of the most-prized herbs of Ayurveda and is also known as Bhu-Sanjivani. *Ganoderma lucidum* is commonly known as"Lingzhi" in Chinese, "Reishi" in Japanese. Both the mushrooms have broad medicinal effects such as immuno-enhancer, antioxidant, anti-aging, tonic effect, hepatoprotective, neuro-cardioprotective etc.Rathor et al.[1, 2]; Singh et al. [3].

Here,for the first time we present the results of the proximate analysis of the crude powderof *Cordyceps sinensis*and*Ganodermalucidum*(Indiacultured mycelium and fruiting body) in terms of various parameters such as Moisture content,Total ash, Protein,Crude Fat, Crude Fiber,Carbohydrate,Nitrogen and heavy metals. The Preliminary qualitative analysis of crude powder as well as water extract of *C. sinensis* and *G. Lucidum* revealed the presence of Alkaloids, Carbohydrates, Saponins, Proteins, Phenolic Compounds, Fat and Gums. Protein

estimation of all these powders and extracts by 1-D electrophoresis indicated the presence of wide range of proteins. Further, HPTLC analysis also showed the presence of nucleotides and nucleosides in both the medicinal mushrooms.

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P-216

SYNTHESIS OF SOME NOVEL PYRIMIDINE CLUBBED PYRAZOLE HYBRIDS AS ANTIMICROBIAL AGENT

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Abstract

As a part of our on-going endeavours in the exploration of novel antimicrobial agents, we here in report a novel synthesis of hybrid molecules 5-(4-acetyl-5-aryl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-(4-flurophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-ones **4** by combining pyrimidine and pyrazole scaffolds having diverse pharmacological actions. The characterization of these newly synthesized compounds was carried out by IR, ^{1}H and ^{13}C NMR and Mass spectroscopy. All the synthesized compounds were evaluated for their *in vitro* antimicrobial activity against Gram-positive bacteria (*Staphylococcus aureus* and *Streptococcus pyogenes*), Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and fungi (*Candida albicans*, *Aspergillus niger* and *Aspergillus clavatus*) using serial broth dilution method. Among all these synthesized compounds **4l** and **4d** were emerged as highly potent molecules with 12.5 µg/mL potency against *Pseudomonas aeruginosa* and *Aspergillus niger* respectively.

Synthesis and Biological Evaluation of Novel 3-(4-hydroxycoumarino)-3-phenylpropanamide Derivatives as Antithrombotic Agents

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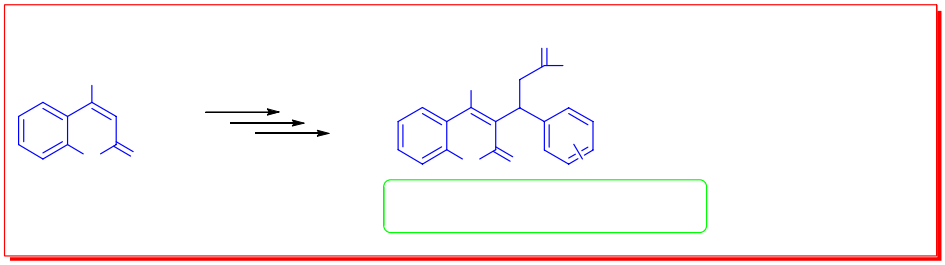
Abstract:

Haemostasis is the normal physiological response that prevents significant blood loss following vascular injury,[1] however the imbalance in the coagulation system (thrombosis) leads to significant morbidity and mortality.[2] The most widely used medications for treating thrombosis are heparins and **vitamin K antagonists** (VKAs).[3] Vitamin K antagonists have been used as anticoagulants for over 50 years for the prevention of thrombosis, systemic embolism in prosthetic heart valves, atrial fibrillation, and myocardial infarction.[4] Bleeding is the major side effect of VKAs therapy. Other limitations are narrow therapeutic window, interactions with drugs and food, delayed onset and offset of anticoagulant effect, need for frequent coagulation monitoring and dosage adjustments, etc.[5] Despite these adverse effect warfarin is still medication of choice in the treatment and prophylaxis of thromboembolic disease.[4] Here a series of novel 3-(4-hydroxycoumarino)-3-phenylpropanamide derivatives were synthesized and evaluated for their antithrombotic effect in mice model of Collagen-epinephrine induced Pulmonary thromboembolism and also assessed their coagulation parameters in plasma of mice (*ex vivo*). Among 45 synthesized compounds, 13 compounds have shown 40% or above activity while remaining compounds exhibited lower activity. Three compounds were most promising showing comparable antithrombotic protection of 40% (Warfarin under the similar conditions showed 50% protection). None of the compounds showed any anti-platelet effect at 30 µM concentration confirming that antithrombotic effect of compound was only due to its anticoagulant effect not due to anti-platelet effect. Further replacing 4-hydroxycoumarin core by 4-hydroxyquinilonones or 4-hydroxybenzocoumarin group resulted in the loss of antithrombotic activity.



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P-217

Abstract

Isolation of Curcuminoids from Curcuma *longa* and further synthesis of its potential ester derivatives

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Plants have been one of the major sources of medicines since ancient civilization. The contribution of plant derived drug in modern times is still significant and has been focused on exploiting the wide diversity of medicinal plants in both traditional systems of medicine and modern drug development. Curcuma .*longa* is a well known

medicinal plant . Curcumin isolated from C.*longa* have variety of pharmacological activities like anti-oxidant, anti-bacterial, anti-cancer, anti-HIV [3] etc. Curcumin is a polyphenolic compound and have many active centres. In this conference, we assess C. *longa* rhizome for isolation and characterization of curcuminoid pigments and synthesized their bioactive conjugates[1]. Column chromatographic separation of curcuminoids (Chloroform extract) was done using silica gel (60-120 mesh) in chloroform methanol as solvent system. Curcumin is major component of curcuminoid pigments [2]. Esterification of this biologically active compound was carried out [4]. These newly synthesized compounds are being purified by column chromatography and are subjected to spectroscopic studies such as ^{1}H NMR, ^{13}C NMR, I.R, HRMS.

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P-218

Design and synthesis of some new novel trisubstituted pyrimidine derivatives as antiviral agents

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ABSTRACT

Hetrocycles are regarded as important compounds possessing pharmaceutical properties and became a major area of research worldwide. Nitrogen containing hetrocycles such as pyrimidine ring is an important pharmacophore in modern drug discovery and its derivatives exhibits diverse biological activity. This inspired us to prepare a series of trisubstituted pyrimidine ring by using multicomponent one spot synthesis.

All the synthesized compounds are characterized busing different spectral techniquesand were screened for their antiviral activity: This study provides valuable directions to our ongoing endevour of rationing, designing more patent antiviral agents.

P-219

In vitro DNA binding studies of new Chiral Quercetin-Valine organotin (IV)conjugates.

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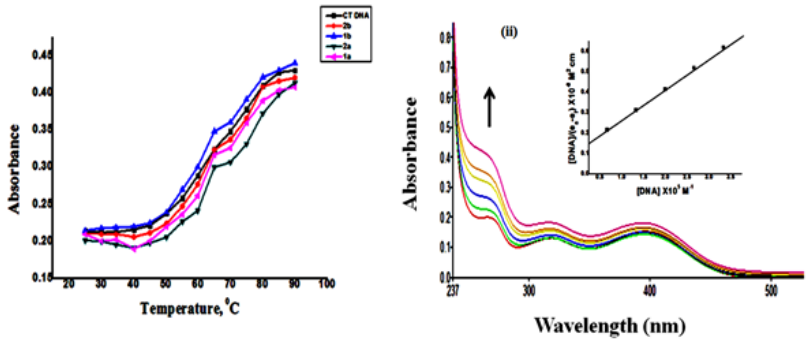
Abstract

New chiral Quercetin-Valine conjugates **1 & 2 (a and b)** were synthesised with L- and D- valine and $(CH_3)_2SnCl_2$ and $(C_6H_5)_2SnCl_2$, respectively and thoroughly characterized by elemental analysis, IR, ^{1}H NMR, ^{119}Sn NMR spectroscopy. *In vitro* DNA binding studies were carried out by UV-vis., Fluorescence and thermal denaturation and circular dichroic techniques, the experimental results revealed that the complexes bind strongly to DNA by electrostatic interaction mode. The extent of binding was quantified by computing their intrinsic binding constant K_b and binding constant K values which showed that both the L-enantiomers of complexes **1** and **2** exhibited higher binding propensity as compared to their D- enantiomeric analogs and followed the trend **2a** > **1a** > **2b** > **1b.** These studies revealed that the binding affinity of L- enantiomer of diphenyltin complex with CT DNA was highest in the order of magnitude than the dimethyltin analogs. Thermal denaturation studies of complexes in the absence and presence of CT DNA has been carried out by peltier- spectrophotometric method and the calculated "T_m was found to be 1-3 ^{0}C depicting electrostatic mode of binding well-corroborated with results of UV-vis and fluorescence studies.



P-220

Comprehensive Quantitative Analysis of Multiple Bioactive Compounds in Different Plant Parts of *Cassia auriculata* and *Cassia fistula* by Ultra-Performance Liquid Chromatography coupled to Triple Quadrupole Mass Spectrometry

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Abstract:

Indian traditional system of medicine is based on empirical knowledge of observations and the experience over millennia and more than 5000 plants are used by different ethnic communities in India. *Cassia* is an indigenous medicinal plant genus, in which *Cassia auriculata* have large biodiversity in south India and *Cassia fistula* in

north India [1]. These plants are known to contain various active principles of therapeutic value and to posses biological activity against a number of diseases. These plants possess various pharmacological activities i.e., antidiabetic, hepatoprotective, antioxidant, anticancer, immunomodulatory, nephroprotective activity, etc [2-5]. In this study, UPLC-ESI-MS/MS method has been developed and validated for simultaneous determination of twenty-three bioactive compounds in multiple reaction monitoring (MRM) acquisition mode in all parts of *Cassia fistula* and *Cassia auriculata*. The analysis was accomplished on an Acquity UPLC BEH C18 (2.1 mm × 50 mm, 1.7 µm) column using gradient elution with 0.1% (v/v) formic acid water and acetonitrile. A good linear regression relationship for each analyte was obtained over the range from 1-500 ng/ml. The proposed method was fully validated in terms of linearity, sensitivity, precision as well as recovery. The intra- and inter-day assay precision ranged from 0.73 to 3.25% and 0.95 to 3.12% respectively. The recovery relative standard deviation (RSD) measured at three concentration levels varied from 0.88-2.64%. The method sensitivity expressed as Limit of Quantitation was typically 0.07-4.18 ng/ml. The analysis results showed that there were remarkable differences in the distribution and contents of the chemical markers between various plant parts. The present study can provide necessary information for the comparative quantitative evaluation and quality control of *Cassia species*.

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IL-6

Natural products-inspired anti-microbial, anti-inflammatory and antiplatelet agents

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We have extensively worked on several plant species and isolated a large number of novel compounds belonging to different classes (alkaloids, polyphenols, steroids, amides, terpenoids, etc.). Several of these compounds have shown interesting biological activities, remarkable of them has been our extensive work on polyphenol acetates leading to the discovery of a fundamental biochemical pathway involving acetyl CoA-independent enzymatic protein acetylation. Our seminal investigations have highlighted the unique biochemical and pharmacological action of polyphenol acetates. These act as the substrates for the well-known protein calreticulin and transfer acetyl groups to certain receptor enzymes, such as cytochrome P-450 linked mixed function oxidases (MFO), NADPH cytochrome c reductase, Nitric Oxide Synthase (NOS), protein kinase c (PKC) and glutathione S-transferase (GST) resulting in modulation of their catalytic activities. The purified enzyme from buffalo liver in the presence of 7,8-diacetoxy-4 methylcoumarin (DAMC) and several other polyphenol acetates was found to significantly enhance the NOS activity in human platelets and caused significant vasorelaxation. These polyphenol acetates and several natural products were also found to lower PKC levels and suppress the ICAM-1 and VCAM-1 expression, and were found to be good anti-inflammatory & anti-asthmatic agents.

Further studies have revealed that acetoxyphenols having the vicinal diacetoxy moiety are also good radical scavengers, thus enabling these compounds to block the formation of superoxide and other reactive oxygen species. Acetyl polyphenols and several other classes of natural products were also found to be excellent inhibitors of chemical and radiation induced clastogenecity, and antifungal agents against various deadly lung fungal infections.

Details of these studies will be discussed in the presentation.

Author Index