14th ISCB INTERNATIONAL CONFERENCE (1SCBC-2010)

CHEMICAL BIOLOGY FOR DISCOVERY; PERSPECTIVES AND CHALLENGES

January 15 – 18, 2010

Organized by

Indian Society of Chemists & Biologists, India

Abstracts of Scientific Papers

Central Drug Research Institute, Lucknow, India

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January 15 – 18, 2010

SCIENTIFIC PROGRAM

Friday, January 15-01-2010

9.30 – 2.30 AM	**Registration**	
2.30 PM-3.20 PM	Inaugural Session	
	Welcome Address:	**Dr. Tushar Kanti Chakraborty, Director, CDRI**
	Introduction to ISCB:	**Dr. P.M.S. Chauhan, Secretary, ISCB.**
	Presidential Address:	**Prof. D.P. Singh, Vice chancellor , BHU, Varanasi**
	Address by Chief guest	**Prof. David St. C. Black, Secretary General ,IUPAC** University of New South Wales , Sydney, Australia
	Vote of Thanks:	**Dr. P.M.S. Chauhan, Secretary, ISCB**
3.20 PM-4.00 PM	High-Tea	

Session – I

Chairpersons: Prof. Vadim T. Ivanov and Prof. Cynthia J. Burrows

PL-1 4.00 PM-4.40 PM	**Colin J. Suckling,** University of Strathclyde, Glasgow, Scotland,UK Heterocyclic chemistry at the edge of biology and medicine
PL-2 4.40 PM-5.40 PM	**Michael D. Threadgill**, University of Bath, Claverton UK Nad^{+}-Requiring Enzymes As Targets For Medicinal Chemistry
5.40 PM-6.30 PM	**ISCB Award Lecture-1 & 2**

6.30 PM – 7.30 PM **Poster Session -1** **(Poster Numbers 1-80)**
7.30 PM – 8.30 PM **Cultural Programme**
8.30 PM **Dinner**

Saturday, January 16-01-2010

SESSION – II: Chairpersons: Prof. Colin J. Suckling and Prof Michael D. Threadgill

PL-3, 9.00 PM –9.40 PM	**V.T. Ivanov ,** Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, Russia Challenges and practical perspectives of peptidomic research
PL-4 9.40 -10.20PM	**Tsann-Long Su,**Institute of Biomedical Sciences, Academia Sinica, Taipei ,Taiwan. Oncologic Drug Development: From Target Identification to Bedside
IL-1, 10.20PM -10.50PM	**Cynthia J. Burrows**, University of Utah, , USA **Lessons from DNA Damage Applied to siRNA**
IL -2, 10.50PM-11.20PM	**Aloysius Siriwardena**, , Université de Picardie Jules Verne, Amiens, France Synthetic tools that modulate the action glycan metabolising enzymes: the simpler the better ?

Tea: 11.20 AM-11.40 PM

Parallel Session-III (HALL A)

Chairpersons: Prof. Jyoti Chattopadhyaya and Dr. Mukund Chorghade

IL-3 11.40 PM-12.10PM	**Asit K. Chakraborti,** National Institute of Pharmaceutical Education and Research (NIPER), S. A. S. Nagar, Punjab – 160062, India Sustainable Development: An Exploration to the Wonderland of Ionic Liquids
IL-4 12.10PM-12.40PM	**Leena Otsomaa**, Orion Corporation, Orion Pharma, Finland Challenges of Medicinal Chemists
IL-5 12.50 -1.20PM	**Sreeni Devidas**, GVK BioSciences Pvt.Ltd., Hyderabad, India. Drug Discovery: Is reliance increasing on India and are we prepared for the challenges?

Parallel Session-IV (HALL B)

Chairpersons: Prof. Graham B. Jones and Dr. Sham Nikam

IL-6 11.40 PM-12.10PM	**Andrea Vasella**, ETH Zurich, Zurich, Switzerland A New Type of Oligonucleotide Analogues
IL-7 12.10PM-12.40	**Prof.V.S.Parmar ,** Delhi University ,Delhi Biocatalytic Synthesis of Pharmaceutically Important Nanomaterials
IL-8 12.40PM -1.10PM	**S. M. S. Chauhan**, Delhi University , Delhi Supramolecular Capsules from Functional Porphyrins and Related Macrocycles

Lunch 1.20 PM - 2.20 PMParallel Session-V (HALL A)

Chairpersons: Dr. K.C. Gupta and Dr. Sudhir K. Singh

IL-9 2.20-2.50	**Graham B. Jones**, Department of Chemistry & Chemical Biology, Northeastern University, Boston, MA Natural Product Inspired Probes of DNA and RNA Microenvironments
IL-10 2.50 PM-3.20 PM	**Sham Nikam** – Nycomed, Germany Optimization of chemical leads in multi-target strategies
IL-11 3.20 PM-3.50 PM	**David Haydon**, Prolysis Ltd. UK Discovery and Development of Novel Antibacterials: Antibacterial inhibitors of the essential cell division protein FtsZ
IL-12 3.50 PM -4.10 PM	**Barbara Zajc**, The City College and The City University of New York MODULAR ASSEMBLY OF FLUOROORGANICS USING JULIA OLEFINATION

IL-13 4.10 PM -4.30 PM	Anil Kumar, **BITS, PILANI, Raj.** Design and Synthesis of Src Tyrosine Kinase Inhibitors as Therapeutic Agents

Tea 4.30 PM -4.50 PM

Parallel Session-VI (HALL A)

Chairpersons: Prof. Barbara Zajc and Prof Mahesh K. Lakshman

O-1 4.50 PM-5.00 PM	**Palwinder Singh**, Department of Chemistry, Guru Nanak Dev University, Amritsar Studies of interactions of acridone derivatives with P-gp, ATP and Mg^{2+} - Search for MDR modulators led to the identification of an anti-candidasis agent
O-2 5.00 PM-5.10 PM	**Mona Semalty,** H.N.B. Garhwal University, Srinagar (Garhwal) Development of formulations of root extract of *Urtica dioica* for hair growth promotion and identification of responsible bioactive constituents
O-3 5.10 PM-5.20 PM	**Akhilesh Kumar Verma**, University of Delhi, Delhi Copper-Catalyzed Regioselective Tandem Synthesis of Indolo, Pyrrolo [2,1-*a*]isoquinolines and Indolo[2,1-*f*][1,6]Naphthyridines by the Preferential Addition of *N*-Heterocycles on *ortho*-haloalkynes followed by Intramolecular C-2 Arylation
O-4 5.20 PM-5.30 PM	**M. Bansal** , Institute of Medical Sciences, Banaras Hindu University, Varanasi An assessment of safflower *(Carthamus tinctorius*) seed extract in the treatment of periodontal osseous defects in humans: A pilot study
O-5 5.30P M-5.40 PM	**Vaibhav P. Mehta,** Katholieke Universiteit Leuven, Heverlee, Leuven, BELGIUM. Transition metal-catalyzed desulfitative c-c bond forming reactions of 2-(1*h*)-pyrazinones
O-6 5.40 PM-5.50 PM	**Neeloo Singh**, Central Drug Research Institute, Lucknow Target-to-Drug Discovery for Novel Leishmaniacidals
O-7 5.50 PM-6.00 PM	**Pannuru Venkatesu ,** Department of Chemistry, University of Delhi, Delhi , India Effects of Osmolytes or Denaturants on α-Chymotrypsin Activity and the Folding/Unfolding Transition States

Parallel Session- VII (HALL B)

Chairpersons: Prof. Manas Chakrabarty and Dr. Kesav Deo

IL-14 **2.20 PM -2.50 PM**	**J. Senn-Bilfinger, Nycomed GmbH** & University Suttgart, Germany Analogue – based Design of Gastric Acid Anti-secretory Agents. Past and Present
IL-15 **2.50 PM-3.20 PM**	**Veena Agarwal** – Nicholas Piramal, Mumbai Innovative Approaches for Discovery and Development of Therapeutics in Oncology and Metabolic Disorders
IL-16 **3.20 PM-3.50 PM**	**Ashvani Singh** – Vertex San Diago,USA **Cystic Fibrosis Drug Discovery**
IL-17 **3.50 PM - 4.10 PM**	**M. S. Shingare,** Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, India Quinoline based various antimicrobials
IL-18 **4.10 PM – 4.30 PM**	**Dalip Kumar** Chemistry Group, Birla Institute of Technology and Science, Pilani India Design and Synthesis of Novel Bioactive Heterocycles as Potential Anticancer Agents

Tea 4.30 PM -4.50 PM

Parallel Session-VIII (HALL B

Chairpersons: Dr. S. B. Katti and Dr. Leena Otsomaa

IL-19 4.50 PM – 5.10 PM	Abhijit Roychowdhury, **Piramal Life Sciences, Mumbai , India** **Small molecule mTOR inhibitors as anti-cancer agents: Is selectivity an issue?**
O-8 5.10PM – 5.20PM	**Ram Sagar**, University of Oxford, Oxford UK. Synthesis and *in-planta* activity of caged/phosphotriester precursors of trehalose-6-phosphate (T6P
O-9 5.20PM-5.30PM	**Islam Khan**, Kuwait University, Kuwait Curcumin ameliorates experimental colitis: Singnal transduction through TLR-4 Receptor and Myd88
O-10 5.30 PM - 5.40PM	**Bandana Bose**, Banaras Hindu University, Varanasi-221005, India. $Mg(NO_3)_2$ primed seeds: A better tool for somatic embryogenesis in rice (variety-Swarna) –A first report.
O-11 5.40 PM - 5.50 PM	**Anjali M. Rahatgaonkar**, Institute of Science, Civil Lines, Nagpur 440001, India Facile polymer supported syntheses of n-pegylated quinoline scaffolds: A convienient drug delivery technique
O-12 5.50PM – 6.00 PM	**Okram M. Singh**, Department of Chemistry, Manipur University, Canchipur, Imphal Facile synthesis of novel coumarins under solvent-free conditions and their antioxidant evaluation
O-13 6.00 PM-6.10PM	**Meenu Aggarwal,** *Lingaya's University, Nachauli , Faridabad* Biological and Toxicological Studies of new derivatives synthesised from the sesquiterpene lactones isolated from medicinal plants

6.00 PM – 7.30 PM	**Poster Session -II**	**(Poster Numbers 81-160)**
7.30 PM – 8.30 PM	**Cultural Programme**	
8.30 PM	**Dinner**	

Sunday, January 17-01-2010

SESSION – IX

Chairpersons: Prof. Graham B. Jones and Prof. David Haydon

PL-5 9.30 AM – 10.10 AM	**S. Chandrasekaran,** Indian Institute of Science, Bangalore-560012, India Studies on the Synthesis of Thiosugars as Glycosidase Inhibitors
PL-6 10.10 AM – 10.50 AM	**Jyoti Chattopadhyaya** , Uppsala University, Uppsala, Sweden The Importance of Being Nucleic Acids – Some Structural and Reactivity Considerations

Tea : 10.50 AM - 11.10 AM

Parallel Session X (Hall A)

Chairpersons: Prof. S.Chandrasekaran and Prof. Dr. Andrea Vasella

IL-20 11.10 AM - 11.40PM	**David St. C. Black**, University of New South Wales, Sydney, Australia The Role of Molecular Activation, in the Generation of New Indole Reactivity
IL-21 11.40 AM – 12.10 AM	**Nancy B. Jackson**, Sandia National Laboratories,Albuquerque,NM The Role of Safety and Security in Chemical Sustainability
IL-22 12.10 AM - 12.40 PM	**John C. Amedio** Jr, ZIOPHARM Oncology, , U.S.A. Palifosfamide (ZYMAFOS™):A Novel Molecule for the Treatment of Soft Tissue Sarcoma
IL-23 12.40 PM – 1.10 PM	Greg Bisacchi, **Infection Chemistry, Astra Zeneca Research, Bostan, USA** The Exploitation of Diverse Lead Generation Paradigms to Identify Novel Antibacterial Agents
IL-24 1.10 PM – 1.30 PM	**Mohan Prasad**, Ranbaxy Research Laboratories, Gurgaon Process Development & Scale up From a Generics Perspective

Parallel Session XI Prof. S.P. Singh and Prof. V.K.Tandon

IL-25 11.10 AM - 11.40PM	**Mukund S. Chorghade,**THINQ Pharma, USA Value Creation and New Opportunities in Medicinal Chemistry, Drug Discovery, Process Development and Project Management of Technology Transfer
IL-26 11.40 AM – 12.10 AM	**Dr. Michael N. Liebman**, Strategic Medicine, Inc. PA 19348,USA
IL-27 12.10 AM - 12.30 PM	**R. A. Mane,** Dr. Babasaheb Ambedkar Marathwada University,Aurangabad Organic Transformations leading to bioactive molecules accelerated by biocatalysts
IL-28 12.30 PM - 12.50 PM	**Ashok K. Prasad ,**University of Delhi, Delhi Nucleosides and Nucleic Acids: Present and Future Drugs
IL-29 12.50 PM - 1.10 PM	**Sanjay Kumar**, Piramal Life Sciences, Mumbai , India Discovery of novel inhibitors targeting HIF-1alpha towards anticancer drug development

Lunch 1.1 0 PM – 2.00 PM

Parallel Session –XII (Hall A) Chairpersons: Prof. Nancy B. Jackson and Dr.R.Tuli

IL-30 **02.00 PM - 02.30 PM**	**Binghe Wang**, Department of Chemistry and Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA 30302-4098, USA Boronolectins and fluorescent boronolectins as potential research tools and diagnostics
IL-31 **02.30 PM - 3.00 PM**	**Mahesh K. Lakshman**, The City College and The City University of New York, USA **Phosphonium ion chemistry *en route* to nucleoside modification**
IL-32 **3.00 PM - 03.20 PM**	**Bipin Pandey,** *CMC and NPR Department, Zydus Research Centre, Zydus Cadila, Ahmedabad* Importance of Salts and Polymorphs during Drug Discovery and Development

IL-33 **03.30- 03.50 PM**	**Kanchugarakoppal. S. Rangappa**, University of Mysore, ,Mysore Implications of heterocycles as chemotherapeutic agents: drug discovery programme
IL-34 **03.50 PM - 4.10 PM**	**Shiv K. Agarwal,**Unimark Remedies Ltd, Hindustan Antibiotic Campus, Pune Anticancer Drugs derived from Natural Products
O-16 **4.10 PM - 4.20PM**	**Raman K Sharma,**Delhi University Delhi Exploring Enzyme Substrate Specificity for the Separation of Anomeric Mixture of *O*-Aryl Nucleosides of Diagnostic Importance

Parallel Session XIII (Hall B)

Chairpersons: Prof. Tsann-Long Su and and Dr. John C. Amedio

IL-35 02.00 PM - 02.30 PM	**Vinod Bhakuni,** Central Drug Research Institute, CSIR, Lucknow 226001, India. An enzymatically active fibrillar film of bacteriophage-associated hyaluronate lyase (hylp2)
IL-36 02.30 PM - 3.00 PM	**Dr. Sajan Joseph** - Lilly & Comp BisIndolyl Maleimides and Indolocarbazoles as Cyclin Dependent Kinase Inhibitors
IL-37 3.00 PM - 03.20 PM	**A.S. Mustafa**, Kuwait University, Kuwait Cell mediated immunity assays identify ESAT6-family of proteins for diagnostic and vaccine relevance using overlapping synthetic peptides corresponding to genomic regions of difference of *Mycobacterium tuberculosis*
IL-38 03.20- 03.40 PM	**Anamik Shah** Department of Chemistry,Saurashtra University, Rajkot- 360 005 Design, synthesis and small library generation of benzo pyrans and other& Their *in vitro* anticancer evaluation
IL-39 03.40 PM - 4.00 PM	**Vishnu K Tandon,** Department of Chemistry,Lucknow University,Lucknow-India Proliferation and Apoptosis in Cancer Cells: The role of Chromophore
IL-40 4.00 PM-4.20 PM	**Surat Kumar,** Dayalbagh Educational Institute,Dayalbagh, Agra, INDIA Nucleic Acid Binding of Alkaloids: Fluorescence, Docking and Molecular Modeling Approaches

SPECIAL SESSION

Chairperson: Prof. David Black

PL-7

4.30 PM - 5.10 PM Prof. Robert H. Grubbs*, Nobel laureate*,
California Institute of Technology, Pasadena, USA

TEA 5.10 PM - 5.30 PM

Parallel Session XIV (Hall A)

Chairpersons: Dr. Yetendra Kumar and Prof.Anil K. Singh

PL-8 5.30 PM – 6.10 PM	**Ram Vishwakarma**,,Indian Institute of Integrative Medicine, Jammu, Chemical biology of GPI molecules
IL-41 6.10 PM – 6.30 PM	**Parthasarathi Das**, Aurigene Discovery Technologies Limited, Hyderabad Macrolide and Ketolide Antibiotics: Synthetic Studies on Narbonolide
IL-42 6.30 PM – 6.50 PM	**Arun K. Sinha**, Institute of Himalayan Bioresource Technology (CSIR), Palampur Exploring environmentally benign chemical and biocatalytic routes for bioactive phenolics

Parallel Session XV (Hall B)

Chairpersons: Dr.Vinod Bhakuni & Dr. S. K.Agarwal

PL-9 5.30 PM – 6.10 PM	**Cemil OGRETIR**,Eskişehir Osmangazi University try ,Turkey Theoretical approaches to drug design case studies on QSAR and QSPR
IL-44A 6.10 PM-6.40 PM	**Dr. Chafique Hamdouchi -** Lilly & Comp
IL-43 6.40 PM – 7.00 PM	**Rajiv Sharma,** Piramal Life Sciences Limited, Mumbai, India Structure-CYP Inhibition Relationships
IL-44 7.00 PM – 7.20 PM	**Ian A Cliffe ,**Ranbaxy,Gurgaon Use of Virtual Compound Libraries for Chemical Hit Finding

7.00 PM - 8.30 PM **Poster session-III (Poster Nos. 160 onward)**
8.30 PM **Dinner**

Monday 18, January, 2010

SESSION –XVI

Chairpersons: Prof. Virinder S. Parmar and Prof. S.M.S.Chauhan

IL-45 9.30 AM -10.10 AM	**Vinod K. Singh**,Indian Institute of Science Education and Research Bhopal Total Synthesis of Bioactive Natural Products
IL-46 10.10 AM -10.40 AM	**Anil K. Singh**, Indian Institute of Technology, Bombay,Mumbai Design, synthesis and antiradical activity of novel Vitamin E compounds
IL-47 10.40 AM -11.10PM	**Dr. Soumitra Banerjee, Fine Solutions Ltd, Israel** Recent advances in containment technologies for Anti cancer drugs
11.10PM-11.40PM	**Prof.Luis Echegoyen** Director, Division of Chemistry, National Science Foundation USA
IL-48 11.40PM-12.10 PM	**Vommina V. Sureshbabu**, , Bangalore University, Bangalore Synthesis of Peptides and Peptidomimetics: Isothiocyanates derived *N*-protected amino acids and their utility in the preparation of thioureidopeptides
IL-49 12.10 PM - 12.30 PM	**Ramesh C. Gupta**,Torrent pharmaceuticals Ltd. Gandhinagar , Gujarat, INDIA Advanced glycation end products and diabetic complications: An overview.
IL-50 12.30 PM - 12.50 PM	**Diwan S Rawat**,Department of Chemistry, University of Delhi, Delhi-110007, India Synthesis and Antimalarial Activity Evaluation of Tetraoxanes, Tetraoxane-aminoquinoline/triazine Conjugates

12.50 AM – 1.30 PM **Award session and Valedictory Session**
1.30 PM – 2.00 PM **Lunch**
2.00 PM **Sightseeing**
2.20 PM - 3.30 PM **ISCB GENERAL BODY MEETING**

Planery Lectures

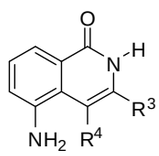
PL-1

NAD^+-Requiring Enzymes as Targets For Medicinal Chemistry

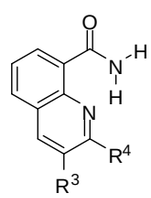
Michael D. Threadgill

Medicinal Chemistry, Department of Pharmacy & Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY, United Kingdom m.d.threadgill@bath.ac.uk

NAD^+ (nicotinamide adenine dinucleotide) is one of the most important small molecular components of the cell, being present at *ca*. 0.3 mM in the cytosol of many mammalian cells [1]. Many important pathways use NAD^+ (or its reduced form NADH) and it is a substrate or co-factor for more than 100 enzymes. Thus selecting only one of these enzymes as a target for selective drug design may seem an impossible challenge but several NAD^+-requiring enzymes have been proposed and exploited as drug targets [2]. The enzymes that use NAD^+ can be divided into two groups, oxidoreductases and those that use NAD^+ as a source of electrophilic ADP-ribose. Amongst these oxidoreductases, the human inosine monophosphate dehydrogenases (IMPDHs), which catalyse the oxidation of IMP to XMP as the rate-determining step of *de novo* purine biosynthesis, have been the target of much drug design research for treatment of cancer and viral infections [3]. The group of enzymes that use NAD^+ as a source of electrophilic ADP-ribose can be sub-divided into four sub-groups: mono-ADP-ribosyltransferases (bacterial toxins and mammalian ARTs), ADP-ribosyl cyclases, sirtuins (N^{ϵ}-AcLys protein deacetylases) and poly(ADP-ribose)polymerases (PARPs). The mammalian ARTs attach single ADP-ribose units to (usually) Arg residues in the target proteins and have roles in extracellular signalling and in regulating activities of target proteins [4]; these have been proposed as potential targets for drug design [5] but few inhibitors are reported. ADP-ribosyl cyclases use NAD^+ to generate cyclic-ADP-ribose to control release of Ca^{2+} from intracellular stores; inhibitors are known but the medicinal applications are unclear [6]. The seven mammalian sirtuins use NAD^+ as an activating electrophile in catalysing the removal of acetyl groups from the side-chains of Lys residues in their substrate proteins; this deacetylation regulates the activities of the proteins, which are important in many cellular functions [7]. Inhibition of sirtuin activity and stimulation of their deacetylation functions have both been proposed and are being researched in medicinal chemistry of diabetes, cancer, aging, *etc*. [8,9]. The PARPs, which poly(ADP-ribose) polymers onto Glu residues of the target proteins, have received the most attention from the medicinal chemists [10]. Pharmacological inhibition of PARP-1 has applications in treatment of cancer, inflammatory diseases and ischaemia-reperfusion injury, although many agents are not isoform-selective.



5-AIQs



Q8Cs

In this lecture, the therapeutic opportunities for selective inhibition of NAD^+-requiring enzymes will be reviewed, with presentation of our recent results on the effects of inhibition of PARP-1 on metastasis of cancer, on selective inhibition of the PARP-2 isoform, on inhibition of the sirtuins and exciting chemistry discovered on the way to potent and selective inhibitors, including the 5-AIQs and the Q8Cs [11-13].

REFERENCES

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PL-2

Heterocyclic chemistry at the edge of biology and medicine

Colin J. Suckling

WestCHEM Research School, Department of Pure& Applied Chemistry, University of Strathclyde, Glasgow, Scotland, c.j.suckling@strath.ac.uk

Heterocyclic compounds feature prominently in nature. In terms of playing active roles in biology, nucleobases and cofactors are especially significant. We have chosen to work in two major fields at the interface between chemistry and biology, namely the chemistry of fused pyrimidines, which include pteridines, pyridopyrimidines, and pyrrolopyrimidines, and the chemistry of DNA minor groove binders (MGBs). In the former case, we have investigated methods of synthesis that lead to highly diversified structures in each of the three classes of fused pyrimidine taking advantage of the ability of pyrimidines to react with electrophiles and nucleophiles in appropriate cases. The products of these synthetic studies have been evaluated in a range of screens for anti-infective activity; important results have been obtained for antitrypanosomal activity leading to a proof of concept of a new treatment trypanosomiasis through the parallel inhibition of pteridine reductase 1 and dihydrofolate reductase. A further novel application of fused pyrimidines concerns the activation of nitric oxide synthases by blocked dihydropterins. These compounds, originally prepared at Strathclyde in the 1980s, have been found to be almost as effective as the natural cofactor, tetrahydrobiopterin, in supporting the oxidation of arginine by nitric oxide synthases. In the DNA field, we have developed new design criteria for minor groove binders that emphasise the importance of the physicochemical properties of these compounds. By introducing alkene links in place of amides and increasing the hydrophobicity of specific regions of the minor groove binders, we have discovered potent antibacterial agents that bind to DNA and owe their selectivity to differential penetration into the target Gram positive bacterial cells compared with Gram negative bacterial cells or mammalian cells. The lecture will firstly describe some new diversity oriented synthetic methods for fused pyrimidines followed by their biological activity, in particular the proof of concept for the treatment of trypanosomiasis. Secondly, the design and properties of antibacterial minor groove binders will be discussed with emphasis upon the role of physicochemical properties and specific hydrogen bonds in determining activity and selectivity.

PL-3

Challenges and practical perspectives of peptidomic research

V. T. Ivanov

Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, Russia

Peptidomic studies, i.e. total screening of biological samples for peptides hold considerable promise for elucidating biochemical regulatory networks and for discovery of new bioactive molecules or disease markers. The following general aspects of peptidomic research will be discussed in the presentation:

- How far one should (or can) go down the concentration axis in the screening process?
- To what extent the extracts of biological samples represent the endogenous composition of peptides? What information can be inferred from the artifacts obtained in the course of sample preparation?
- What are the relative merits and disadvantages of peptidomic studies of different types of biological material (tissues, cell cultures, fluids, etc.)?
- How general are the conclusions derived from peptidomic studies of animal samples? Do they apply to plants? To prokaryotes?
- What is the biological function of separate peptidome components and of the whole peptidome?
- To what extent is the human peptidome disease sensitive? Can it be applied to human diagnostics?
- Answers to these questions will be attempted basing on 10 years of studies in the title Institute. Data will be presented and discussed, obtained on peptides from rat tissue and plant extracts, human erythrocytes, several tumor cell cultures and clinical blood samples.

PL-4

Oncologic Drug Development: From Target Identification to Bedside

Tsann-Long Su

Laboratory of Bioorganic Chemistry, Institute of Biomedical Sciences, Academia Sinica, Taipei, 115, Taiwan.

Cancer is one of the top ten leading causes of death in the world. Many strategies for treating cancer patient have been applied clinically. These include chemotherapy, radiation therapy, surgery, and other treatment methods. However, the advances in the treatment of malignant diseases have been limited because of the failure to identify unique biochemical and/or biological properties which are able to clearly distinguish cancer from normal cell population. Consequently, current available anticancer agents lack tumor selectivity and possess a narrow therapeutic index. In the recent years, there have been marked advances in the understanding tumor cell biology and oncogenes, leading to the identification of novel targets for designing new anticancer agents (Targeted Cancer Therapies) or Gene Therapy. These new treatment strategies have prolonged patient lives significantly and in some cases provided cures to certain oncologic diseases. Despite these advances, it is important to know that there are still tumor cells that remain very difficult to kill due to their heterogeneity. Multi-drug resistance (MDR), tumor invasion and metastasis are the leading cause of death in cancer patients and major barrier in cancer patient treatment. In this presentation, the past, present and future of anticancer drug research and development from target identification to bedside will be discussed.

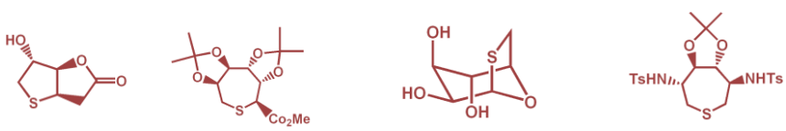
PL-5

Studies on the Synthesis of Thiosugars as Glycosidase Inhibitors

S. Chandrasekaran

Department of Organic Chemistry,Indian Institute of Science, Bangalore-560012, India

Thiosugars possess unusual physicochemical properties and differ from their oxygen analogs in terms of geometry, conformation and flexibility . Many functionalized thiosugars occur naturally and a large number of this class of compounds have been studied extensively as glycosidase inhibitors and as HIV protease inhibitors. The chemistry of thiosugars poses unique synthetic problems and we have tried to develop new synthetic methodologies involving the use of benzyltriethylammonium tetrathiomolybdate as the sulfur transfer reagent for the construction of a wide range of functionalized thiosugar derivatives. The interesting redox chemistry of molybdenum –sulfur systems has been exploited to carry out intriguing , multi-step , tandem processes for the synthesis of thiodugars. Studies related to the synthesis of enantiopure thiepane derivatives, conformationally locked thiosugars and deoxy thiosugars will be discussed in this lecture.



PL-6

The Importance of Being Nucleic Acids – Some Structural and Reactivity Considerations.

J. Chattopadhyaya

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The intrinsic dynamic and architectural flexibility of DNA and RNA, resulting in to specific function, are the result of cooperative interplay *of pentofuranose, nucleobase and phosphodiester* moieties. At least following components are found to be important to account for the structure-activity of nucleic acids.

A. Stereoelectronics in Nucleosides and Nucleotides

We have earlier shown [for a free download of our monograph on "Stereoelectronic Effects in Nucleosides & Nucleotides and their Structural Implications", see our website http://www.boc.uu.se/] that the interplay of various stereoelectronic *gauche* and *anomeric* and associated steric effects energetically drive the sugar-phosphate conformation, which, in turn, is dictated by the electronic nature of the aglycone and other substituents of the sugar ring, as well as by stacking, H-bonding and electrostatic interactions:

B. Nucleobase Reactivity of DNA and RNA is sequence-dependent

Our pH-dependent chemical shift changes of different aromatic marker protons in a set of dimers, trimers, tetramers, pentamers, hexamers and heptamers in the single-stranded DNA and RNA series show that the nearest-neighbor nucleobases in ssRNA are electronically coupled as a result of *variable* electrostatic interaction (Stacking and Destacking). This interaction of the nearest-neighbor nucleobases modulates chemical reactivities of the participating nucleobases, giving variable pK_a perturbations in the nucleobases, meaning that, for example, all adeninyl residues are not chemically equivalent within a sequence context.

C. Phosphate Reactivity of DNA and RNA is sequence-dependent

The internucleotidic phosphates are chemically non-uniform owing to their different local microenvironments owing to change of the sequence context.

References:

All relevant publications from the author's lab can be found at the author's website: see http://www.boc.uu.se/]

PL-7

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PL-8

Chemical biology of GPI molecules

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Since the discovery [1,2] of glycosylphosphatidylinositol (GPI) molecules as a novel and alternative mode of membrane-anchoring of specialized cell-surface proteins, the biology of these complex glycolipids has remained in focus. Subsequently, several GPI-anchors and protein-free GPIs have been isolated all across the biology. The GPIs are produced in high abundance by protozoan parasites (*Leishmania, Trypanosoma* and *Plasmodium*) and are essential virulence factors that help the parasites to infect, proliferate and subvert the human host immune system. Marked differences in the structure and biosynthesis of GPIs from the parasites and human cells have been identified providing valuable targets for drug and vaccine design. Even among the parasites, various species express GPIs with subtle structural differences that manifest in remarkable and, at times, opposing biological functions in the host. Their structural complexity and biological activity presents substantial challenges to synthetic chemistry. Despite the concerted efforts of several leading groups, total synthesis of a given full-length GPI molecules remains a daunting task which is further complicated by the presence of (a) structural and functional differences among the species and (b) significant micro-heterogeneity in their lipid and glycan domains. In our efforts [3-9] on chemical biology of parasitic GPI molecules, we designed [10] new and efficient approaches for the synthesis of the full-length GPI molecules and their structural and functional mimics. We have extended this work for the preparation of novel fluorescent GPIs as valuable biological probes and used them to address specific questions pertaining to the biosynthesis [11,12], inhibitor design [13] and membrane (lipid-raft) organization [14]. Some of our recent work [15] will be discussed in the presentation.

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PL-9

Theoretical Approaches To Drug Design Case Studies On QSAR And QSPR

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After giving a historical development in theoretical drug design an introduction to theoretical methods which have been used up to date will be surveyed. Some examples of the applications will be presented [1-14].

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Invited Lectures

IL-1

Lessons from DNA Damage Applied to siRNA

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Knockdown of specific genes of interest by siRNA is one of the very promising approaches of current drug design. One important problem that needs to be addressed is the off-target effects of siRNA. Many off-target effects can be attributed to the interaction of siRNA with double-strand RNA binding proteins such as protein kinases, and these interactions divert siRNAs in the cell, lowering their efficacy. One approach to this problem incorporates a switchable base that can inhibit PKR binding in one conformation while permitting activity in the RISC in another conformation. 8-Oxo-2'-deoxyguanosine (OG) is a common product of DNA damage formed from oxidative stress in the cell. OG is known to exist in both *anti* and *syn* conformations based on the complementary base in the opposite strand, and this bipartisan property accounts for its mutagenicity in DNA. In current work, a series of 8-oxo-2'-deoxyguanosine and other purine analogs has been synthesized and then incorporated into various positions of siRNA known to knock down caspase-2. The results obtained from these experiments will be used for designing better siRNA with fewer off-target effects and better knock-down capability.

IL-2

Synthetic Tools That Modulate The Action Glycan Metabolising Enzymes: The Simpler The Better ?

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We have for some time been interested in designing and synthesizing chemical tools with which to modulate the action of oligosaccharide-metabolising enzymes. We were primarily motivated by the possibility that these synthetic tools might be exploited to modulated and probed various physiological events and also as strategy for the treatment of various diseases. Inhibiting the enzymes that guarantee the fidelity of N-glycan biosynthesis is have been targeted as a strategy to fight cancer, Heptatitis C and a host of other diseases.

Natural products with inhibitory activity against glycosyl hydrolases (GH) have been the primary inspiration for the design of analogs promising to display improved selectivity and potency for their target GH. However, the syntheses' of such analogs is often laborious and has more often than not led to compounds with poorer characteristics than those desired.

The design and synthesis of a number of alternative synthetic inhibitors will be described in this presentation that deviate from their natural counterparts in important ways. Moreover, rapid strategies for the syntheses' of these compounds that we have recently developed will be presented.

For selected compounds, biological results will be discussed and inhibition, crystallographic, thermodynamic and computational data will be evoked to rationalize the observed activities.

IL-3

Sustainable Development: An Exploration to the Wonderland of Ionic Liquids

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While a sea change is being witnessed in the drug development strategies due to the advent of molecular biology and more recently proteomics/genomics, organic synthesis still holds the central stage. However, there has been a tremendous influence of green chemistry tools on medicinal chemistry and chemistry research based organizations1 due to the adverse effect of the chemical processes on the environment. To comply with the triple bottom line philosophy2 in the chemical processes a few major directives of the environment protection agency are to: (i) maintain atom economy, (iii) replace stoichiometric reactions by catalytic methods, (iii) use solid acid catalysts, (iv) use alternate reaction media. Towards the fulfillment of these objectives we introduced various synthetic strategies/concepts: 'electrophile-nucloephile dual activation' for atom economical methylation/ethylation,3 novel concept of 'demand based thiolate anion generation' for chemo-selective functional group transformations,4 discovery of novel solid acid catalysts5 that are being actively pursued by researchers globally for various synthesis, and provided a mechanistic rationale for rate acceleration in aqueous medium as 'electrophile nucleophile dual activation through cooperative hydrogen bonded network'6 that would promote a rational selection of water as the reaction medium. The emergence of ionic liquids (ILs) has inspired a major culturer change in sustainable development and are being touted as the future green solvents7 to replace volatile organic solvents that amounts to >80% of the mass utilization in the manufacture of drugs and pharmaceuticals and with recovery efficiency of ~50 – 85% are the major culprits in causing damage to the environment.8 However, the environment friendly image of ILs is under critical assessment on issues pertaining to combustibility, toxicity, and biodegradability that generates the need to redefine their use other than reaction medium. Organocatalysis using ILs shows a new horizon. However, the wonder is how ILs accelerate organic reactions! An exploration of the wonderland of ILs with a view to understand the molecular level interaction of ILs with the reactants reveals for the first time the role of ILs as 'electrophile nucleophile dual activation' organo-catalysts through 'cooperative hydrogen bond and charge-charge interaction network'9 that would form the basis of rational choice of ILs as organocatalysts for a desired reaction with a prior knowledge/assessment of the hydrogen bond donor ability of the C-2 hydrogen atom of the bmim based ILs and the substrates as well as the hydrogen bond acceptor property of the counter anion of the ILs and the reactants.

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IL-4

Challenges Of Medicinal Chemists

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Productivity of R&D in pharmaceutical industry has been an issue since late 90's due to the decreasing number of approved NCE's as R&D spending has been continuously growing.[1] Many new technologies have been adapted to drug discovery, but their significance to overall R&D productivity is still waiting for their final proof.[2] Naturally emphasis on productivity has put pressure to the key players in drug discovery, like medicinal chemists. At the same time concern on innovativeness, open-mindedness and enabling serendipity in discovery has been invokening.[3] Part of characteristics of medicinal chemists' work have changed along with new possibilities that the new technologies have given for drug discovery. Along with these new possibilities new challenges have come up as well. Some characteristics of medicinal chemist's work have remained the same, but today's continual increase of urgency has forced chemists to look for new solutions and to change their way of working.
In this presentation some of the many challenges of medicinal chemists will be highlighted and Orion's solutions will be presented.

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IL-5

Drug Discovery: Is reliance increasing on India and are we prepared for the challenges?

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The Indian pharmaceutical industry has been noted for its innovation in the generics space for several decades. The Indian Contract Research industry has been noted for its cost effective yet high quality delivery systems across the entire drugs discovery value chain ranging from early discovery through to running clinical trials. However, India has rarely been a destination for conducting innovative drug discovery. However, over the past Four years, India has seen a rapid increase in the number of collaborations that foster true innovation. There has been an exponential increase in the number in the past two years. While India has traditionally been very strong in some of the basic areas of drug discovery such as Chemistry, the number and experience of qualified personnel and infrastructure in some of the other critical areas is lacking or limited. The talk will focus on the current state of the industry and discuss some of the challenges seen by the industry.

IL-6

Towards Novel Oligonucleotide Analogues

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Nucleic acids and their analogues all possess a contiguous backbone to which the nucleobases are attached. We wondered if this differentiation is necessary for pairing, for the formation of defined structural elements (helices, loops, bulges etc.), and for their function. We set ourselves the goal of designing analogues where the backbone is replaced by elements directly linking nucleobases to each other and to evaluate the pairing of such analogues to form defined structural elements. The ultimate goal is the design and synthesize analogues of this type that possess useful properties.
The first such analogues possess an acetylenic moiety linking adenosine (A) and uridine (U) units. To minimize the synthetic effort we analysed the association of partially protected, self-complementary dinucleosides of this type in organic solvents. Association may lead to linear or to cyclic aggregates, pairing leading to duplexes that are cyclic by virtue of the hydrogen bonds between complementary nucleobases. Pairing was analysed by ^{1}H-NMR spectroscopy (dilution experiments), molecular weight

determination, and the temperature dependence of CD-spectra, denoting base stacking. These analogues pair, unless unfavourable H-bonds bias the conformation.
Thiomethylene-linked analogues are synthesized more readily, and pair. Guanosine-derived, thiomethylene or aminomethylene-linked dinucleosides form quartetts. Cytidine-derived di- and oligonucleosides are soluble in water. Pairing of a A and U derived tetranucleoside results in an incipient helix. An octanucleoside comprising all nucleobases forms a helix, and is soluble in water.
Of theseveral analogues devoid of a carbohydrate moiety that were designed and synthesized, one octa-nucleoside linked by amide bonds pairs in aqueous solution.
The stage is set for the design of analogues that possess the correct geometry to interact with nucleic acids and/or proteins.

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IL-7

Biocatalytic Synthesis of Pharmaceutically Important Nanomaterials

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The charter of pharmaceutical industries and chemical research in general is changing today because of the pressing need to develop environmentally benign methodologies for the synthesis of well-defined molecules having precise structural features and pharmacological action. Biocatalytic reactions in synthetic sequences provide unique advantages of efficiency, selectivity, economy and environmental friendliness.
We have successfully used lipases from different sources, *i.e.* procine pancreas, and *Candida*, *Pseudomonas* and *Aspergillus* species in carrying out selective organic reactions and in polymerization reactions. A few highly novel amphiphilic polymer systems based on PEGs having a broad range of chemical functionalities under mild conditions have been prepared. These novel copolymers that aggregate in aqueous medium to form nanospheres have been found to be very useful in the encapsulation of small hydrophobic drugs. Our investigations have enabled the design and development of a model polymer system that has high drug affinity (from small drug aspirin to high molecular mass drugs, insulin and inulin), controlled release profile for the incorporated drug, and good compatibility between the core forming block and incorporated drug. The detailed results in these areas would be presented at the Symposium.

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IL-8

Supramolecular Capsules from Functional Porphyrins and Related Macrocycles

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Formation of supramolecular capsules using noncovalent interactions is an important area in supramolecular chemistry. Supramolecular capsules are suitable for separations, sensors, catalyst and medical applications. Porphyrins specially chlorophylls are tetrapyrrolic macrocylcles ubiquitous in nature. Porphyrinic assemblies are of fundamental importance to develop the models for light-harvesting antenna and photosynthetic reaction centres as well as building blocks for the construction of different photonic materials.[1]

The noncovalent interactions such as hydrogen bondings, metal coordination, ionic interactions and hydrophobic interactions are involved in the formation of supramolecular capsules.[2] The formation of four hydrogen bonds between a tetracarboxy calixarene with *meso*-tetra(2-pyridyl)porphyrin form the self-assembled capsules. The metal-coordination with heteroatoms containing porphyrins have been used in the formation of boxes and capsules

The ionic-interactions between cationic calix[4]pyrroles with anionic porphyrins form capsules in aqueous solution.[3] Similarly anionic calix[4]arenes with cationic porphyrins form capsules which are characterized by UV-Visible, fluorescence, NMR and mass spectroscopy.

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IL-9

Natural Product Inspired Probes of DNA and RNA Microenvironments

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Nucleic acids can have richly diverse structures, including hairpins, knots, pseudoknots, triple helices, loops, helical junctions, and bulges [1]. Such bulged structures in nucleic acids are of general biological significance [2-3] and have also been suggested as binding motifs for regulatory proteins involved with viral replication, including the TAR region of HIV-1 [4-6]. Additionally, the etiology of at least 12 human neurodegenerative genetic diseases has been attributed to genetic variations in the lengths of triplet repeats in genomic DNA (e.g. myotonic dystrophy, Huntington's disease, Friederich's ataxia, and fragile X syndrome). The unstable expansion of triplet repeats has been attributed to reiterative synthesis due to slippage and *bulge formation in the newly formed DNA strand* [7]. As such, compounds capable of binding to bulges could have significant therapeutic potential. Despite these obvious ramifications, few previous attempts have been made to prepare compounds with affinity for bulged sequences. Success has been hindered by lack of an available substrate which can effectively mimic the base pairing involved at a bulged site, which requires a unique wedge-shaped template. The most promising bulge-specific agent discovered to date originated from work on the enediyne natural product NCS-chrom [8]. Based on this

finding we have designed libraries of compounds and have achieved nM affinity for specific bulged sequences [9-10]. This presentation will focus on recent findings, including the selective alkylation of bulged sites, library design criteria, and the development of molecular biology probes which induce the slippage process.

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IL-10

Optimization of chemical leads in multi-target strategies

Sham Nikam

Nycomed, Germany

IL-11

Discovery and Development of Novel Antibacterials: Antibacterial inhibitors of the essential cell division protein FtsZ

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Prolysis Ltd. UK

Alkyl derivatives of 3-Methoxybenzamide (3-MBA), a weak inhibitor of the essential bacterial cell division protein FtsZ, were found to have potent anti-staphylococcal activity with poor drug-like properties. Analogues of these FtsZ inhibitors were synthesised in order to improve the drug-like properties. Exploration of the structure–activity relationships led to the identification of potent anti-staphylococcal compounds with improved pharmaceutical properties demonstrating efficacy in a murine model of infection.

IL-12

MODULAR ASSEMBLY OF FLUOROORGANICS USING JULIA OLEFINATION

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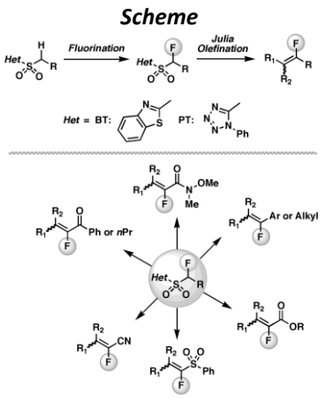
A variety of functionalized fluoroolefins can be readily synthesized via use of the Julia-Kocienski olefination. For this, we have been developing metalation-fluorination approaches to individual fluorinated heteroaryl building blocks, which now constitute a toolbox for modular assembly. Examples of

fluoroolefins we have synthesized include ?-fluoro acrylates, ?-fluorovinyl Weinreb amides and ?-fluoroenones, ?-fluoro acrylonitriles, ?-fluorovinyl sulfones, ?-fluorostyrenes and stilbenes as well as ?-fluoroalkylidenes. This talk will focus on the methodological and stereochemical (where applicable) aspects, and comparisons to other literature methods.

Scheme



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IL-13

Design and Synthesis of Src Tyrosine Kinase Inhibitors as Therapeutic Agents

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Protein tyrosine kinases play a key role in cell signaling pathways and regulate biological processes such as proliferation, differentiation, and apoptosis.[1-2] The Src family of protein tyrosine kinases, Src, Yes, Lck, Fyn, Lyn, Fgr, Hck, Blk, and Yrk, are non-receptor tyrosine kinases. Src family kinases are involved in the regulation of a wide variety of normal cellular signal transduction pathways, such as cell growth, differentiation, survival, adhesion and migration. Inhibition of this family of protein tyrosine kinases represents a viable strategy for regulation of the cellular signal transduction and is of considerable interest in the therapy of many human cancers, osteoporosis, cardiovascular disorders and immune system dysfunction. There is a need in the art for kinase inhibitors which are more potent and selective than those currently available.

To generate Src tyrosine kinase inhibitors we have followed three different approaches, i) synthesis of small molecules based on pyrazolopyrimidine scaffold, ii) converting weak peptide inhibitor by structural modification, and iii) synthesis of bisubstrate analogs by conjugating small molecule with peptide templates. Peptide Ac-CIYKF(NO_2)Y, in which the nitrophenylalanine is located at position 5, exhibited a significantly higher inhibitory potency (IC_{50} = 0.53 μM) by approx. 750-fold vs. Ac-CIYKYY. Furthermore, a constrained peptide synthesized by linking side chains Y3 and K4 exhibited an approximate 1400-fold increase in inhibitory potency (IC_{50} = 0.28 μM) when compared to the corresponding linear peptide.[3] In an another approach, covalently linked bisubstrate analogs were designed by attaching a N-heteroaromatic moiety to the side chain of different amino acids in the peptide template.[4] The inhibitor (3-phenylpyrazolopyrimidine-CIYKYY) inhibited the phosphorylation of E_4Y by active Src significantly higher (IC_{50} = 0.38 μM) than the carboxylic acid derivative of pyrazolopyrimidine (IC_{50} = 250 μM) or peptide Ac-CIYKYY (IC_{50} = 400 μM), this suggests that there is a synergistic inhibition effect of conjugation of the ATP

mimic with the peptide by possibly creating favorable interactions between the conjugate and the kinase domain. The details of synthetic schemes, inhibitory potencies and SAR will be presented.

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IL-14

Analogue-based Design of Gastric Acid Anti-secretory Agents. Past and Present

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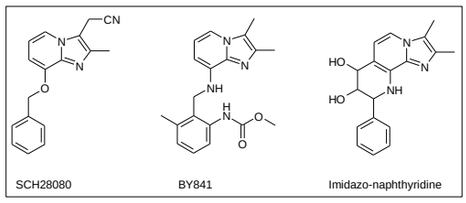
Acid related diseases are currently treated by the highly efficient proton pump inhibitors (PPIs), They are prodrugs that undergo an acid-catalyzed chemical rearrangement that is necessary for their activity. This acid-catalyzed conversion from prodrug to drug occurs rapidly in the secretory canaliculus of the parietal cell where in addition there is accumulation of the prodrug due to a protonation dependent trapping mechanism. Since the acid pump is involved in the final common step of acid secretion, this class of drug showed superior acid suppression as compared to the H_2 receptor antagonists (H_2RAs). PPIs show marked superiority in the treatment of gastro esophageal reflux disease (GERD) and have become the standard of therapy in this disease. There are currently five PPIs available on the market, omeprazole, lansoprazole, pantoprazole, rabeprazole and esomeprazole.

More recently, the development of new anti-secretory drugs which inhibit the acid pump reversibly by binding to its K-binding site (acid pump antagonists, APAs) has attracted much interest. Such inhibitors would circumvent the inherent acid instability of PPIs as well as their slow on-set of action. The first APA was SCH 28080 (K_i = 68 nM). Its metabolic instability prevented the further development of this drug. Other analogues such as BY841 (K_i = 7 nM) or Linaprazan , show improved metabolic stability as well as high activity on the enzyme. Even higher metabolic stability along with high potency could be achieved with the unprecedented imidazo-naphthyridines (K_i = 7 - 25 nM). Their preclinical characterization in comparison to other candidates (e.g. YH-1885, K_i = 32 nM) will be discussed in detail.



IL-15

Innovative Approaches for Discovery and Development of Therapeutics in Oncology and Metabolic Disorders

Veena Agarwal

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There is a need of novel approaches for R & D in the current scenario of the skyrocketing R & D cost and shrinking pipeline of blockbuster drugs. This presentation will discuss the scientific advances and innovative R & D strategies that have led number of molecules in clinical trials globally for unmet medical needs. As examples, Piramal Life Sciences's lead molecules in oncology (P276), and in diabetes (P1736) undergoing various clinical trials in different countries will be discussed. PLSL's vision for leveraging the strengths of R & D in India with global partnerships, to accelerate the discovery and development of drugs for worldwide markets will also be presented.

IL-16

Cystic Fibrosis Drug Discovery

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Impaired processing and trafficking of membrane-target proteins to the cell surface can lead to partial or complete loss of function and is the basis of number of misfolding diseases, including cystic fibrosis (CF). Cystic fibrosis is a fatal genetic disease caused by mutations in *cftr*, a gene encoding a PKA-regulated Cl^- channel. The most common mutation is a deletion of phenylalanine at position 508 (□F508CFTR) that results in impaired protein folding, trafficking, and channel gating in epithelial cells. These defects alter salt and fluid transport in the lung, leading to defective mucociliary clearance, chronic infection, inflammation, and bronchiectasis. There are no drugs that specifically target mutant CFTR and optimal treatment of CF may require repair of both the membrane trafficking and gating defects. We have discovered two classes of novel, potent small molecules identified from screening compound libraries that restore the function of □F508CFTR in both recombinant cells and primary human bronchial epithelial (HBE) cultures isolated from human CF airway tissue. The first class potentiates cAMP-mediated gating to levels similar to wild type CFTR. The second class is able to correct the trafficking defect to approximately 10% of wt CFTR. The effects of the two mechanisms are additive. We discuss the implications of these findings for CF drug discovery. The CFTR-activating effects of the two mechanisms are additive and support the drug discovery strategy based on rescue of the basic genetic defect responsible for CF.

IL-17

Quinoline based various antimicrobials

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Quinolines and their derivatives are important constituents of pharmacologically active synthetic compounds. The quinoline nucleus can also be frequently recognized in the structure of numerous naturally occurring alkaloids. They have been associated with broad spectrum of biological activities. The fusion of quinoline to the tetrazole ring is known to increase the biological activity. The tetrazole group which is considered as analogues to carboxylic group as a pharmacore possesses wide range of biological activities. Several substituted tetrazoles have been shown to possess anticonvulsant, anti-inflammatory, CNS dispersant, antimicrobial, anti-AIDS and antifertility agents.

The phosphonate (PO_3^{2-}) moiety is a common structural fragment present in a wide range of biologically active compounds. A wide range of natural phosphorus based biologically active compounds which plays important roles as metabolic intermediates as common regulatory switches for proteins and as a backbone for the genetic information. However, aside from prodrugs applications, phosphate esters are normally considered impractical functional group for drug design because they are subject to cleavage by digestive phosphatases. Despite structural and electronic differences between phosphonate and carboxylic functionalities (in terms of size, shape, acidity and geometry), the phosphonate functionality is regarded as a bioisostere of the carboxylic acids, many of catalytic enzymes antibody generation and as transition state analogue inhibitors of different proteolytic enzymes exhibiting a wide spectrum of biological properties including antimicrobial, antitumor, antihypertensive and antibacterial activities.

Keeping in view, the importance of quinoline nucleus and organophosphorous compounds, we have synthesized some quinoline based biological active compounds such as α-hydroxyphosphonates, α-acetoxyphosphonates, α-aminophosphonates, alkyl phosphonates and others.

IL-18

Design and Synthesis of Novel Bioactive Heterocycles as Potential Anticancer Agents

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Synthetic and naturally occurring bioactive heterocycles are known to display a wide variety of biological properties [1]. With a special place among pharmaceutically significant natural products and synthetic compounds, many of these heterocycles can be exploited for medicinal purposes. Particularly, there has been a considerable interest on the design and synthesis of *N,O*-heterocycles due to their diverse biological activities viz. anticancer. Cancer is a one of the fatal diseases that has posed serious threat to human health. In the past, many classes of anticancer drugs have been developed. However, most drugs cause undesirable side effects due to lack of tumor specificity and multi-drug resistance [2]. Therefore, the development of novel and effective anticancer agents remains a major challenge. In our efforts to design novel and selective anticancer agents, we have prepared various 3,5-disubstituted-1,2,4-oxadiazoles and indolylazoles, and screened for their anticancer activity against various human cancer cell lines [3,4]. The *in vitro* cytotoxic effects of these heterocycles have been demonstrated across a wide array of tumor cell types and a few compounds exhibited specificity towards specific cancer cells. Detailed synthesis and results of biological evaluation of these heterocycles as anticancer agents will be presented in the conference.

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IL-19

Small molecule mTOR inhibitors as anti-cancer agents: Is selectivity an issue?

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In last decade Mammalian target of rapamycin (mTOR) has emerged as a validated therapeutic target for various diseases like cancer, inflammation & metabolic disorders. Over the past few years mTOR has been extensively used as an emerging target for anticancer drug development. mTOR is closely associated with its upstream signaling kinases phosphatidyl-3-inositol (PI3K) and AKT and thus selectivity is always an issue for any small molecule program. Most of the mTOR inhibitors do inhibits PI3K & AKT. In this oral presentation efforts of various groups in achieving a selective mTOR inhibitor will be discussed and its implication with respect to the signal transduction pathway will be evaluated.

IL-20

The Role of Molecular Activation in the Generation of New Indole Reactivity

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Simple indoles undergo ready electrophilic substitution and addition at C3. Over recent years, we have been investigating the chemical reactions of activated indoles, especially those with methoxy substituents in place to activate the benzene ring. In addition to such specific activation of the benzene ring, there is significant general activation that also affects the C2 and C3 positions. For example, activated 4,6-dimethoxyindoles are capable of being nucleophilic in a variety of positions, including C3, C2, and C7, depending on the overall substitution pattern. The special chemistry of activated indoles allows the formation of diindolylmethanes, triindolyldimethanes, and tetraindolyltrimethanes, and these can further lead to interesting macrocyclic structures. Also, the ambident nucleophilicity enables further ring fusion to take place and generate new heterocyclic ring systems. A selection of new reactions and new ring structures will be described.

IL-21

The Role of Safety and Security in Chemical Sustainability

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The first steps towards making chemical processes and industries more environmentally benign and sustainable begin with the adoption of safe practices in the chemistry laboratory and the secure management of chemicals. The safe use of chemicals is necessary not only for the health and safety of scientists, but in order to maintain community relationships and protect the environment. A loss of trust with your neighbors due to an accident or a chemical release can interfere with how your facility is operated. On a larger scale, accidents and accidental chemical releases affect the way the public perceives chemistry, and ultimately, their willingness to support chemistry. The best safety and security is achieved through a culture of safety and security and not by a rule-based compliance attitude. This presentation will address the ingredients necessary for creating a culture of safety and security and the role that instilling this culture can have in creating an environmentally sustainable future for the chemical and pharmaceutical sciences.

IL-22

Sustainable Development: An Exploration to the Wonderland of Ionic Liquids Palifosfamide (ZYMAFOS™): A Novel Molecule for the Treatment of Soft Tissue Sarcoma

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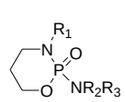
Palifosfamide (ZYMAFOS™, Isophosphoramide Mustard, IPM), **1** (Figure 1), a bi-functional DNA alkylator, is the active metabolite of ifosfamide (IFOS, 2, Figure 2). Ifosfamide, **2** and the related drug cyclophosphamide, 3 (CPA, Figure 2) are widely used anti-cancer drugs: both are pro-drugs that need to be metabolized to be active [1]. Their clinical use is limited by toxicity associated with specific metabolites. ZYMAFOS™ has shown efficacy in diverse cancer models, including activity in CPA-resistant osteosarcoma cell lines and xenografts [2]. It has a favorable safety profile since the toxic metabolites of Ifosfamide, **2**, acrolein and chloracetaldehyde, are absent [2]. Initially the pharmaceutical development of ZYMAFOS™ had been hindered by its poor aqueous solubility. In an effort to find a suitable formulation of **1**, a series of salts were evaluated. The tromethamine salt, **1a**, was found to offer several advantages such as enhanced solubility and stability over a wide pH range, improved non-deliquescence characteristics and a more favorable dissolution rate relative to the free acid and alternative salts. These characteristics allowed the development of both intravenous and solid dosage forms [3].

Figure 1. Structures of ZYMAFOS™, 1 and ZYMAFOS™ tromethamine salt, 1a.



2 $R_1 = R_2 = CH_2CH_2Cl$, $R_3 = H$ (ifosfamide)
3 $R_1 = H$, $R_2 = R_3 = CH_2CH_2Cl$ (cyclophosphamide)

Figure 2. Structures of Ifosfamide 2 and Cyclophosphamide 3.

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A scaleable process for the bi-functional DNA alkylator, ZYMAFOS™ (Palifosfamide, Isophosphoramide Mustard, IPM), **1** has been developed; three operations were conducted in one pot. Stoichiometry, solvent selection, wash and extraction procedures, and reaction temperatures were optimized to obviate the need for intermediate isolation and to effect final purification of ZYMAFOS™, **1**. Several variables were addressed during the development of the improved process and are discussed herein. The improved

process provided **1** in 74% yield, whereas the original process afforded 48% yield. ZYMAFOS™, **1**, free acid, is converted to a tromethamine salt, **1a**, which exhibits properties suitable for solid dosage and injectable formulations.

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IL-23

The Exploitation of Diverse Lead Generation Paradigms to Identify Novel Antibacterial Agents

Greg Bisacchi

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At AstraZeneca a key strategy, used to discover and develop antibacterial agents that will address the growing challenge of bacterial resistance, has focused on the design of new chemical scaffolds for new or under-exploited bacterial targets. We have championed the application of a diversity of lead generation techniques such as HTS and fragment based screening (using NMR and high concentration techniques), supported by strong structure based design capabilities to provide a range of novel compound starting points that have yielded novel lead scaffolds for these targets. This presentation will describe some case studies where this approach has successfully generated novel lead scaffolds that could be transformed into compounds that display excellent on-target potency, antimicrobial activity and in more recent cases, efficacy in animal models bacterial disease.

IL-24

Process Development & Scale up From a Generics Perspective

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The last decade has seen a major change in the area of process development in pharmaceutical industry. Indeed it opens an opportunity to explore the use of process development as an attractive tool in drug manufacturing organizations. Chemical process development is generally not taught as part of degree courses in higher education. The transformation of a synthetic route used for making mg/gram quantities of a chemical into a process for manufacturing multi kilogram and tones quantities is typically learnt “on the job” by chemists in industries. First of all it is very important to understand the generic drug development, stages of process development and scale up and generic approval requirements. I sense an all pervasive mood of optimism and buoyancy as process development is reflecting increasingly scientific talent in its use in the large scale manufacturing. Worldwide companies are struggling with the competing priorities of rising customer’s low cost expectations, ever-increasing safety and regulatory burden. Only insightful process development will bring the lower affordable cost.
The presentation will cover an overview of global generic pharma industry, insight of process development and case studies during scale-up at commercial scale.

IL-25

Value Creation and New Opportunities in Medicinal Chemistry, Drug Discovery, Process Development and Project Management of Technology Transfer

Mukund S. Chorghade*

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The pharmaceutical sector has traditionally been a vibrant, innovation-driven and highly successful component of the chemical enterprise. In recent years, a confluence of spectacular advances in

chemistry, molecular biology, genomic and chemical technology and the cognate fields of spectroscopy, chromatography and crystallography have led to the discovery and development of numerous compounds and technologies. In order to facilitate this process, there has been a significant and noticeable effort aimed at improving the integration of discovery technologies, chemical outsourcing formulations, and refined deployment of information technologies. Multi-disciplinary and multi-functional teams focusing on optimization have replaced the traditional, specialized research groups. To progress from conception to commercialization, the entrepreneurial industry has reached out and established global strategic partnerships with numerous companies overseas.

Simultaneously, industry in the U.S.A. and Europe has undergone unprecedented changes in recent years primarily due to mergers and acquisitions, blockbuster drugs losing patent protection and above all a paucity of new drugs that have been introduced, thereby creating an "innovation deficit". Rapidly increasing pace of regulatory reform allied with the necessity of effecting drastic reductions in costs have also resulted in marked shifts in the strategic paradigms. Numerous corporations are seeking strategic partnerships overseas to enhance their global capabilities. Pre-requisites like a highly trained and motivated work force, political stability, and the formidable research skills of the chemists make for a winning combination. As might be expected, significant international collaborations are on the increase. Strategic Sourcing, for long a preserve of the process and information technology industries, has now extended to virtually all activities in the chemical industry. India is well placed to take advantage of these scenarios.

Chemists today have an enviable armamentarium of techniques and methodologies in organic synthesis but are facing premium demands on their efficiency and creativity. An oft- repeated criticism that chemists prefer to research molecules that can be made rather than the ones that should be made An old quip concerned an inebriated individual losing his car keys in the darkness and looking for them far away from the site. His reasoning: "There is more light here". Chemists operate in familiar areas with methods they are comfortable with. The need of the hour is to improve productivity and efficiency and explore new approaches, tactics and strategies for compound synthesis. We are pleased to review herein, approaches pioneered by our group. In this lecture, we will discuss how some serendipitous observations in our laboratories led to discovery of NCEs and explore how mutual benefits can be obtained by eliminating current challenges faced by industry via sophisticated technology, strategic off shoring, global commerce and refined logistics.

Process Chemistry / Route Selection are important activities in the path of a drug from discovery to market. The medicinal chemistry routes for synthesis are usually low yielding and are fraught with capricious reactions, tedious chromatography and problems in scale-up. Considerable research efforts have to be expended in developing novel, cost efficacious and scalable processes and seamlessly transferring these technologies to manufacturing operations. We will exemplify this by discussing the route selection efforts on anti-asthma and an anti-phthalassemia drug candidate

IL-26

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IL-27

Organic Transformations leading to bioactive molecules accelerated by biocatalysts

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Heterocylces are well explored as bioactive molecules and several numbers of heterocylces are found to be established as clinical agents. Heterocylces which are used as medicaments are mostly obtained by synthetic routes. The present multistep multicomponent synthetic routes which are used to generate value added heterocylces bearing sulfur and or nitrogen as heteroatoms. Need non recyclable acid/base catalysts and require longer time. It seems that there is urgent need to provide environmentally accepted alternative rapid routes for getting the value added heterocylces.

In view of this, in the presentation focus will be directed to discuss various environmentally benign cyclocondensation routes which are being used to obtain five/six/seven membered sulfur and or nitrogen containing bioactive heterocylces using nature's catalysts, enzymes.
Attempts will also be made to present some of the synthetic routes developed by our group using cheaper and readily available enzymes for getting benzothiazoles, 1, 4 benzothiazines etc.

IL-28

Nucleosides and Nucleic Acids: Present and Future Drugs

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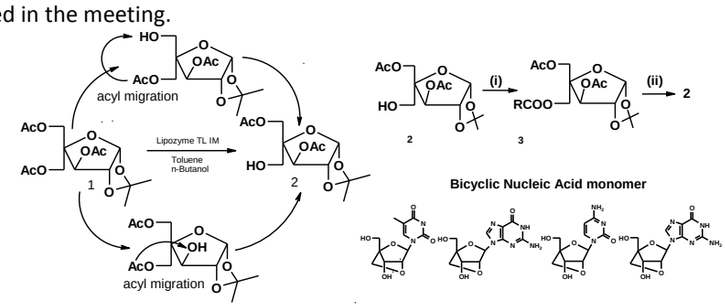
One of the important components of Nucleic Acids is deoxyribose and ribose sugars. The discovery of sugar modified nucleoside derivatives as potential antiviral agents and the emergence of antisense and antigene oligonucleotides as potential and selective inhibitors of gene expression have led to the considerable rise in the synthesis of modified nucleoside derivatives. The intrinsic problem in such synthesis is the selective manipulation of different hydroxyl and amino functions present in the compound under mild reaction condition.
We have developed an efficient biocatalytic methodology for the selective manipulation of different hydroxyl groups in the sugar during the synthesis of nucleosides of biological importance. Detailed results will be presented in the meeting.



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IL-29

Discovery of novel inhibitors targeting HIF-1alpha towards anticancer drug development

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Hypoxia-inducible factor-1alpha (HIF-1α) is a critical regulatory protein of cellular response to hypoxia, and regulates the transcription of many genes involved in key aspects of cancer biology, including immortalization, maintenance of stem cell pools, cellular dedifferentiation, vascularization and invasion / metastasis. HIF-1α has been implicated in the regulation of genes involved in angiogenesis e.g. VEGF and

is associated with tumor progression. In last decade, the over expression of HIF-1α has been demonstrated in many common human cancers and has emerged as a validated target for anticancer drug discovery. In the present talk design and synthesis of pyridyl-pyrimidine/ pyridyl-oxadiazole based HIF-1α inhibitors will be discussed[1]. As a consequence of HIF-1α inhibition, their impact on the signal transduction pathway will also be explored.

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IL-30

Boronolectins and fluorescent boronolectins as potential research tools and diagnostics

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Variations of glycosylation patterns in glycoproducts are often indicators of pathological changes. Sensors/binders capable of recognizing differences in glycosylations are potential diagnostics and important research tools in glycobiology. Based on the strong interactions between the boronic acid moiety and hydroxyl groups, we have developed a number of boronic acid-based lectin mimics, boronolectins, including (1) fluorescent boronic acids capable of fluorescent property changes upon sugar biding, (2) small molecule bisboronic acids capable of specific recognition of certain carbohydrates, and (3) DNA-based aptamers capable of differentiating glycosylation variations in glycoproteins. This presentation will focus on our recent effort in developing boronolectins for carbohydrate sensing and recognition.

IL-31

PHOSPHONIUM ION CHEMISTRY *en route* TO NUCLEOSIDE MODIFICATION

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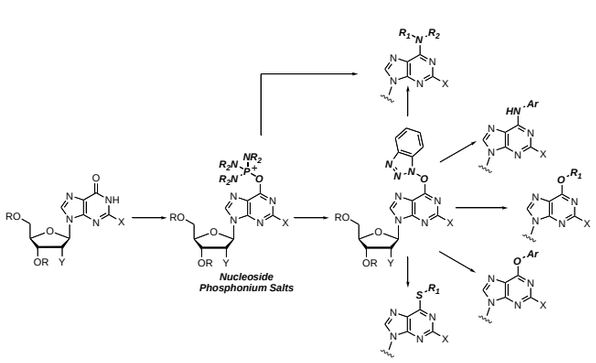
Over the past 3 years research in our group has expanded to include nucleoside activation by phosphonium ion formation. These intermediates have led to a new family of reactive nucleoside derivatives: O^6-(benzotriazol-1-yl)inosine, 2'-deoxyinosine, guanosine and 2'-deoxyguanosine. In addition, the isolable, stable phosphonium derivative of 2'-deoxyxanthosine is a valuable synthetic intermediate. This talk will present selected aspects from the discovery, mechanisms and applications of nucleoside phosphonium ion chemistry from our research, as well as applications of the underlying concepts to functionalizing simple organic molecules.Scheme



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IL-32

Importance of Salts and Polymorphs during Drug Discovery and Development

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Selection of an appropriate salt and polymorph for a new chemical entity is of utmost importance to pharmaceutical chemist and formulation development scientist. Salts and Polymorphs offer opportunities to modify the characteristics of Drug Substance eg, bioavailability, stability, manufacturability, impurity profiling and patient compliance. Such modifications influence a range of physico-chemical properties eg, melting point, hygroscopicity ,chemical stability, dissolution rate, solution pH, electrostatic, crystal shape and forms. Additionally, for well established, block buster Drugs, when they are about to go off-patent and generic, Salts and Polymorphs offer opportunities as 505-B(2) and for early launch. During that period, evaluation of I.P. perspectives, safety and equivalent efficacy of Salts and Polymorphs becomes essential. All these and related issues will be described with practical examples.

IL-33

Implications Of Heterocycles As Chemotherapeutic Agents: Drug Discovery Programme

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During the past twenty years, a multitude of novel bioactive heterocycles have been developed and several of these are being considered as therapeutic agents for various diseases. In this context, we synthesized some 3- (4-substituted-1-piperidinyl)-6-halogeno-1, 2-benzisoxazole hydrochlorides, 3-(2-butyl-4-chloro-1*H*-imidazolyl)-substituted-δ^2-isoxazolines and piperazine derivatives and found that 1, 2-benzisoxazole heterocycle was an appropriate bioisosteric replacement for the benzyl functionality present in the N-benzylpiperidine class of inhibitors for acetylcholinesterases. Further we synthesized and characterized several alkyl/aryl derivatives of arecoline thiazolidinones**,** arecoline emides and arecoline morpholines as M1 receptor agonist and screened by several *in vitro* and *in vivo* pharmacological studies.
Novel derivatives of 5-(4-methyl-benzylidene)-thiazolidine-2,4-dione and diazaspiro bicyclo hydantoin were synthesized and evaluated for their cell antiproliferation activity by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay viable human skin fibroblast cell line and carcinoma cell lines namely HeLa cells, HT-29 cells, MCF-7 cells, HepG-2 cells and human leukemia, K562 (chronic myelogenous leukemia) and CEM (T-cell leukemia) cells respectively. Various aspects of the above mentioned studies including *in vitro* and *in vivo* will be discussed.

IL-34

Anticancer Drugs derived from Natural Products

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The most consistently successful source of drug leads is natural products; continue to provide greater structural diversity. They offer major opportunities for finding novel lead structures that are active against a wide range of assay targets. As less than 10% of world's biodiversity has been tested for biological activity, many more useful lead compounds are awaiting discovery. For decades, natural products have been a wellspring of drugs and drug leads. Approximately, 74% of anticancer compounds are natural

products or have been derived from, or inspired by, a natural product. Many natural products possess diverse bioactivities, which attract both biomedical and synthetic interests and eventually lead to the applied fields[1]. However, their structural complexity, low natural concentration and unstableness frequency, hinder the industrial development of natural products. It is not unusual that bioactive natural compounds are discarded from clinical or preclinical trials due to one or more other reasons. An effective solution of this problem is provided by semi-synthesis of new structural analogues from natural products.
Terpenes are widely spread group of natural compounds and at least 400 known triterpenes. A variety of biological properties have been ascribed to pentacyclic triterpenes such as bactericidal, fungicidal, antiviral, cytotoxic, analgesic, anticancer, spermicidal, cardiovascular, antiallergic etc. In recent years, a number of studies have been carried out on three compounds of pentacyclic triterpenes namely lupeol, betuline and betulinic acid. Betulin is present in birch bark, as a main component along with trace amounts of lupeol and betulinic acid. National Cancer Institute (NCI), USA, screened around 3000 plant extracts for anticancer activity and identified betulinic acid as a potential anticancer agent.

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IL-35

An Enzymatically Active Fibrillar Film Of Bacteriophage-Associated Hyaluronate Lyase (HYLP2)

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The *in vitro* assembly of a soluble protein into its mature fibrillar form is usually accompanied by loss of its functional activity. Our study is the first demonstration of a natural enzyme (HylP2) retaining its enzymatic activity on conversion from pre-fibril to mature fibril and supports the contention that minor conformational changes in the native folded form of a protein can lead to the formation of a functional fibril. Interestingly, the mature fibrillar film of HylP2 also retains about 68% and 20% enzymatic activity for hyaluronic acid and chondroitin sulfate respectively. Hence, we demonstrate that fibrillar film formation owes novelty for hyaluronidase enzymes and its functionality in the organism establishes fibrils as a genuinely acquired protein fold/structure.

IL-36

BisIndolyl Maleimides and Indolocarbazoles as Cyclin Dependent Kinase Inhibitors

Sajan Joseph, *Lilly & Comp. India*

IL-37

Cell mediated immunity assays identify ESAT6-family of proteins for diagnostic and vaccine relevance using overlapping synthetic peptides corresponding to genomic regions of difference of *Mycobacterium tuberculosis*

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The advances in whole genome sequencing and comparative genomics have identified 11 genomic regions of differences (RDs) in *M. tuberculosis*, which are deleted/absent in all vaccine strains of BCG [1]. These RDs (RD1, RD4 to RD7, RD9 to RD13 and RD15) cover open reading frames (ORFs) of 89 proteins of *M. tuberculosis* and could be useful in specific diagnosis and developing new vaccines for tuberculosis (TB) [1]. To determine their diagnostic, pathologic and vaccine potential, overlapping synthetic peptides were used in this study in cell mediated immunity (CMI) assays.
A total of 1,648 peptides were synthesized using fluonerylmethoxycarbonyl chemistry [2, 3]. CMI responses to peptide pools of each of the 11 RDs were determined in relation to protective Th1-type

responses (antigen-induced proliferation and secretion of IFN-γ and the non-protective/pathologic Th2-type reactivity (IL-10 secretion) using peripheral blood mononuclear cells (PBMCs) obtained from pulmonary TB patients and healthy humans [3-5]. Furthermore, Th1 and Th2-biases of these responses were determined from the ratios of secreted IFN-γ :IL10 [3-5]. The results showed that highest Th1-responses were induced by RD1 peptides and the highest Th2 responses were induced by RD12 and RD13 peptides [3, 4]. Moreover, strong Th1-biases were observed with peptides of RD1, RD7 and RD9, whereas strong Th2-biases were obtained with peptides of RD12 and RD13 [3, 4]. In addition, experiments were performed by mixing peptides of RD with highest Th1-bias, i.e. RD1, with peptides of RDs having strongest Th2-bias, i.e. RD12 and RD13, to determine if IL-10 secreted by PBMCs of healthy subjects in response to peptides of RD12 and RD13 could inhibit Th1 reactivity of RD1. The results showed that peptides of RD12 and RD13 inhibited Th1-cell reactivity [3, 4], and the extent of inhibition of RD1-induced Th1 cell responses correlated with the ability of RD12 and RD13 to induce secretion of IL-10. It is well established that IL-10 helps to maintain mycobacterial infections by acting primarily at the level of macrophages and compromises anti-mycobacterial signals delivered by the Th1 cytokine IFN-γ [1], therefore it is essential that IL-10 inducing proteins of RD12 and RD13 are avoided in any future vaccine design against TB.

To identify individual proteins of Th1 cell-reactive RDs, further testing of the peptide pools corresponding to each protein of RD1, RD7 and RD9 was performed in Th1 cell assays. The results showed that three proteins of RD1, i.e. PPE68, ESXA and ESXB, and two proteins of RD7 (ESXO and ESXP) and RD9 (ESXV and ESXW) were the best stimulators of Th1 cells. Interestingly, six of these proteins belonged to ESAT6 (ESXA) family, and two of them (ESXA and ESXB) have already been shown to have vaccine potential in animal models of TB. However, ESXA and ESXB are also antigens recommended for the specific diagnosis of active and latent TB, and are widely used for this purpose, especially in the industrialized countries. Therefore, these antigens can't be used as vaccines against TB. Hence other Th1-stimulating antigens, i.e. PPE68, ESXO, ESXP, ESXV, ESXW, must be investigated for protective efficacy in animals. If found promising in such studies, these antigens may further be explored in clinical trials as new generation or alternative vaccines to replace/supplement BCG for vaccination of humans against TB.

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IL-38

Design, Synthesis And Small Library Generation Of Benzopyran Related Other Heterocycles & Their *In Vitro* Anticancer Evaluation

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Coumarins & other pyran analogs have shown excellent anticancer activity. The careful structural changes in several benzopyran derivatives at benzenoid part and also several synthetic modifications at C_3 and C_4 positions have led generation of several new small libraries. In the current work, more than 15 different reaction schemes were employed to design new chemical entities and primary screening was carried out of these library & screening of selected molecules were done on a panel of cell lines representing various cancers. Thus, the MTT assays were performed against cancer cell lines namely SW620 (colon), MDA, MB453, MCF-7 (Breast), L132 (Lung), ECV.304 (endothelial), MiaPaCa (Pancreas), HuTu80 (Stomach), G401 (Renal), PA-1 (Ovary), KB (ORAL), Hep2 (Larynx). In total, more than 200 compounds were prepared and studied.

The entire work was carried out in collaborative Project with Dabur Research Foundation, Ghaziabad and mini review of the work will be presented.

II-39

Proliferation And Apoptosis In Cancer Cells: The Role Of Chromophore

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Abnormal activation of proliferative pathways is observed in many types of cancer.The inhibition of apoptosis might play a role in the carcinogenic process.The role of chromophore in antiproliferation and cell apoptosis shall be discussed.

IL-40

Nucleic Acid Binding of Alkaloids: Fluorescence, Docking and Molecular Modeling Approaches

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A group of Alkaloids, derived to cure various diseases and cancers have been studied for their nucleic acid binding profile. Some of them having planar structural moiety, which could be easily inserted between the base pairs of nucleic acids were intercalating or partially intercalating drugs between DNA or RNA bases. Vinblastine was shown to bind in the minor groove of DNA duplex using fluorescence spectroscopy and molecular modeling studies. The binding of berberine to B-DNA (in the range of 10^5 $mole^{-1}$) was characterized by hypochromism in the absorption spectrum, enhancement of steady-state fluorescence emission intensity and stabilization of DNA against thermal denaturation. The DNA interaction of coralyne and palmatine by intercalation may be correlated with the biological activity. The DNA binding constants (10^6 $mole^{-1}$) showed a relatively high GC specificity of coralyne. It was revealed that the binding affinity of berberine to poly (rA) by a mechanism of partial intercalation was the highest compared to t-RNA and DNA. Coralyne was also found to bind strongly to poly (rA) structure and the binding process was enthalpy driven with a stoichiometry of one coralyne to four adenine bases. Berberine, palmatine and coralyne are partially intercalated on the $t\text{-}RNA^{PHE}$ molecule with lower contribution from electrostatic forces. These alkaloids are known to bind to DNA and RNA triple helices.

IL-41

Macrolide and Ketolide Antibiotics: Synthetic Studies on Narbonolide

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Ketolides[1] are a new class of macrolide antibiotics that have been shown to be active against a variety of bacteria including macrolide-resistant bacteria and mycobacteria. Ketolides differ from erythromycin A by harbouring a 3-keto group instead of a L-cladinose group. The 3-ketone modification has imparted this class of compounds with
excellent activities against drug resistant bacterial infections especially the clinically important respiratory tract
pathogen *Streptococcus pneumoniae*.[2] The therapeutic promise shown by ketolides has led to a resurgence in macrolide antibiotic research in the pharmaceutical industry,[3] with successful clinical candidates such as telithromycin[4] (**1**) from Aventis Pharma, and cethromycin (**2**) from Abbott Laboratories[4] (Fig. 1). Narbonolide **3** is a 14-membered polyketide macrolactone biosynthesized by the pikromycin polyketide synthase (PKS) system of Streptomyces venezuelae ATCC 15439, exhibited significant therapeutic potential and structural similarity to the macrocytes in telithromycin and cethromycin. Stereoselective preparation of various fragments[5] of the natural product will form the basic premise of my presentation.

Figure 1

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IL-42

Exploring environmentally benign chemical and biocatalytic routes for bioactive phenolics

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Phenolic compounds are characterized by the presence of hydroxylated aromatic ring system and are widely distributed in plant kingdom. Owing to the immense biological importance of phenolics, interest in accessing these molecules has reached a new high. However, exploration of these compounds is severely hindered by low percentage in their natural resources as well as use of hazardous chemicals. Consequently, the utilization of green chemical practices has provided a fresh stimulus to counter the longstanding problems for their isolation and synthesis. In the above context, various green methodologies have been developed for bioactive phenolics using contemporary tools like ionic liquids, water, biocatalysts, besides energy efficient microwave and ultrasound which will be discussed in details during presentation.

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IL-43

Structure-CYP Inhibition Relationships

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Drug-drug interaction is the result of a drug affecting the activity of another drug i.e. the drug effects are increased or decreased in the presence of another drug. This generally happens due to changes in the metabolism of one drug in the presence of another drug. Drug-drug interactions should be avoided due to the possibility of adverse or unexpected outcomes. Cytochrome P450 (CYP) mediated metabolism is a major focus for drug-drug interactions in the pharmaceutical industry as it represents approximately 55% of all metabolic processes. Of late, medicinal chemists all over the world have been dealing with increased incidences of CYP inhibition. This talk will detail various structural modifications and strategies that have been found to be useful in overcoming CYP inhibition.

II-44

Use of Virtual Compound Libraries for Chemical Hit Finding

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The high-throughput screening (HTS) of large chemical libraries is a means for the pharmaceutical industry to generate chemical starting points for “hit-to-lead” drug discovery exercises. Such HTS campaigns are usually expensive and require access to large quantities of biological reagents, a significant level of automation, and a large screening library consisting of hundreds of thousands of compounds obtained through costly in-house synthesis and/or acquisition. In order to circumvent the need for such significant investment, the Novel Drug Discovery Research group at Ranbaxy has employed various computer-based approaches for chemical hit generation. A description will be given of the successful ligand-based *database mining* of a commercially-available compound repository in the identification of chemical hits for a medicinal chemistry project. In addition, the creation of virtual libraries of chemical reagents allows small and focussed compound libraries to be designed and synthesised by parallel organic syntheses.

IL-45

Total Synthesis of Bioactive Natural Products

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Nature being the best craftsman provides synthetic organic chemist with ample opportunity for discovery and creative endeavor of various bioactive natural products with an incredible variety of complexity and stereochemical diversity. However, lesser availability and cumbersome isolation techniques have attracted organic chemist for their synthesis from readily available source in an efficient and economical way. In my talk, I will discuss how we have crafted the chirality in sugar for total synthesis of Dihydrokawainol,[1] (+)-Cardiobutanolide,[2] Pentenocin-B and (+)-Verbalactone and biologically active □-lactones.[3]

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IL-46

Design, synthesis and antiradical activity of novel Vitamin E compounds

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IL-47

Recent advances in containment technologies for Anti cancer drugs

Soumitra Banerjee,

Fine Solutions Ltd, Israel

IL-48

Synthesis of Peptides and Peptidomimetics: Isothiocyanates derived *N*-protected amino acids and their utility in the preparation of thioureidopeptides

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The research theme of our group is to synthesize novel peptidomimetics such as ureas, carbamates, carbonates, etc. Thioureas are valuable class of compounds and have found wide range of applications in bioconjugate and heterocyclic chemistry. They are medicinally valuable as antibacterial, antiviral and antimicrobial agents. Precursors to these thioureas are the isothiocyanates which are versatile intermediates. The reported class of amino acid derived isothiocyanates was limited to α-isothiocyanato esters obtained by converting the α-amino group by treating with thiophosgene into isothiocyanate. We have now synthesized and isolated *hitherto* unreported class of *N*-protected amino alkyl isothiocyanates *via* a simple protocol employing TsCl mediated decomposition of dithiocarbamic acid salt which in turn was prepared from the corresponding vicinal diamine. Further, they have been employed as synthons for the preparation of dipeptidyl thiourea esters. Some of these results will be presented in this talk.

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IL-49

Advanced glycation end products and diabetic complications: An overview.

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Diabetes is a multi-factorial disease associated with very high incidence of stroke, peripheral artery disease, macrovascular and microvascular diseases such as heart failure, neuropathy, nephropathy and retinopathy etc. Prolonged hyperglycaemia is now recognized as a primary cause of diabetic complications. Despite considerable progress in the therapy for hyperglycaemia and hypertension, the presence of vascular complications is still around 20-25% among diabetics of over 5 years duration. A global increase in diabetic population has generated considerable amount of interest in therapies targeted for treatment of macrovascular and microvascular complications of diabetes.

One of the major causes of these complications is formation of Advanced Glycosylation End products (AGEs). Maillard in 1912 found that reducing sugars such as glucose and ribose react with proteins to form brown pigments. The aldehyde or keto groups of reducing sugars and lipids oxidized are capable of reacting with amino groups of amino groups of amino acid to form Schiff bases, which can rearrange to the more stable Amadori type of early glycosylation products. These early glycosylation products undergo a slow, complex series of chemical rearrangements to become irreversible Advanced Glycosylation Endproducts (AGE)[1-3] .These AGEs contribute towards many pathologies of diabetes, atherosclerosis, heart disease, stiffness, kidney diseases and arthritis,There are three main mechanisms responsible for the AGE related complications.1)Glycosylated and oxidized proteins are immunogenic and cause low-grade vascular inflammation and widespread endothelial dysfunction; a key component of Metabolic Syndrome X.2)Glycoxidated Lipoproteins lead to accelerated Atherosclerosis and 3) AGE related cross-link formation with collagen ,Myelin ,Glomerular membrane , retinal and various structural proteins cause different diabetic complications[4-6].

Considering all these diabetic complications, We have initiated research programme at Torrent Research Centre to find out potent and safe AGE breaker compounds .To achieve this series of compound were synthesized and screened in vitro and in vivo efficacy. Further ADMET profile led to the identification of TRC 4186 as a drug candidate for clinical studies. The recents advances in AGEs related pathologies and developments of AGE breakers will be discussed.

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IL-50

Synthesis and Antimalarial Activity Evaluation of Tetraoxanes, Tetraoxane-aminoquinoline/triazine Conjugates

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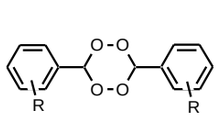
Malaria is still one of the deadly diseases causing deaths of more than 1-3 million people per year all over the world. Aminoquinolines have been used for the treatment of malaria for a long time, but *Plasmodium falciparum* has developed resistance against these compounds, and artemisinin and its derivatives are the only alternative for the treatment of *Plasmodium falciparum* related infections [1,2]. Heme and dihydrofolate reductase are the most commonly used targets in malaria chemotherapy [3,4]. Aminoquinoline and artemisinin based compounds stop the hemozoin formation *via* different mechanism, while cycloguanil, a triazine derivative exhibit antimalarial activity due to its ability to inhibit dihydrofolate reductase enzyme. Recently another class of compound named tetraoxanes received considerable amount of interest due to it artemisinin like activity, however, the structural diversity of this important class of compounds is not available [5,6]. To this end, synthesis, characterization, x-ray crystal structure,

antimalarial activity and cytotoxicity of symmetrically and asymmetrically substituted tetraoxanes (**1**), tetraoxane-aminoquinoline (**2**), and tetraoxane-triazine (**3**) conjugates will be presented [7-12].



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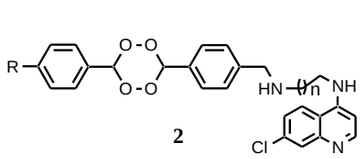

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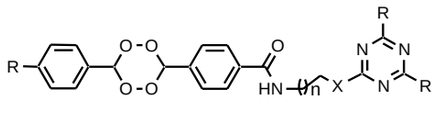

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IL-51

Chafique Hamdouchi –

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Oral Presentations

OP-1

Studies of interactions of acridone derivatives with P-gp, ATP and Mg^{2+} - Search for MDR modulators led to the identification of an anti-candidasis agent

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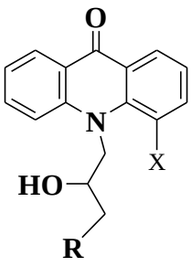
The practice of chemotherapy of various diseases like malaria, AIDS, cancer, fungal and many more viral diseases thwarted from the development of resistance to drugs in the infected cells/microbes. Amongst many other transporter proteins, the over expression of P-glycoprotein (P-gp) in higher organisms and cdrp1, cdrp2 in *Candida albicans* has been found to be responsible for the development of multi drug resistance.

Targeting P-gp, ATP and Mg^{2+} which collectively constitute the efflux pump, we have synthesized acridone based compounds (Figure 1) and evaluated for their interaction with the three components of efflux pump. The experimental results were also supported by the docking studies. It was observed that the acridone based molecules under present investigation interact with P-gp/ATP/Mg^{2+}. Further the influx/efflux experiments on *Candida albicans* indicated that these compounds cause cell wall rupturing of this microbe and hence could also be the suitable candidates for anti-candidasis therapy. The results of these experiments will be discussed.



X = -H, -COOH, -Cl

R = morpholine
piperidine
pyrollidine
piperidino piperidine
diethyl amine
diisopropyl amine

Figure 1

OP-2

Development of formulations of root extract of *Urtica dioica* for hair growth promotion and identification of responsible bioactive constituents

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Alopecia (baldness), a dermatological disorder is a common problem throughout the world and has been estimated to affect between 0.2 and 2 % of the world population. Herbal drugs have been widely used for hair growth promotion since ancient times in Ayurveda, Chinese and Unani systems of medicine. The present study aims to prepare and characterize the herbal formulation of *Urtica dioica* of Garhwal Himalayan region for promoting the hair growth for the treatment of alopecia.

Aloe vera based herbal preparations of light petroleum and ethanolic root extract of *Urtica dioica* were prepared by a simple method. Both the prepared formulations were nonirritant and nontoxic on skin of rats. The prepared herbal gels showed hair growth initiation time of 5 days and rapid completion time of 15 days for both the formulations. It was also observed that the prepared herbal gels showed the better hair growth initiation and completion activity than that of standard (2 % minoxidil solution) even. It was observed that formulation prepared with ethanolic extract of roots of *Urtica dioica,* showed the best hair lengthening properties as compared to others. In order to explore the probable active compounds responsible for the hair growth, the chemical analysis of the roots of *Urtica dioica* was performed. From

the roots of *Urtica dioica* five compounds namely β- Sitosterol, Ursolic acid, Sitosterol-β-D glucoside, Quercetin and Rutin were isolated and identified. Rutin and Quercetin showed good *in-vitro* antioxidant as well as good hair growth initiation activity. Rutin was found to be better in hair growth activity, which might be due to its better antioxidant activity.

Therefore, it was concluded that Rutin and Quercetin were among the chief active constituents that might be responsible for the promising hair growth activity of roots of *Urtica dioica.*

OP-3

Copper-Catalyzed Regioselective Tandem Synthesis of Indolo, Pyrrolo [2,1-*a*] isoquinolines and Indolo[2,1-*f*][1,6]Naphthyridines by the Preferential Addition of *N*-Heterocycles on *ortho*-haloalkynes followed by Intramolecular C-2 Arylation

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Indolo[2,1-*a*]isoquinoline has a unique nitrogen containing tetracyclic structure, characterstic of dibenzopyrrocoline alkolids, cryptaustoline **P** and cryptowpline **Q** isolated from the bark of Cryptocarya bowiei, which are reported to possess antileukemic, tublin polymerization inhibitory and antitumour activities. In continuation of our recently developed methods for the copper-catalyzed *N*-arylation of N-heterocycles using benzotriazole and its derivatives as a ligand[1-3] and the electrophilic cyclization of alkynes[4], Polyheterocycles **4** were synthesized regioselectively in one pot by the copper-catalyzed tandem addition of *N*-heterocycles **1** onto *ortho*-haloarylalkynes **2**, followed by intramolecular arylation without isolating intermediate **3** [5]. This chemistry appears to involve the preferential nucleophilic addition of *N*-heterocycles onto the *ortho*-haloarylalkynes over *N*-arylation of the aryl halide. Developed novel chemistry allows direct access to the various types of diversely substituted *N*-heterocycles, Carbocycles, Natural products, Synthetic drugs and π-conjugated organic materials. A relatively inexpensive ligand $BtCH_2OH$, is used along with inexpensive CuI for this novel transformation, increasing the overall utility of this reaction.

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OP-4

An assessment of safflower *(Carthamus tinctorius*) seed extract in the treatment of periodontal osseous defects in humans: A pilot study

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Recently, herbal medicines have been evaluated for their effects in periodontal diseases *i.e.* antibacterial, anti-inflammatory and periodontal tissue regeneration because interest in the search for a new non-toxic biodegradable material that would be free from side effects has been growing. Therefore, the present study was designed to evaluate the regenerating potential of safflower seed extract in the treatment of human periodontal osseous defects. Twenty one, two-wall infrabony defect sites from fifteen patients were randomly and equally divided into three groups to be treated with safflower seed extract. These groups were comprised of safflower seed extract (SSE)/collagen (test), saline/collagen (saline control) or access flap surgery alone (surgical control).The soft and hard tissues were evaluated at baseline along with 6 months surgical re-entry. Statistical analyses of data suggest that all three groups show significant difference for both soft and hard tissue parameters after comparing with baseline. Test and saline control groups have significant improvements in soft and hard tissues over the surgical control. However, they did not differ significantly themselves. Data in the present pilot study indicated that Safflower seed extract may be a promising natural drug in periodontal regeneration.

OP-5

Transition Metal-Catalyzed Desulfitative C-C Bond Forming Reactions of 2-(1*h*)-Pyrazinones

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Transition-metal-catalyzed reactions [1] are among the most attractive methodologies for the decoration of heterocyclic compounds. As a result of the development of a large number of metal-catalyzed coupling reactions of various C-X containing compounds (X = I, Br, Cl, OTf, OMs), efficient methods are now available for the direct formation of bonds between of sp^3,sp^2 and sp hybridized carbon atoms.

As a part of our ongoing research on the development of transition metal-catalyzed cross-coupling reactions [2] under microwave irradiation conditions, we are presently investigating several new methodologies for the decoration of the 2(1*H*)-pyrazinone scaffold with focus on desulfitative[1c] C-C cross-coupling reactions using palladium catalyst. A detailed overview will be given describing our recently developed and optimized protocols.[3]

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OP-6

Target-to-Drug Discovery for Novel Leishmaniacidals

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Leishmaniasis is endemic in >85 developing countries with >1.5 million estimated cases occurring each year and an additional 350 million people at risk of infection. Transmission of leishmaniasis most commonly occurs via an infected phlebotomine sandfly. Clinical manifestations of leishmaniasis range from cutaneous, mucocutaneous to visceral leishmaniasis, the latter if untreated is fatal. Patients of leishmaniasis are faced with limited treatment options, as there are no vaccines and existing therapies are expensive having pharmacological liabilities.

As opposed to whole parasite phenotypic anti leishmanial drug discovery pathway, our interest is based on significance of pteridine reductase 1 enzyme as a molecular target to parasite growth and survival. Targeting this pathway, we developed a multi-tiered compound screening paradigm to identify and confirm novel leishmaniacidal lead molecules. Transgenic *Leishmania* were used in flow cytometry screen, aided with structural modeling of target recombinant enzyme we developed biochemical and biological screening assay formats to identify and characterize new potent *L. donovani* growth inhibitors targeting the amastigote found in the human host. Confirmed growth inhibitors were filtered further for desirable

drug-like properties using computational predictions. Lead molecules were identified that display in vivo activity without toxicity to human cells. Monastrol, which is an established anticancer drug, was identified as a novel leishmaniacidal lead molecule. We confirmed the leishmaniacidal effect of these molecules is triggered by programmed cell death (PCD).
With the whole genome sequencing of *L. donovani* clinical isolates being carried out in our laboratory, molecular target driven approach to antileishmanial drug discovery will be further strengthened.

OP-7

Effects of Osmolytes or Denaturants on α-Chymotrypsin Activity and the Folding/Unfolding Transition States

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Enzymes are very sensitive and highly complex systems, exhibiting a substantial degree of structural variability in their folded state. In the presence of co-solvents, the fluctuations among vast numbers of folded and unfolded conformations occur via many different pathways, alternatively, enzymes can be stabilized or destabilized. To understand the osmolytes and denaturants contribution on the stabilization, related to the associated structural changes and enzyme activity of α-chymotrypsin (CT), we have monitored the differential scanning calorimetry (DSC), circular dichroism (CD), enzyme activity and gel electrophoresis as a function of osmolyte or denaturant concentrations. The present investigation compares the compatibility of osmolytes and deleterious effects of denaturants on the structure, function and enzyme activity of CT. This comparison has provided new important insight on the contribution of co-solvents effects on protein folding/unfolding, enzyme activity and the understanding of protein-solvent interactions. Evidently, we observed that naturally occurring osmolytes (trimethylamine N-oxide (TMAO), betaine, sarcosine, proline and sucrose) play dominant contribution on stabilization of CT while not enhances its enzyme activity. In contrast, our results revealed that the denaturants enhanced surface of enzyme by binding to the surface of CT, which leads to zero enzyme activity. The modifications in the secondary structure of this β/β protein, as quantified by the CD spectra, reasonable enhancement was observed for β–strands in the presence of the osmolytes as compared to buffer, which contributes its stabilization power.

OP-8

Synthesis and *in-planta* activity of caged/phosphotriester precursors of trehalose-6-phosphate (T6P)

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Trehalose is a non-reducing disaccharide sugar that is made up of two glucose units joined by an α,α-1,1 linkage with wide spread occurrence in bacteria, insects, fungi, and plants.[1] However, its existence and biosynthesis in mammals is not known.[2] Trehalose-6-phosphate (T6P), an intermediate in the trehalose pathway (Figure 1), has come out of obscurity over ten year to be appreciated as signaling molecule that regulates plant metabolism and development.[3] Its significance began to dawn when genetic modification of trehalose pathways produced dramatic phenotypes in plant. Two main enzymes namely trehalose phosphate synthase (TPS) and trehalose phosphate phosphatase (TPP) are the key enzymes in this pathway. TPS1-knockout is embryo lethal showing that the pathway is indispensable for embryo development.[4] Vital beneficial phenotypes emerged from these T6P intervention experiments. a) Those expressing E. coli TPS and elevated T6P produced more biomass than wild type when fed glucose or sucrose means T6P is important for carbohydrate metabolism [5] b) Parallel experiments in *Nicotiana tobacum* demonstrated that these genetic modifications were an effective means of altering photosynthetic capacity. [6]
Recent research has demonstrated that T6P regulates sugar utilization and starch metabolism and interacts with other signaling pathways, including those mediated by plant hormones. [7] Such wide ranging and significant biological effects through modification of one pathway are unprecedented. In spite

of this we still don't know clearly the mechanism and site of interaction of T6P with its binding partner. Our effort towards finding the answer of above questions and synthesis of *in-planta* active T6P as prodrug will be presented briefly therein.

Figure 1. Trehalose biosynthetic pathway

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OP-9

Curcumin ameliorates experimental colitis: Singnal transduction through TLR-4 Receptor and Myd88

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Recent surge of interest in herbal medicine for inflammatory bowel diseases has prompoted us to investigate the anti-inflammtory effects of curcumin and its mechanism in experimental colitis. Expression of Toll like receptor-4 (TLR4), MyD88 and NFkB was examined in inflamed colonic tissues. Sprague-Dawley male rats having colitis induced by intrarectal administration of trinitrobenzenesulphonic acid were treated daily with an aqueous suspension of curcumin (100 mg/Kg body weight) or phosphate buffered saline (PBS) 2 hr prior to inducing colitis. Non colitis animals controls received curcumin or PBS in a similar manner. Colonic levels of TLR-4, MyD88 and NFkB proteins were measured using ECL western blot analysis, and TLR-4 mRNA by a competitive RT-PCR method. Curcumin suppressed the induction of TLR-4, MyD88 and NFkB proteins in inflammed colon. Interestingly the expression of TLR-4 mRNA remained unaltered in inflamed. Furthermore inflammatory makers such as myeloperoxidase activity, malodialdehyde concentrations and colon histology were also significantly reversed by curcumin. These findings suggest that curcumin mediates its effects through that TLR-4 and MyD88 and may serve as therapeutic target in IBD treatment.

OP-10

$Mg(NO_3)_2$ primed seeds: A better tool for somatic embryogenesis in rice (variety- Swarna) –A first report.

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Present study deals with the regeneration potentiality of rice (var.Swarna; MTU 7029) plants through somatic embryogenesis. It is established that the use of $Mg(NO_3)_2$ primed seeds can raise the plants having the capacity of stress amelioration (Anaytullah and Bose, 2007). On the basis of this in the present study a comparative characterization of the calli were made by using the dehusked and sterilized whole rice seeds (caryopses), obtained from $Mg(NO_3)_2$ primed and non-primed one. During the establishment of regeneration potentiality of rice (var. Swarna) the best concentration of 2,4-D was found $2mgl^{-1}$;hence in the present investigation the same concentration was taken into consideration for the preparation of medium. Different concentrations (2-8 mM) of the $Mg(NO_3)_2$ while used as priming treatment before using the rice seeds on calli culture, showed promising results in respect to non-primed seeds. 4mM concentration of $Mg(NO_3)_2$ had taken minimum days for callus induction, maximum callus induction frequency and embryogenic calli percentage and also it has taken the least time to form green bud formation in regeneration medium in respect to other used concentrations of $Mg(NO_3)_2$ and non primed one. Further some physiological and biochemical studies were made to find out the inner potentiality of the regenerated calli. The fresh and dry weights were found maximum in the calli obtained from the 4mM $Mg(NO_3)_2$ primed seeds; in the same treatment the proline content, which reflects the osmoregulatory capability of a particular plant regarding stress was also found maximum, although it is at par with the proline content found with 8mM concentration of $Mg(NO_3)_2$. Calli of non-primed seeds was found to be poor performer for these parameters. The $Mg(NO_3)_2$ primed sets showed more root regeneration capacity, which is the main problem in the Indica rice.

OP-11

Facile Polymer Supported Syntheses Of N-Pegylated Quinoline Scaffolds: A Convienient Drug Delivery Technique

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A library of N-PEGylated quinoline derivatives of PEG molecular weights 400 has been prepared rapidly after the activation of PEGs using maleic anhydrides. Quinolines with a polymer backbone obviously are important as new materials. In 1995, Zalipsky S. et al and Herman S. et al [1] reported the functionalization of polyethylene glycol for preparation of biologically relevant conjugates along with some reactive end groups. Polyethylene glycol conjugation chemistry represents an emerging trend for generation of potential therapeutic agents. Woodle M. C. et al. and Allen T. M et al. [2] have demonstrated that PEG-modified biological molecules can benefit from extended plasma lifetimes, induced by reduced uptake by the reticuloendothelial system and more generally from a decrease of the undesired consequences of electrostatic and van der Waals interactions. A future direction towards nonviral gene therapy is the use of PEG grafted synthetic vectors as long- circulating carriers for receptor mediated gene delivery [3]. Norfloxacin, a member of the fluoroquinolone antibiotics was conjugated to mannosylated dextrin in order to increase the drugs's intake by cells, enabling faster access to microorganisms, reported by Roseeuw E. et al and Coessens et al [4]. The backbone of polyurethanes and other ordinary low-density polyethylenes having antimicrobial norfloxacin drug have been tested by Yang et al [5] against several Gram positive and Gram negative bacteria displayed excellent antimicrobial activities. Recent advances in tumor therapy demonstrated that successful anticancer strategies can be developed by employing proper carrier systems able to deliver probes, drugs or genes to tumor targets reported by Paolo et al [6]. Quinolines and their derivatives have been extensively explored for their biological [7], anti-filarial, anti-bacterial and anti-malarial activities and additionally, for their cardiovascular, anti-neoplastic and receptor agonist activities. PEG, a water soluble non ionic polymer, having non toxic character is widely used as carrier for drug delivery system, in many biochemical cosmetic pharmaceutical and industrial applications. We report the facile synthesis of a novel family of N-

PEGylated of quinolines by coupling PEG 400 with 2-formyl, 3-chloro, 6-amino quinolines via maleic anhydride as an activator. Antimicrobial activities of Quinoline-PEG polymer and quinolines were tested against Gram positive and Gram negative bacteria. The results indicate that the new polymers have potential as potent antimicrobial agents, although the mode of activity is not clear. Since these polymers are relatively stable to high temperatures, they can be used for medical and biomaterial applications with prior thermal sterilization. The present facile synthetic strategy can be an effective approach for incorporating the polymeric carriers conjugated with drug moieties either in the backbone of polymer or as terminal and pendent groups on the polymer chains.

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OP-12

Facile Synthesis Of Novel Coumarins Under Solvent-Free Conditions and Their Antioxidant Evaluation

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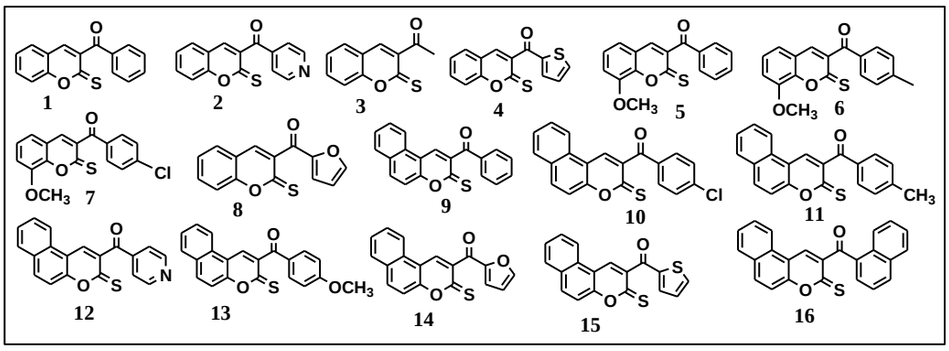
The defensive effects of coumarins as antioxidants is well known [1]. Nishiyama *et al*. reported the stronger antioxidative activities of hydrocoumarins than α - tocopherol for the oxidation of tetralin and linoleic acid in a homogeneous solution [2]. In conjunction with our works related with the synthesis and biological evaluation of heterocycles [3,4], we are reporting herewith a facile, convenient and high yielding synthesis of a combinatorial library of 3-alkanoyl/aroyl/heteroaroyl-2*H*-chromene-2- thiones by the condensation of easily accessible β-oxodithioesters and salicylaldehyde/substituted 2-hydroxybenzaldehydes under solvent-free conditions. The assessment of radical scavenging capacity of the compounds towards the stable free radical 2,2-diphenyl-1-picrylhydrazyl (DPPH) was measured and these compounds were found to scavenge DPPH free radical efficiently. Five selected compounds were able to protect curcumin from the attack of sulfur free radical generated by radiolysis of glutathione (GSH). The newly synthesized compounds exhibited profound antioxidant activities. Five of them (compounds **3-7** of Table 1) rendered comparatively high antioxidant capacity.

Table 1.



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OP-13

Biological and Toxicological Studies of new derivatives synthesised from the sesquiterpene lactones isolated from medicinal plants

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Sesquiterpene lactones having α – methylene –γ – lactone moiety have been established as potent plant growth regulators. With a view to increase the water solubility of lactones, diethanolamine adducts of parthenin [4] (isolated from *Parthenium hysterophorus*) , isoalantolactone & alantolactone (isolated from *Inula racemosa*) were prepared. In order to introduce diethanolamine group in epoxyalantolides [2], isoalantolactone & alantolactone [3] were allowed to react with an excess of perbenzoic acid followed by diethanolamine. In order to prepare more compounds for biological screening, diethanolamine was treated with isotelekin and isotelekin acetate. The structures of all the compounds were elucidated by spectroscopic techniques like IR, ^{1}H NMR, ^{13} C NMR and Mass spectra. All the compounds so obtained were subjected for biological evaluation as plant growth regulators and tested for their toxicological behaviour [1]. The parameters studied in biological activity include adventitious root formation in hypocotyl cuttings of *Vigna radiata, Cucumis melo* cotyledon expansion test and seed germination studies in *Triticum aestivum.* The parameters studied for toxicological behaviour include record of mortality, change in diet intake, change in body weight, change in organ weight indices, lipid peroxidation of blood and tissues and haemolysis of erythrocytes (*in vitro*). The results were fairly good over the parent compounds.

OP-14

Exploring Enzyme Substrate Specificity for the Separation of Anomeric Mixture of *O*-Aryl Nucleosides of Diagnostic Importance

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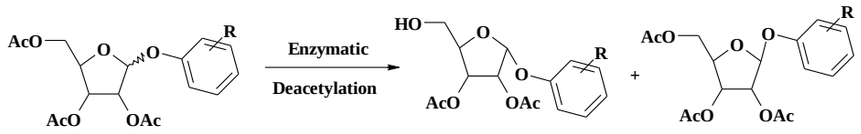
One of the recent applications of *O*-arylglycosides is the detection of / assay of nucleoside hydrolases or nucleoside phosphorylases in microbial parasites, which has adverse effect on human health and animal population. The *O*-arylglycosides are used as chromogenic substrate, which on reaction with the enzyme releases phenolic chromophore that can be detected and assayed spectrophotometrically and thus provide an easy method for the presence of enzymes.

It is the □-*O*-arylglycosides that serve as substrates for the nucleoside hydrolases or nucleoside phosphorylases, however most of the synthetic methodologies reported for the preparation of these compounds lead to the formation of mixture of □ /□anomers. The separation of anomeric mixture o̩f □ /□

O-arylglycosides is almost impossible by simple chromatographic methods. We have developed a highly efficient separation methodology based on lipase-mediated selective deacetylation of one of the acetoxy functions of the peracetylated □-*O*-arylglycoside from the mixture of □ /□anomer. Detailed results will be presented in the poster.



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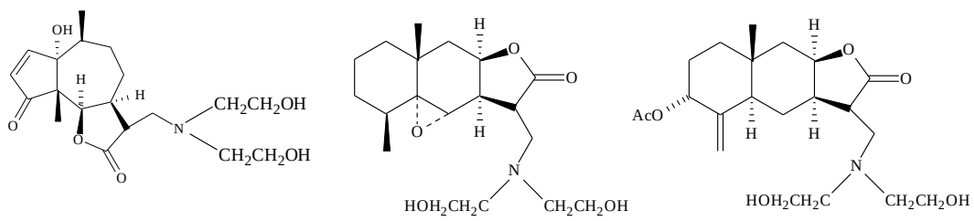

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Poster Presentations

P-1

In-vivo phytoprotective effect of *Thuja occidentalis* Linn against DMBA induced mammary carcinoma

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Breast cancer is the most lethal cancer affecting women throughout the world. More than 10.5 Lakhs new breast cancer cases occur worldwide among which 3.76 Lakhs death occurs annually. In India, breast cancer is the leading cancer site in its female residents. The present trend in the management of breast cancer development involves studies on the pharmacological mechanisms and search for chemical structures of herbal extracts responsible for anticancer activity. Considering, the recent realization that any plant already established for some pharmacological properties should be further explored for newer bioefficacies has motivated us to explore in-vivo protective effect of *Thuja occidentalis* (leaves) against 7,12 dimethyl benz(a)anthracene induced mammary tumor in ICRC mice. In vivo experiment has been conducted to observe the preventive role of *Thuja occidentalis* Linn (leaves) against DMBA induced mammary cancer. Ethyl acetate and methanolic extracts in two doses (5 & 10 mg/kg body weight) of the plant were tested in terms of tumor incidence, weight, volume and life span against the reference drug doxorubicin using standard animal protocol. EtOAc extract (10 mg/kg body weight) of the plant exhibit reduction of tumor incidence (34%), tumor weight (39%) and tumor volume (50%) compared to cancerous control group with the increase in body weight & life span in comparison with cancerous control and doxorubicin treated group. The plant *T. occidentalis* (leaves) possess significant potential for phytopreventive bioefficacy against DMBA induced mammary carcinogenesis.

P-2

HPTLC Determination of Caffeine in newly launched Energy Drinks and it's co-relation with Frustration Tolerance

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Caffeine is a mild central nervous stimulant that occurs naturally in tea & coffee and added in newly launched energy drinks. Such energy drinks are becoming highly popular in younger generation, due to instant energy supply and reducing the sleep time. The present piece of work is focused to the estimation of caffeine in newly launched energy drinks using the High Performance Thin Layer Chromatography (HPTLC). Qualitative and Quantitative analysis using Camag HPTLC system using precoated silica plate has been carried out against reference caffeine. Efforts have been devoted to establish co-relation of caffeine content in energy drinks with the frustration tolerance among the students of same age group, sex and economical status. Frustrations causing psycho motive puzzles were given to the students for co-relating caffeine-frustration relationship. Peak of caffeine was identified at 275 nm, using solvent system [EtOH + EtOAc: 1:9] with the R_f value of 0.13. Caffeine content was found to be in the range of 512-840 ng/spot in energy drinks under study. Single group repeated measures designed for twenty subjects (ANOVA test); indicate increase in unit dose (100mg) of caffeine results into statistically significant increase in the frustration tolerance. However, increase in caffeine dose (>300 mg), showed no further increase in the frustration tolerance of the subjects. Energy drinks selected for the study were found to be safe and contain caffeine within prescribed WHO limit.

P-3

SYNTHESIS OF ARYL PIPERAZINE DERIVED DPP-IV INHIBITORS

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Inhibition of dipeptidyl peptidase IV (DPP-4) is a promising new approach for the treatment of type 2 diabetes. DPP-4 is the enzyme responsible for inactivating the incretin hormones glucagon-like peptide 1 (GLP-1) and glucose dependent insulinotropic polypeptide (GIP), two hormones that play important roles in glucose homeostasis. The potent, orally bioavailable and highly selective small molecule DPP-4 inhibitors sitagliptin (piperazine derivative) and saxagliptin have been approved by the FDA as novel drug for the treatment of type 2 diabetes. So DPP-IV inhibitors have emerged as potential new type of antidiabetic agents free of side effects such as hypoglycemia and exhaustion of pancreatic β-cells. Several DPP-IV inhibitors are currently being evaluated in human clinical trials including alogliptin, dutagliptin and PF-00734200 (piperazine derivative).

In several studies, it has been found that conformationally restricted DPP-IV inhibitors are more potent than their flexible structures. DPP-IV inhibitors having (S)-2-cyanopyrroldine moiety at P1 position are chemically unstable due to intramolecular cyclization between amine group and their electrophilic nitrile. Thus proline mimetics (Thiazolidine, pyrrolidine, piperidine, and morpholine) placed at P1 position provides chemical stability to DPP-IV inhibitors [1], [2]. Therefore, to find potent and selective DPP-IV inhibitors we have synthesized the constrained aryl piperazine derivatives with proline mimetics in which piperazine structure provides natural constraint. They may be potent DPP-IV inhibitors. The details of the study will be presented.

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P-4

Protein-Binding Vesicle: Asymmetry/Cooperativity

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Electrostatics role is studied in cationic protein adsorption to zwitterionic phosphatidylcholine (PC) and anionic mixed PC/phosphatidylglycerol (PG) small unilamellar vesicles (SUVs) [1]. Protein interaction is monitored vs. PG content at low ionic strength [2]. The adsorption of lysozyme–myoglobin–bovine serum albumin (BSA) (isoelectric point, p*I* 5–11) is investigated in SUVs, along with changes of the fluorescence emission spectra of the proteins, via their adsorption on SUVs [3]. The partition coefficients and cooperativity parameters are calculated [4]. At p*I* the amount of binding obtains the maximum, while at lower and higher p*Hs* the binding is significantly decreased [5]. In Gouy–Chapman formalism activity coefficient goes with square charge number. Deviations from ideal model indicate the asymmetric location of anionic phospholipid in bilayer inner leaflet, in mixed zwitterionic/anionic SUVs for both lysozyme– and myoglobin–PC/PG systems, in agreement with experiments–molecular dynamics simulations. SUVs bind myoglobin anti-cooperatively while lysozyme–BSA cooperativitivey. Apparently the structures of the attached lysozyme–BSA layer on protein–SUVs play a significant role. A model for both proteins, which composes two protein sub-layers with different structures–properties, is proposed. Hill coefficient reflects subunit cooperativity of bi/tridomain proteins. Further protein binding is difficult because the repulsion of like charges becomes dominant. In terms of conventional binding mechanisms this would correspond to a negative cooperativity. Lysozyme–albumin binding to SUVs follow a model of positive cooperativity, representing the interaction between the protein considered as a dipole moment and the anionic phospholipid headgroups.

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P-5

Synthesis and antimalarial evaluation of 4-aminoquinoline-triazine and aminoquinoline-triazole conjugates.

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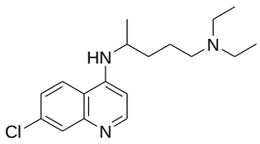
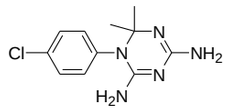
Malaria is one of the most deadly parasitic infection affecting millions of people worldwide especially in Africa and Asia. It has been estimated that approximately 250 million people worldwide are affected by malaria and around 2-3 million deaths occur every year due to malaria (8% of all deaths) [1]. 4-Aminoquinolines such as chloroquine, hydroxychloroquine, amodiaquine and triazines like cycloguanil are long been used as antimalarial drugs for the treatment of malaria. But due to the development of drug-resistant *Plasmodium* strains, the control of malaria in most part of the world has become a challenging problem. Hence the search and development of new antimalarial agents has always found considerable interest.

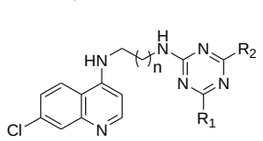


chloroquine



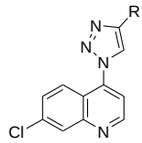
cycloguanil

As a part of our ongoing research on malaria [2-5], we have synthesized a series of 4-aminoquinoline-triazine (**1**) and aminoquinoline-triazole (**2** and **3**) conjugates and evaluated their antimalarial activity against D6 (chloroquine-sensitive) and W2 (chloroquine-resistant) strains of *Plasmodium falciparum.* Some of the tested compounds have shown potent antimalarial activity compared to chloroquine [6].

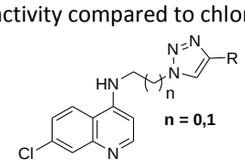


1

n = 0-3,5,7
R_1, R_2 = different primary and secondary amines



2



3

n = 0,1

R = different aromatic and aliphatic groups

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P-6

Metronidazole-triazole conjugates as antibacterial and antiamoebic agents

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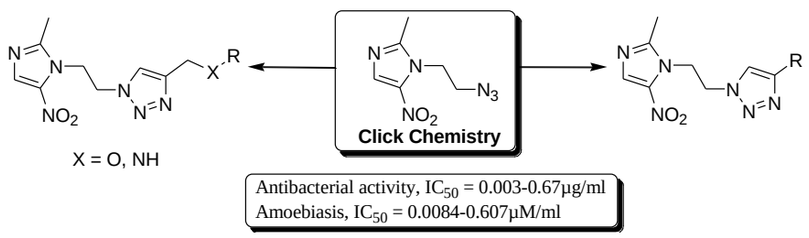
Metronidazole, (MTZ, 1-[2-hydroxyethyl]-2-methyl-5-nitroimidazole) has been a drug of choice for the treatment of anti-infectious diseases against protozoa such as Trichomonas Vaginalis, Entamoeba histolytica, Giardia intestinalis, and infections caused by Gram-negative anaerobes such as bacteroides and Gram-positive anaerobes such as clostridia[1]. However, resistance to these compounds have been demonstrated in trichomonads and *Bacteroides fragilis*, in both natural and *in vitro* under drug pressure-induced populations. We anticipated that hybrid molecule that contains metronidazole and triazoles, one of the most active and widely studied pharmacophore [2-3] will lead to a molecule of biomedical importance.

Metronidazole-triazole conjugates were synthesized and their antibacterial and antiamoebic activities were studied [4-5]. In order to study the role of different substituent on biological activity, variation in substitution pattern was done in the triazole ring. These compounds showed potent to weak antibacterial activity against Gram-positive and Gram-negative bacteria. Six compounds showed equal or better activity than the reference compound with IC_{50} value from 0.003 to 0.67 µg/ml. Some of these compounds were also screened *in vitro* antiamoebic activity and eight compounds (IC_{50}= 0.0084 to 0.607 µM/ml) were found to be more potent then metronidazole which is currently used for the treatment of amoebiasis [6]. No haemolysis was observed up to 1000 µg/ml concentration.



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P-7

Tetraoxane: Future Prospective Drug: Design, Synthesis, Characterisation and Antimalarial Activity of the Tetraoxane based Compounds

Nitin KumarError! Bookmark not defined.,[1] H. Atheaya,[1] **Mukul Sharma**,[1] Shabana I. Khan[2] and Dr. Diwan S. Rawat[1]

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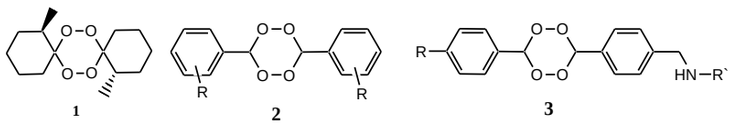
Malaria is still one of the deadly diseases causing deaths of more than 1-3 million people per year all over the world. Since last two decades endoperoxides have attracted the attention of chemist and biologist due to their potent antimalarial activity [1]. Artimisinin and its semisynthetic derivatives shows good antimalarial activity against chloroquine-resistant strain of *Plasmodium falciparum.* Structure activity relationship study revealed that presence of peroxide linkage is a crucial pharmacophore for the antimalarial activity.[2,3]. Dispiro-tetraoxane is one of such class of compounds which was found to be equally potent as artemisinin [4]. However, the structural diversity of this important class of compounds is not available [5]. To this end, synthesis, characterization, x-ray crystal structure, antimalarial activity and cytotoxicity of symmetrically and asymmetrically substituted tetraoxanes (**2,3**) will be presented [6-10].



1 2 3

P. falciparum (D6 Clone); IC_{50} = 0.35 - 13.90 µM

P. falciparum (W2 Clone); IC_{50} = 0.45 - 9.34 µM

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P-8

Interaction Studies of Novel Cell Selective Amphipathic Antimicrobial Peptides Using Microscopic Techniques

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Cationic antimicrobial peptides (CAMPs) with broad range of activity and novel mode of action represent their candidature as future therapeutics against multidrug resistant bacterial strains [1-4]. In the present study six cationic peptides were designed using Schiffer-Edmundson projection diagram. Amino acid residues occurring most frequently in the sequences of CAMPs including ornithine as representative of non gene encoded amino acid were included in the sequences of designed peptides. Keeping length (12) and charge (+5) of the peptide constant, changes were done in the hydrophobic segment of the amphipathic sequence using amino acids such as proline, tryptophan and Ornithine. Designed peptides were found to be active in the concentration range of 1-64 µg/ml against susceptible as well as multi drug resistant bacterial strains. With the exception of peptide SA-1 all peptides were found to be non hemolytic up to 512 µg/ml. Designed peptides were found to affect bacterial killing within minutes after incubation with peptides at concentrations higher than MIC. Although precise mode of action of CAMPs has not been deciphered as yet, it is believed that CAMPs target bacterial membrane as the major site of action [5, 6].To have an insight into the mode of action of the designed peptides, biophysical studies including CD, Tryptophan fluorescence and calcein dye leakage were performed using LUVs composed of phospholipid membranes. Microscopic techniques including SEM, TEM and confocal scanning microscopy studies using *E. coli* and SUVs composed of bacterial mimic membrane gave visual evidences of morphological alteration caused by peptides over the surface of bacterial membrane. Out of the six peptides studied, peptides SA-3 and SA-4 were found to be potent with negligible hemolytic activity. With the potential to combat multi drug resistant bacterial strains, peptides designed in the present study can be further optimized for use in clinics.

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P-9

Design And Synthesis Of Gallic Acid Based Molecules As Anticancer Agents

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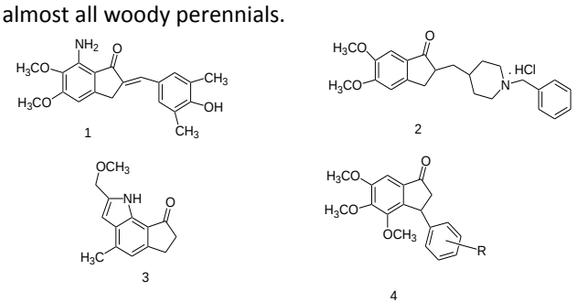
Indanones and related compounds are important bioactive molecules. These compounds have been studied for various biological activities including cancer and Alzheimer's type of diseases. Indanones are also used as drug intermediates, ligands of olefinic polymerisation catalysts [Schumann et al. and Herzog et al.] and discotic liquid crystals [Sato et al.]. Indanocine (**1**) and its analogues are being developed to combat drug resistant malignancies [Leoni et al.]. Another indanone analogue Donepezil hydrochloride (**2**) has been approved by US-FDA for the treatment of mild to moderate Alzheimer's disease. This drug acts as an AChE (Acetylcholinesterase) inhibitor [Sugimoto et al.]. Dilemmaone A (**3**) [Beukes et al.] and some other indanones have been isolated from natural products. Being such a useful moiety, several synthetic strategies have also been developed for their synthesis. Gallic acid, a plant phenolic acid is present as hydrolysable tannins in almost all woody perennials.



[Structures of Indanocine (**1**), Donepezil hydrochloride (**2**), Dilemmaone A (**3**) and gallic acid based indanone (**4**)].

The modified gallic acid moiety i.e. a 3, 4, 5-trimethoxy phenyl unit has been established as an essential structural requirement for several anticancer leads [Srivastava et al.] like Combretastatin A4, Podophyllotoxin, Colchicine etc. In the present communication, gallic acid based indanone derivatives **(4)** have been synthesized and evaluated for their anticancer activity. Some of the indanone molecules showed very good anticancer activity in MTT assay. All the compounds showing potent anticancer activity were further evaluated for toxicity to human erythrocytes by performing erythrocyte fragility test.

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P-10

An Improved Process to Isolate Camptothecin From *Nothapodytes Foetida*

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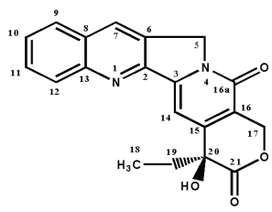
Camptothecin is one of the most significant anticancer molecule due to its property to block the topoisomerase (Topo-I), a DNA replication enzyme, by stopping cell division. This compound was originally isolated from Camptotheca acuminata by Prof Wall et al [1].

Camptothecin was isolated from the plant *Nothapodytes foetida* (*Mappia foetida*) Miers (Icacinaceae) in India. It is a small tree mainly found in Western Ghats. Govindachari et al [2] reported the isolation of Camptothecin from the plant. There are various reports in the literature on extraction, fractionation, isolation and precipitation of Camptothecin, but none of the method is found to be effective due to poor yield, time consuming, requirement of more solvent etc.



CAMPTOTHECIN

The improved process for the isolation of Camptothecin not only avoids the use of tedious and time consuming extraction and purification methods, but also increases the yield of the compound.

Dried and powdered *N.foetida* plant was hot extracted with Methanol under continuous stirring. The solvent was removed in vacuum to obtain crude extract, which was defatted cold with Hexane. The defatted material was treated with Dichloromethane in order to obtain the soluble portion. The dried Dichloromethane fraction was then precipitated with a mixture of Acetonotrile and Dichloromethane to get pure Camptothecin.

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P-11

Hepatoprotective Effect of L-ornithine Hydrochloride in D-galactosamine Induced Hepatotoxicity in Wistar Rats

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L-ornithine, a non essential amino acid and constituent of L-Ornithine-L-aspartate which is a known hepatoprotective agent [1]. It aids in the disposal of excess nitrogen in the body and supports insulin and growth hormone in the body. It also demonstrates putative anabolic and imunomodulatory activities.

The aim of this study was to evaluate the hepatoprotective effect of L-ornithine HCl in D-galactosamine induced hepatotoxicity in Wistar rats. D-galactosamine causes liver cirrhosis whose pattern is similar like viral hepatitis[2].

Animals were divided in to five groups with six animals in each group. First group was sham control without any treatment, second was D-galactosamine control (400 mg/kg, i.p), third group was given a treatment of L-ornithine-L-aspartate (50mg/kg), fourth and fifth groups were treated with L-ornitine HCl with two different dose (50 mg/kg and 100 mg/kg respectively). L-ornithine L-aspartate (LOLA) was used as standard at 50mg/kg. D-galactosamine was given orally on 7th day. On 8th day blood was withdrawn,

serum was separated and analysis of enzyme parameters like AST, ALT, ALP and total bilirubin was performed. Liver was dissected out for histopathology.
Level of serum parameters were elevated in D-galactosamine treated group which was significantly reversed by L-ornithine HCl treatment. All the parameters showed significant decrease at $p<0.05$. Histologically also, L-ornithine HCl was able to prevent D-galactosamine induced damage to the hepatocytes which was comparable to L-ornithine- L-aspartate.

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P-12

Ethanol extract of *Lepidum sativum* prevents the bone loss induced by overactomy in experimental animals

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Lepidum sativum is a small herbaceous plant that has been traditionally used in the treatment of asthma, rheumatism and bleeding piles [1]. Its seeds contain phytoconstituents like β-sitostearol, α-tocopherol etc., which have been hypothesized to have beneficial effects on osteoporosis. Our study involved to evaluate the effect of ethanol extract of seeds of *L. sativum* on ovariectomized rat model [2]. Swiss albino female rats were divided into five groups of six animals each. All the animals except in group I (Sham served as normal control) were ovariectomized by bilateral incision. Group II served as ovariectomized control and received only vehicle. Groups III, IV and V were treated with Raloxifen (5.4 mg/kg), Ethanol extract at two dose levels 250 and 500 mg/kg respectively for 90 days starting from 9th day of ovariectomy. The efficacy was assessed by the estimation of biochemical markers like serum alkaline phosphatase, calcium, phosphorous and urine hydroxyl proline; biomechanical parameters like three point bending, compression of IV lumbar vertebra and load testing of femoral head; and histopathological changes in the bone matrix. All the assessed parameter showed a definite and dose dependant effect on bone mineralization after treatment with ethanol extract.

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P-13

A Concise Synthesis Of 1,4-Benzodiazipines Fused With 1,4-Naphthoquinone

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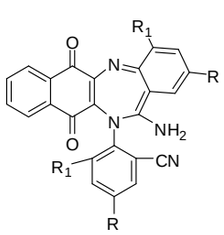
A general and concise practical method of synthesizing 1,4-benzodiazepines fused with 1,4-naphthoquinone nucleus in one pot from 2,3-dichloro-1,4-naphthoquinone has been developed. This method tolerates a variety of alkyl/aryl amines and gives 12,13-disubstituted 1,4-benzodiazepines **1** and **2** in good to excellent yields.



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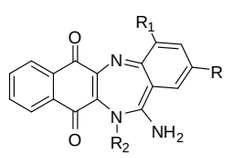

2

P-14

Synthesis And Biological Evolution Of Novel Nitrogen And Sulfur Containing Hetero 1, 4-Naphthoquinones As Potent Antifungal And Antibacterial Agents

Manoj K. Verma,[a] Hardesh K. Maurya,[a] Nripendra N. Mishra,[b] Praveen K. Shukla[b] and Vishnu K. Tandon[a,*]

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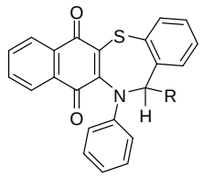
Novel hetero-1, 4-naphthoquinones (**1**) have been synthesized and evaluated for their antifungal and antibacterial activity.



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P-15

On Water" Assisted Nucleophilic Substitution Reaction: Synthesis Of Novel Naphthothiazine-5,10-Dione As Potent Antifunagal And Antibacterial Agents

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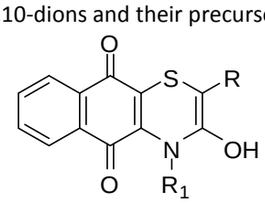
The amino and thioether derivatives of naphthoquinones are a component of molecular frame work of several biologically active compounds. These compounds have been found to possess marked antitrypanosomal, antiviral, antiplatelet, antiallergic, antineoplastic, antimalarial, antiinflammatory, antibacterial, antifungal, antiproliferative, cytotoxic, antitumor, and anticancer activities. These applications have motivated us to develop a green methodology to synthesize medicinally important novel hetero quinone derivatives using water as an economic solvent having environmental safety and societal implications and Unique nucleophilic substitution and addition reactions of 1,4-quinones in aqueous suspension as well as in organic solvents are studied for synthesis of potent antifungal and antibacterial agents naphthothiazine-5,10-dions and their precursors.



P-16

Synthesis and Antibacterial Evaluation of Novel 8-Fluoro Norfloxacin Derivatives with morpholine and Substituted Piperazines at C-7 as Potential Probes for methicillin-resistant and vancomycin-resistant *Staphylococcus aureus*

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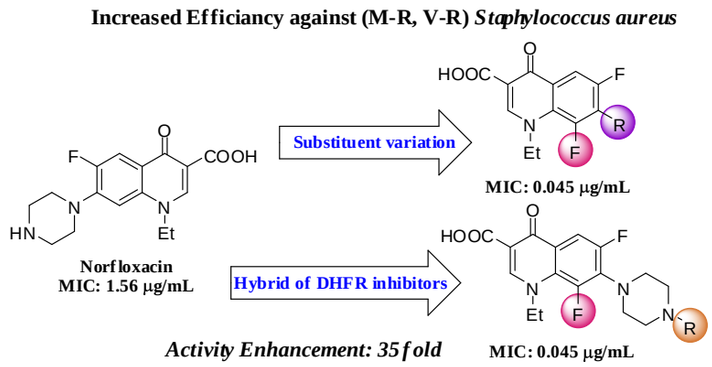
During 1980s, the introduction of norfloxacin the first fluoroquinolone, and later on, the discovery of other fluoroquinolones like ciproploxacin, sparfloxacin and trovafloxacin have changed the landscape of antibacterial chemotherapy.[1, 2] The rapid emergence of drug resistance pathogens like, penicillin-resistant *Streptococcus pneumoniae,* vancomycin-resistant *Enterococci*, methicillin-resistant *Staphylococcus aureus* and multi-resistant *Salmonellae* have now become a serious public health problem.[3] To develop new effective antibacterials that may work out in increasing the efficacy against resistant bacteria, first we evaluated the antibacterial activity of certain novel norfloxacin derivatives (**I**) with an additional functional moiety like fluorine atom at C-8 position and ethyl-4-(trifluoromethyl)benzene at N-1 position (to provide extra hydrogen bonding capacities with the DNA gyrase), against methicillin-resistant *S. aureus* (MRSA), methicillin-resistant and vancomycin-resistant *S. aureus* (VRSA) and Gram-negative bacteria *Klebsiella pneumoniae*. After that aiming them towards multiple targets, a series of hybrids (**II**) of above norfloxacin derivatives with DHFR inhibitors like 1,3,5-triazines and pyrimidines was designed, synthesized and were tested against above mentioned resistant strains. This approach made us successful in identifying the new substitutes for piperazine, like Morpholine, *N*-methyl/phenyl/benzyl/pyrimidinyl piperazines and *n*-butylamine at C-7 position of fluoroquinolones for the development of future antibacterial agents.



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P-17

Design and synthesis of Coruscanone A mimics as new antifungal agents

Vikas Tyagi[a], Ravi Kumar[a], Shahnawaz Khan[a], P. K. Shukla[b], Prem M. S. Chauhan[a]*

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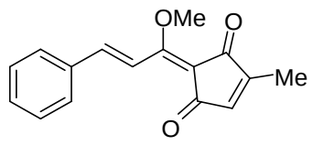
Fungal infections are still the most serious threats to immunocompromised patients. Currently available drugs for treatment of fungal infections are limited. [1] Couscanone A, a plant derived cyclopentenedione derivative, was isolated from the ethanolic extract of Peruvian plant, *Piper coruscans* showed potent in vitro antifungal activity against *candida albicans* (IC_{50}<2ug/ml).[2,3] In our effort towards discovery of novel antifungal agents, a series of coruscanone A mimics having 2-thiohydantoin moiety in place of cyclopentendione ring have been synthesized and evaluated for their antifungal activity.



Coruscanone A

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P-18

Isonaamine C and its analogues: Development of an expeditious, highly versatile, protecting group free synthesis and discovery of their antileishmanial potential

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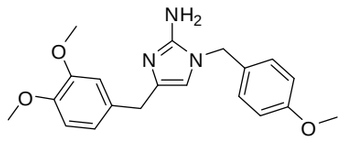
Marine sponges are still the main source of bioactive natural products.[1] Since the late 1980's, several marine alkaloids possessing 2-aminoimidazole moiety have been isolated from the genus *Leucetta* and many of them demonstrated interesting biological activities.[2] One such secondary metabolite Isonaamine C (**1**) was isolated from *L. Chagosensis* collected from Australian Bougainville Reef, which showed cytotoxicity against HM02, HepG2, Huh7 tumour cell lines with GI_{50} values of 5.3, 2.2, 2.1 µg/ml respectively.[3] To investigate the antileishmanial potential, a series of nine Isonaamine C derivatives, corresponding thiohydantoins, imidazolinones have been synthesized and screened against *Leishmania donovani*.



Isonaamine C (**1**)

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P-19

$SnCl_2.2H_2O$: An efficient reagent for direct conversion of 2-thiohydantoins to corresponding hydantoins

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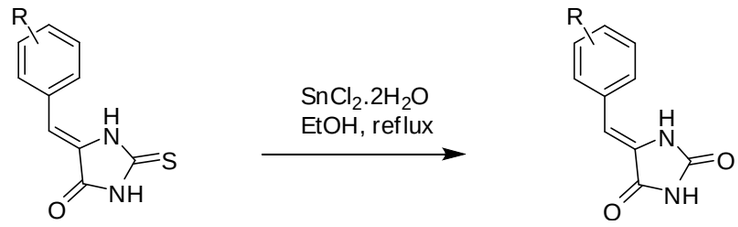
Thiohydantoins, hydantoins and their derivatives represent an important class of biologically active molecules that have broad medicinal [1-4] and agrochemical [5] (herbicidal and fungicidal) applications. Classical methods involves refluxing of 2-thiohydantoins in aqueous mineral acids for conversion to their corresponding hydantoins, [6] which may not be applicable in many cases involving acid sensitive functional groups. Herein, we report discovery of an efficient reagent $SnCl_2.2H_2O$ for the synthesis of hydantoins from 2-thiohydantoins.



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P-20

Synthesis of Chloroquine-Aplysinopsin Hybrids as Novel Antimalarial Agents

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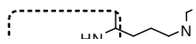
At the border between bio-inspired and rational drug design, one can imagine preparation of hybrid molecules with a dual mode of action to create efficient new drugs. Hybrid molecules are defined as chemical entities with two or more structural domains having different biological functions and dual activity.[1] Aplysinopsin has recently been discovered as a potential antimalarial agent.[2] As a part of our ongoing research devoted for the synthesis of diverse hybrid heterocycles of chloroquine with immense success against resistant strain of *Plasmodium falciparum*, a series of hybrid molecules containing chloroquine and aplysinopsin has been prepared and evaluated for its antimalarial activity.



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P-21

Designing and synthesis of Pentamidine-Aplysinopsin hybrid molecules as antileishmanial agents

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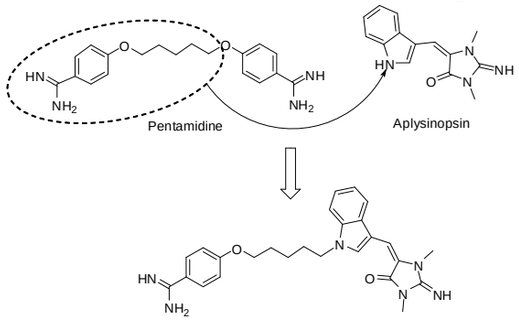
Leishmaniasis is a growing health problem in many parts of the world, with about 350 million people living in areas of disease endemicity and about 2 million new cases each year. Leishmaniasis is a vector born parasitic disease of the tropics and subtropics which is manifested in four major clinical forms (cutaneous leishmaniasis, mucocutaneous leishmaniasis, visceral leishmaniasis, and post kala-azar dermal leishmaniasis or PKDLa) depending on the causative species of the protozoan. Among all above, visceral leishmaniasis is lethal, if left untreated.

Pentamidine(dicationic class of molecules in general) is a second line drug for visceral leishmaniasis. In spite of some side effects of pentamidine, it has broad range of its biological activities[1,2] and relatively low propensity towards the development of resistance. Aplysinopsin, a class of natural products possessing cyclic guanidine function[3], acts on similar biological targets (plasmepsin II and serotonin receptors) as a dicationic class of molecules[4]. On the basis of above observations we designed a hybrid molecule where one amidinophenoxy function of pentamidine has been replaced with aplysinopsin and synthesized its analogues and discovered a new class of antileishmanial agents.



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P-22

Design, synthesis and antimalarial activity of the hybrid triazine thiosemicarbazones

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Dihydrofolate reductase (DHFR) plays an essential role in cellular biochemistry and has been a well-recognized drug target of antimalarial antifolates namely pyrimethamine and cycloguanil for half a century [1]. Malaria parasite *Plasmodium falciparum* required a network of cysteine and aspartyl proteases for the degradation of host protein (Haemoglobin)[2], further to inhibit these parasite

proteases, molecule of hydrazide and thiosemicarbazone[3] family have been identified through computational screens and validated through *in vitro* and *in vivo* screenings [4,5]. Resistance of *Plasmodium falciparum* (*Pf*) to antifolates is an important problem in antimalarial chemotherapy and has been shown to be associated with mutations in the dihydrofolate reductase (DHFR) domain of the bifunctional dihydrofolate reductase-thymidylate synthase (DHFR-TS)[6].

Therefore to circumvent the emerging threat of resistant malaria, here we design the hybrid molecule with two dimensional intrinsic potency by extrapolating the lead of these targets or hits which may be a viable option at this intersection.

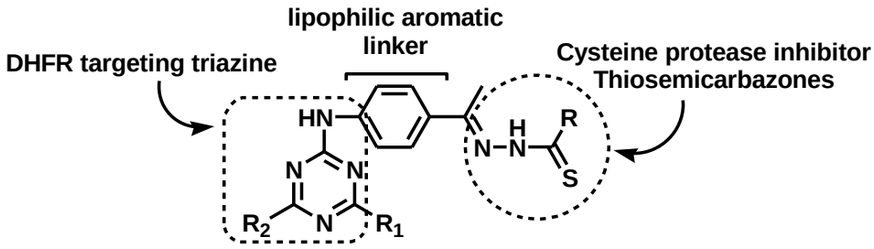

Fig. Hybrid of Triazine and thiosemicarbazone

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P-23

Synthesis and antimalarial activity of Hybrid 4-aminoquinoline triazine derivatives

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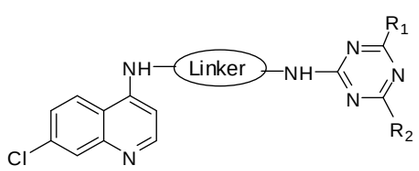
Malaria is by far the most important tropical parasitic disease, and it kills more people than any other communicable disease except tuberculosis[1]. The causal agent of the most lethal form of malaria, *Plasmodium falciparum*, has developed resistance to a multitude of drugs including the efficacious, safe and cheap drug chloroquine. This development of resistance has in part been responsible for the global rise of malaria[2]. Designing hybrid drugs with multiple effects is a common strategy in today's search for new treatment of malaria[3]. CQ and other structurally related antimalarials exert their effect by binding to heme molecules released from the hemoglobin that is digested by malaria parasites[4] on the other hand Triazine derivatives, are potent DHFR inhibitors have been reported to possess antimalarial activity[5] .

With the aim of generating antimalarials based on novel pharmacophores, we hybridized the heme interacting 4-aminoquinoline moiety of CQ with triazine (DHFR inhibitor) systems to overcome the resistance against chloroquine.

7. 

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P-24

Synthesis of novel tetracyclic lactones from 1- Naphthoxepines

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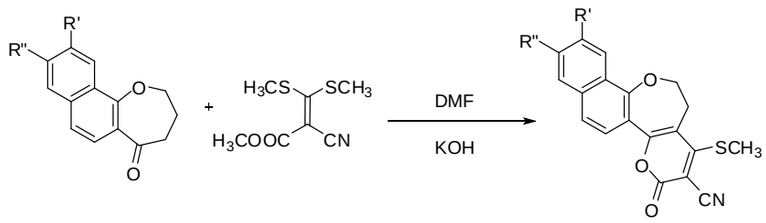
1-Naphthoxepines react with in presence of thio acital (methyl 2-cyano-3,3-bis(methylthio)acrylate) to form tetracyclic Lactones. The derivatives synthesized will be discussed.



P-25

Alum: An efficient catalyst for one-pot synthesis of α-aminophosphonates

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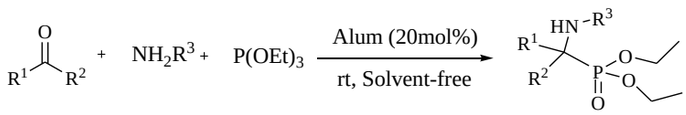
Alum ($KAl(SO_4)_2{\cdot}12H_2O$) is an inexpensive, efficient, non-toxic and mild catalyst for the one-pot synthesis of α-aminophosphonates. A three component reaction of an aldehyde/ketone, an amine and triethyl phosphite was carried out under solvent-free conditions to afford the corresponding α-aminophosphonates in short reaction times and high yields with the green aspects by avoiding toxic catalysts and solvents.



P-26

Synthesis and in vitro antimicrobial activity of new ethyl 2-(ethoxyphosphono)-1-cyano-2-(substituted tetrazolo[1,5-a]quinolin-4-yl)ethanoate derivatives

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A series of new ethyl 2-(ethoxyphosphono)-1-cyano-2-(substituted tetrazolo[1,5-a]quinolin-4-yl)ethanoate derivatives have been synthesized for the first time of tetrazolo [1,5-a] quinoline derivatives. Elemental analysis, IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and mass spectral data elucidated the structures of the all newly synthesized compounds. *In vitro* antimicrobial activities of synthesized compounds have been investigated against Gram-positive *Bacillus subtilis*, Gram-negative *Escherichia coli* and two fungi *Candida albicans* and *Aspergillus niger* in comparison with standard drugs. Significantly microbiological behavior of these newly synthesized derivatives possesses significant antibacterial and antifungal activity.

P-27

Synthesis of bis(indolyl) methanes using aluminium oxide(acidic) in dry media

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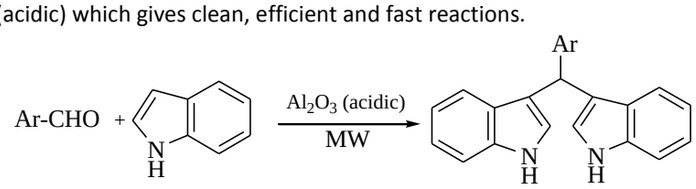
Heterogeneous catalyst aluminum oxide (acidic) is found to be an effective catalyst for the solvent-free condensation reaction of indole with aldehydes in microwave irradiation with shorter reaction time and higher yields. The role of aluminium oxide as a heterogeneous catalyst on several organic reactions, such as oxidation, reduction and displacement reactions is known from the previous work of Posner. Keeping all these facts in mind, we go for synthesis of bis(indolyl) methanes using heterogeneous catalyst aluminum oxide (acidic) which gives clean, efficient and fast reactions.



P-28

A new protocol for one-pot three-component synthesis of amidoalkyl naphthols in acidic ionic liquid

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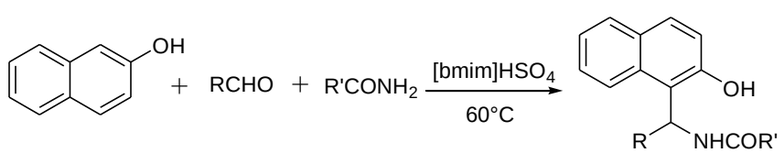
An efficient and easy method for one-pot three-component synthesis of amidoalkyl naphthols by the condensation of aromatic/heteroaromatic/aliphatic aldehydes, 2-naphthol and amides or urea under thermal condition at 60 °C in the presence of acidic ionic liquid 1-butyl-3-methylimidazolium hydrogen sulphate ([bmim]HSO_4) has been described. The operational simplicity of the procedure, shorter reaction time, cost effective recovery and reusability of ionic liquid make this method much attractive.



P-29

Chamomile: A New Hope Against Wide Range Of Cancers

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German Chamomile (*Matricaria chamomilla*), is one of the most popular medicinal herbs of the western world. This plant is known for centuries for its therapeutic values against the variety of human ailments. Due to Its excellent antioxidant properties, its standardized extracts are also available in the market claiming to have ~1.2% bioactive apigenin. Antioxidant, anti-inflammatory and mild sedative properties of chamomile are well documented but the plant has not been evaluated before for anticancer properties. We assessed the anticancer properties of chamomile against variety of human cancer cell lines. Methanolic extract was prepared, sterilized and applied in cell culture studies. Treatment with methanolic extract resulted in significant decrease in cell viability of various cancer cell lines *viz*. LNCaP, PC-3 and DU145 (prostate carcinoma); HeLa (cervical adenocarcinoma); RKO (colon carcinoma); HT 1080 (fibrosarcoma) and T47D (breast carcinoma). The IC_{50} values evaluated after 72 h of exposure ranges from 100-200 g/ml in various prostate cancer cell lines. Similar effects were observed in other cancer cell lines. Chamomile treatment also resulted in induction of apoptosis in prostate cancer cells whereas minimal growth inhibitory responses were observed in normal counterparts at similar doses. HPLC analysis confirmed that the extract contains 50-60% apigenin-7-O-glucoside along with 1-1.2% free apigenin amongst the total polyphenolic contents. In bio-phase the break down of glucoside moiety releasing bioactive apigenin was demonstrated. Pharmacokinetic and toxicity evaluation were also conducted in albino mouse . The LD_{50} for chamomile in single dose administration in these animals was determined as15g/kg body weight. Per oral administration of 50 mg/mouse chamomile extract exhibited the presence of apigenin-7-O-glucoside as early as 3 h in the plasma which peaked at 24 h post-administration. Apigenin-7-O-glucoside was detected in the liver, intestine and kidneys as early as 24 h post administration and was traced up to 48 h in the liver and intestine. Additional, long term administration of chamomile extract (10mg/mouse for 10 weeks) did not exhibited any apparent signs of toxicity or histopathological changes in the liver, kidney or spleen in these mice. Taken together, the abundance of plant availability, with promising anticancer efficacy against wide range of cancer cells , along with minimal toxicity prompted us to move forward with the developmental work to establish chamomile as an anticancer agent.

P-30

Synthesis And Biological Activities Of Novel Nalidixic Acid Based Hydrazones

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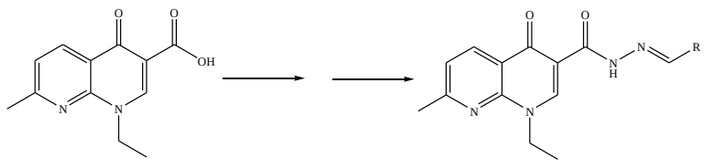
Nalidixic acid (1,8-naphthyridine derivative) is a quinolone antibacterial agent for oral administration. It inhibits DNA gyrase (topoisomerase II), an enzyme involved in uncoiling super coiled DNA which leads to rapid cell death (1). The nalidixic acid hydrazide and its quinazolone derivatives have been found to be potential antibacterial and antifungal agents against fourteen clinically isolated microbial strains as compared to parent nalidixic acid (2). To explore the bio potential of nalidixic acid derivatives, thirty one substituted hydrazones of nalidixic acid hydrazide were synthesized and characterized by spectral techniques. These compounds were evaluated for various biological activities namely antifungal, insecticidal and nitrification inhibition. The antifungal activity was evaluated against five pathogenic fungi namely, *Rhizoctonia bataticola, Sclerotium rolfsii, Rhizoctonia solani, Fusarium oxysporium, Alternaria porii.* The above compounds were able to inhibit the growth of *A. porii* (ED_{50} value in the range from 34.23-133.81 µg/mL). The activity was comparable to commercial fungicide, hexaconazole (ED_{50} value-25.45 µg/mL). These compounds were also screened for insecticidal activity against third instar larvae stage of *Spodoptera litura* (field insect) and adults of *Callsobruchus analis* and *Tribollium castaneum* (storage insect). Most of them were found to be potent insecticidal agents at 0.1% dose against *S. litura*

through feeding method with mortality range of 70-100%. Therefore, these molecules hold promise for further detailed bioefficacy study especially against insect pest.



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P-31

In-Vitro Evaluation Of Total Reducing Property Of The Synthesized Molecule Having Variable Atomic Electronegativity

Kiran Manubhai Patel*, Hardik Arvindbhai Patel, Dhrubo Jyoti Sen, Bibhuranjan B. Panigrahi and R. Badmanaban

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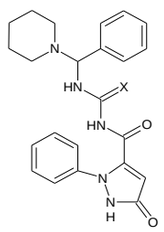
Three different compounds have been synthesized by keeping X as variable: X=O/S/NH for Compound-A/Compound-B/Compound-C respectively. Electronegativity of oxygen for urea X:O=3.5 and of sulfur for thiourea X:S=2.4 and of nitrogen+hydrogen for guanidine X:NH=3.1+2.2=5.3. So the X=NH shows the maximum electronegativity with combined effect of electronegativity of nitrogen and hydrogen, whereas X=O has two lone pairs and X=S has also two pair of electrons, but in case of NH moiety the electronegativity of nitrogen and hydrogen exceeds the electronegativity of oxygen and sulfur:

NH (5.3) > O (3.5) > S (2.4).

X=O: Urea, X=S: Thiourea, X=NH: Guanidir



The spectral data for the absorption for the three compounds was compared with gallic acid for the plot was calculated by the equation: y=0.022x-0.1458 (R^2=0.982) and found that the antioxidant property of the compounds have the mentioned profle: **Compound-C>Compound-B>Compound-A**. Compound-C is guanidine moiety having X=NH so according to the highest electronegativity profile this is more potent than other two when compared with the total reducing capacity property. (Compound-A: 272.8µg, Compound-B:317µg, Compound-C:384.9µg) It was expressed as GAE means that reducing power of 10mg of each compound is equivalent to reducing power of µg of gallic acid or expressed as µgGAE/mg of compound.

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P-32

RAS: New Targets in Cancer Research

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The identification of intracellular signalling cascades important for the growth and survival of cancer cells has led to the development of targeted cancer therapeutics aimed at blocking these signals[1].One of the most frequently detected genetic alterations in cancer is in the ras oncogene family, which plays a pivotal role in the control of both normal and transformed cell growth. Ras genes were first identified in the 1960s as homologues to the viral oncogenes of transforming retroviruses. This gene family includes N-ras (neuroblastoma cell line), H-ras (Harvey murine sarcoma virus), and the alternatively spliced K-ras (Kirsten murine sarcoma virus), which is the type of ras most frequently activated in human cancers. Advances in our understanding of the basic molecular mechanisms underlying cell signaling have led to the identification of key pathways, such as the Ras-Raf-MEK-ERK (ERK) pathway which plays a critical role in many aspects of tumorigenesis. Novel anticancer agents targeting this signaling pathway are currently being evaluated and may prove to be more effective and less toxic than conventional cytotoxic therapies[2].The RAS proteins control signalling pathways that are key regulators of several aspects of normal cell growth and malignant transformation. They are aberrant in most human tumours due to activating mutations in the RAS genes themselves or to alterations in upstream or downstream signalling components. Rational therapies that target the RAS pathways might inhibit tumour growth, survival and spread. Several of these new therapeutic agents are showing promise in the clinic and many more are being developed[3].

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P-33

Lewis Acid Mediated Synthesis Of Some Biologically Active Pregnane Derivatives.

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The origin and development of modern and traditional medicine is fascinating. Indeed human progress and development of modern medicine are inseparable. In recent years there has been a resurgence of interest in the chemistry and biochemistry of natural as well as synthetic steroids and amongst them particularly of C-21 steroids commonly called pregnanes. With an objective of synthesizing model compounds belonging to this group, diosgenin, easily obtainable from plant source was converted to 16-dehydropregnenolone acetate (16-DPA) which was subsequently converted to it hydroxy derivative. Novel and convenient method/s were adopted for the introduction of groups like neopentyl glycol, 1,5-pentanediol, 2-butene-1,4-diol, o-bromoaniline and m-bromoaniline in the presence of boron trifluoride etherate. Through these C-16 substituted derivatives, introduction of hydroxyl and amino groups at C-20 position of the steroidal chain is also in our proposed scheme.

Steroidal oximino ether derivatives are medicinally important and very important and have clinically been used for the treatment of breast cancer in women. A novel steroidal oximino ether derivative was synthesized by introduction of 1,6-dibromoderivative at C-20 position.

Conjugation of these biologically active pregnane derivatives with different sugars and then evaluating these glycosides as potential anti-oxidant and anti-dyslipidemic agents is the major goal or our research programme.

P-34

The influence of ionic liquids on the folding and activity of α-chymotrypsin

Pankaj AttriError! Bookmark not defined., **P. Madhu Sudhan Reddy**, Awanish Kumar and P. Venkatesu*

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To understand the influence of a series of ionic liquids from different families such as simple ammonium ionic liquids, imidazolium salts and phosphonium salts on α-chymotrypsin (CT), we have investigated activity and folding studies of transition state. For the first time, it is shown that enzyme stabilization by different family ionic liquids seems to be related to the associated structural changes of the protein that can be observed by circular dichroism (CD) and enzyme activity studies. All tested ionic liquids acted as enhancers, with varying efficacies and efficiencies. The results of the folding screening could be interpreted by taking into account the effect of the studied ionic liquids on protein aggregation, together with the systematic variations of their influence on the stability of native protein in solution. Our results reveal that more hydrophobic imidazolium cations and phosphonium cations, which are carrying longer alkyl chains, are weak stabilizer on enzyme while small alkyl chain molecules of ammonium salts are strong stabilizer for CT. Evidently, we observed that all ionic liquids play dominant contribution on stabilization of CT while not enhances its enzyme activity because ionic liquid-induced folding is not specific.

P-35

Synthesis and Antiplatelet Activity Studies on Some Novel oumarinyldihydropyridines

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Coumarin is a widely natural occurring secondary metabolite of plant families. Now a days more than 1000 naturally occurring coumarins have been reported and many more are synthesized by structural variations. The pharmacological and biochemical properties, therapeutic applications of coumarins depend upon the pattern of substitution. It has long been recognized that many coumarin derivatives posses anti-inflammatory, anti-oxidant, anti-allergic and anti-viral activities. Moreover, among the calcium channel blockers, 1,4-dihydropyridine nucleus serves as the scaffold important for cardiovascular activity. Derivatives of dihydropyridines exhibit a wide range of biological activities such as anti-hypertensive, anti-platelets and anti-anginal actions. The present work aims the synthesis of compounds containing biologically active scaffolds, coumarin and DHP in a single molecule (**Figure I**). A series of new coumarin-DHP hybrid derivatives have been synthesized and biological activity evaluation of these compounds are in progress. The detailed synthetic scheme and biological activity of these compounds will be presented during the poster session.

Figure I

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P-36

Synthesis of Novel alkyl ( )-4-(7,8-dimethoxycoumarin-4-yl)-6-methyl-3,4-dihydropyrimidin-2-one-5-carboxylates

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Coumarins (2*H*-Chromen-2-ones) continue to be investigated because of their importance to medicinal chemist due to a variety of biological activities. Naturally occurring as well as synthetic derivatives of coumarin scaffold possesses antibacterial, antiviral and anticancer activities as well as inhibition of platelet aggregation and inhibition of steroid 5α-reductase. Coumarins are used in drug and pesticidal preparations, they have also found applications as photosensitizers, fluorescent and laser dyes.
Moreover, derivatives of dihydropyrimidinones (DHPM) exhibit a wide range of biological activities and are antihypertensive, antitumor and anti-inflammatory agents. In the past decade, 4-aryl dihydripyrimidinones have attracted considerable attention owing to their high activity as calcium channel blockers. The present work aims at the synthesis of compounds containing both biologically active scaffolds, coumarin and DHPM. A series of novel coumarin-DHPM hybrid derivatives have been synthesized and biological evaluation of these compounds are in progress. The details of the work will be presented in the poster.

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P-37

Synthesis of Backbone Modified Nonionic Thioacetamido-linked Dimer of LNA of Biological Importance

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The last two decades have witnessed an upsurge in the synthesis of several modified nucleic acid derivatives. The intentions have been to synthesize therapeutically suitable and commercially viable nucleic acid analogues. Oligonucleotide-based antisense strategies represent a unique paradigm for the treatment of a wide variety of human disease states. The novel utility of these agents resides in their ability to selectively prevent the expression of a particular disease-associated gene in a sequence specific manner. Successful drug development based on this technology requires the synthesis and use of chemically modified oligonucleotides that render stability to nucleolytic digestion, enhance cellular uptake, and hybridize with high affinity and specificity toward the target mRNA. Ongoing synthetic studies into this broad class of compounds have focused on the chemical modification of the backbone, sugar, and base functionalities of natural DNA.[1-6]
We have designed and synthesized the five atom thioacetamido-linked LNA based dimers **I** and **II** mentioned in (**Figure 1**). The detailed synthetic scheme will be presented during the poster session.

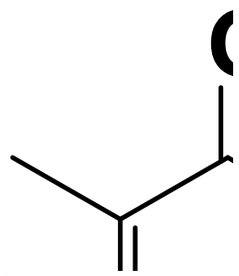

Figure 1

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P-38

Antimicrobial Activity Of Oxazolone Derivatives

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Heterocyclic compounds having more importance in recent years due to diverse pharmacological activities. Nitrogen, sulphur, oxygen containing five/six membered heterocyclic compounds have occupied enormous significance in the field of medicinal chemistry. Oxazolone derivatives are highly versatile intermediates used for the synthesis of several organic molecules, including amino acids, peptides, antimicrobial or antitumor compounds, immunomodulators, heterocyclic precursors for biosensors coupling. In view of this, it was of considerable interest to synthesize the title compound with a hope to obtain potent biologically active compounds.

The compounds have been synthesized by reported literature[1], characterized by UV, IR, NMR, Mass spectra and evaluated for in vitro antibacterial activity. The synthesized compounds were screened for their antibacterial activity by cup-plate method[2] against S. aureus, S. paratyphi, E. coli, V. cholera and S. dysenteriae. From the activity data it was concluded that all the compounds showed significant antibacterial activity against gram +ve and gram –ve bacteria as compared to standard streptomycin. All compounds showed equivalent antibacterial activity and the results are statistically significant.

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P-39

Kinetics and Mechanism of Oxidation of Primary Alcohols by Acidic Solution of Quinolinium Fluorochromate in the presence of Ru(III) as Homogeneous Catalyst

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The mechanistic study of ruthenium(III)-catalyzed oxidation of n-hexanol and n-heptanol (primary alcohols) has been studied by quinolinium fluorochromate (QFC) in aqueous perchloric acid medium at

308 K. The reaction followed zero order kinetics with respect to [primary alcohols]. First-order kinetics with respect to [QFC] and [Ir(III)] were observed for the oxidation of primary alcohols. The variation of $[H^+]$, $[Cl^-]$ and ionic strength of the medium had no significant effect on the rate of the reaction. The values of rate constants observed at four different temperatures were utilized to calculate the activation parameters. The reaction between QFC and primary alcohols, in acidic medium, exhibits 1:1 stoichiometry. A plausible mechanism conforming to the kinetic results has been proposed.

P-40

Purification of Chloroperoxidase from Musa paradisiaca stem juice

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Chloroperoxidase [CPO: E. C. 1.11.1.10] is a potential versatile biocatalyst for organic synthetic reactions Spreti et al. [1].Chloroperoxidase is the catalyst of the choice in oxygen transfer reactions of variety of organic compounds i e N-oxidation Corbett et al. [2] , S-oxidation Allenmark et al. [3], epoxidation Zhu et al. [4] , hydroxylation Ullrich [5], oxidation of alcohols Kiljiunen et al.[6] and indole Van Deurzen et al. [7].In all these reactions, chloroperoxidase from *Caldariomyces fumago*, a marine fungus has been used La Rotta Hernandez et al. [8]. Heme containing chloroperoxidases from other sources have not been available since long for the above reactions. It is recently that a heme containing chloroperoxidase from *Agrocybe aegerita* has been purified and studies on its potential as a biocatalyst in synthetic organic chemistry have been initiated Ullrich et al. [9]. Though the presence of chloroperoxidase in plants have been detected but the enzyme has not been purified Speicher et al. [10]. We have purified a chloroperoxidase from a plant source, *M. paradisiaca* stem juice, for the first time.The results of the studies done will be presented in the form of poster.

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P-41

Rational Development and Computational Structure – activity relationship of organo-sulphur functional active compounds in garlic

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Garlic has been used medicinally since antiquity because of its antimicrobial activity, anticancer activity, antioxidant activity, ability to reduce cardiovascular diseases, improving immune functions, and antidiabetic activity. Recent studies identify the wide variety of medicinal functions of garlic can be attributed to the sulphur compounds present in garlic and epidemiological observations and laboratory studies, both in cell culture and animal models have also showed anticarcinogenic potential of organo-sulphur compounds of garlic, which has been traditionally used for varied human ailments around the world. In this paper we are reporting a computational design of organ- sulphur compounds of garlic . The methods of theoretical chemistry have been used to elucidate the molecular properties. The analysis of molecular descriptors defined by Lipinski has been done. The solubility of drug in water has been determined as it is of useful importance in the process of drug discovery and development from molecular design to pharmaceutical formulation and biopharmacy. All toxicities associated with candidate drug have been calculated. P-gp expressed in normal tissues as a cause of drug pharmacokinetics and

pharmacodynamics been examined. Drug plasma-protein binding and volume of distribution has also been calculated. To avoid rejection of drugs, it is becoming more important to determine pKa, absorption, polar surface area and other physiochemical properties associated with a drug, before synthetic work is undertaken. Our goal is to examine organo- sulphur compounds of garlic to evaluate its possible efficacy and toxicity under conditions of actual use in humans.

P-42

Purification, Characterisation And Coal Depolymerising Activity Of Lignin Peroxidase From *Lenzitus Betulina* MTCC – 1183

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The lignin decomposing basidiomycete white rot fungi secrete a hemeprotein, lignin peroxidases (LiP) [E.C.1.11.1.14] which in presence of H_2O_2 degrades lignin and lignin model compounds Steven et al. [1]. LiP is a biotechnologicaly important enzyme having wide potential applications in delignification of lignocellulosic materials Harley et al. [2] which are seen as an alternative to the depleting oil reserves, (ii) in the conversion of coal to low molecular mass fractions Catcheside et al. [3] which could be used as feed stock for the production of commodity chemicals, (iii) in biopulping and biobleaching Eriksson et al. [4] in paper industries, (iv) in removal of recalcitrant organic pollutants Bumpus et al. [5], Sin et al. [6], Satwinder et al. [7], Levin et al. [8] and Cenek et al. [9]and (v) in the enzymatic polymerization Uyama et al. [10] in polymer industries. We have purified and characterized lignin peroxidase from the liquid culture growth medium of *Lenzitus betulina* MTCC-1183. Its enzymatic characteristics like Km, pH and temperature optima and thermal stability using veratryl alcohol and H_2O_2 as the substrate have been determined. Depolymerisation of coal by the purified enzyme has been demonstrated using humic acid as a model of coal. The results of our studies will be presented in the form of a poster.

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P-43

Water pollution with special reference to pesticide contamination in India

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The pesticides belong to a category of chemicals used worldwide as herbicides, insecticides, fungicides, rodenticides, molluscicides, nematocides, and plant growth regulators in order to control weeds, pests and diseases in crops as well as for health care of humans and animals. The positive aspect of application of pesticides renders enhanced crop / food productivity and drastic reduction of vector-borne diseases. However, their unregulated and indiscriminate applications have raised serious concerns about the entire environment in general and the health of humans, birds and animals in particular. Despite ban on application of some of the environmentally persistent and least biodegradable pesticides (like organochlorines) in many countries, their use is ever on rise. Pesticides cause serious health hazards to living systems because of their rapid fat solubility and bioaccumulation in non-target organisms. Even at low concentration, pesticides may exert several adverse effects, which could be monitored at biochemical, molecular or behavioral levels. The factors affecting water pollution with pesticides and their residues include drainage, rainfall, microbial activity, soil temperature, treatment surface, application rate as well as the solubility, mobility and half life of pesticides. In India, organochlorine insecticides such as DDT and HCH constitute more than 70% of the pesticides used at present. Reports from Delhi, Bhopal and

other cities and some rural areas have indicated presence of significant level of pesticides in fresh water systems as well as bottled drinking mineral water samples. The effects of pesticides pollution in riverine systems and drinking water in India has been discussed in this review.

P-44

Ultrasound assisted green synthesis of bis(indol-3-yl)methanes catalyzed by 1-hexenesulphonic acid sodium salt

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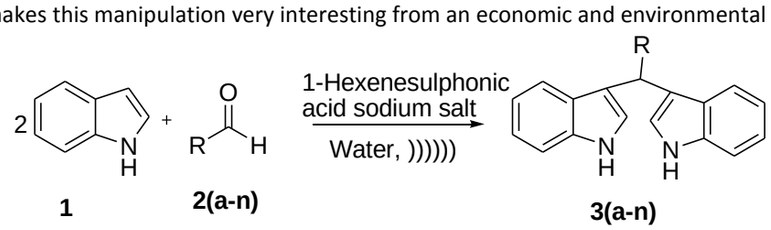
1-Hexenesulphonic acid sodium salt as catalyst for green synthesis of bis(indol-3-yl)methanes was described. The reaction of indole with various aldehydes in water using ultrasound irradiation at ambient temperature for appropriate time using 1-hexenesulphonic acid sodium salt furnish the desired product in good to excellent yield. Utilization of aqueous medium, simple reaction conditions, isolation, and purification makes this manipulation very interesting from an economic and environmental perspective.



1 **2(a-n)** **3(a-n)**

P-45

Mechanistic Aspects For The Oxidation Of Glycerol By Potassium Bromate In Presence Of Sodium Hydroxide Catalyzed By Chloro Complex Of Ru(Iii) In Its Nano Concentration Range As Homogeneous Catalyst: A Kinetic Approach.

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The present paper deals with the kinetics and mechanism of Ru(III) catalyzed oxidation of Glycerol in an alkaline solution of $KBrO_3$ carried out in the temperature range 30-45^{0}C.Mercuric acetate has been used as a scavenger for Br^- ion formed in the reaction mixture to prevent parallel oxidation by bromine. First order kinetics with respect to each [$KBrO_3$] and [Ru(III) chloride] was observed in the oxidation of Glycerol. The reaction shows zeroth order with respect to Glycerol and [OH^-] , whereas a negative effect is observed for [Cl^-]. Negligible effect of mercuric acetate and ionic strength of the medium has been observed .The reactive species of Ru(III) in alkaline medium is [$RuCl_2(H_2O)_3(OH)$]. A suitable mechanism in conformity with the kinetic observation has been proposed. The various activation parameters such as energy of activation (ΔE*), the Arrhenius factor (A), entropy of activation (ΔS*) etc. were calculated from the rate measurements at 30, 35, 40 and 45^{0}C.The rate has been derived on the basis of obtained data.
Keywords: Kinetics, mechanism, oxidation, polyhydric alcohol, potassium bromate, Ru(III) catalyst.

P-46

Targetting MAP Kinase pathway for anticancer drug

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Cancer can be perceived as a disease of communication between and within cells. The aberrations are pleiotropic, but mitogen-activated protein kinase (MAPK) pathways feature prominently(Dhillon et al.) The mitogen-activated protein kinase (MAPK) pathway (including Ras or Rapl, Raf-1 or B-Raf and the MAPKs Erk-1 and Erk-2) is involved in the regulation of cell growth, differentiation and apoptosis of both

small cell and non-small cell lung cancers (SCLC and NSCLC)(Qui et al). Recent evidence may be summarized for the molecular mechanism of this MAP kinase pathway. Initially, Ras oncogene product activates Raf1, which in turn phosphorylates and activates MEK1 on 2 distinct Ser residues; Activated MEK1 phosphorylates p44 ERK1 and p42 ERK2 (ERK= extracellular signal-regulated kinase) on Thr183 and Tyr185; These activated MAP kinases phosphorylate a variety of factors such as transcription factors to result in cell proliferation and/or differentiation. The mitogen-activated protein kinase (MAPK) superfamily consists of three main protein kinase families: the extracellular signal-regulated protein kinases (ERKs), the c-Jun N-terminal kinases (JNKs) and the p38 family of kinases. Each is proving to have major roles in the regulation of intracellular metabolism and gene expression and integral actions in many areas including growth and development, disease, apoptosis and cellular responses to external stressesv (Kyra et al). The blockers of phosphorylation are new types of anticancer agents, and being nontoxic, cytostatic, and oral in some of them may open a new avenue for the development of antitumor drugs with a novel mechanism of action and may end up being able to extend the survival of the patient with enhanced quality of life.

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P-47

New Strategic Approach for Bifunctional Protein Modeling and Docking Studies on Pyrimidine Based Derivatives as Antifolates on Toxoplasma gondii (Tg).

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Toxoplasmosis is a parasitic disease caused by the protozoan Toxoplasma gondii (Tg). The parasite infects most genera of humans and warm blooded animals. Toxoplasma gondii is predominant as opportunistic pathogen associated with AIDS[1]. Protozoans contain Thymidylate Synthase (TS) and Dihydrofolate Reductase (DHFR) on the same polypeptide. In bifunctional proteins, the DHFR domain is on the amino terminus and TS domain is on the carboxy terminus. The two domains are separated by a junction polypeptide, whose length is determined by the source of the protein. The bifunctional proteins have been popular targets in development of drugs for chemotherapy, since inhibition of either enzyme DHFR or TS disrupts the dTMP cycle and result in the death of cells due to lack of thymine. In our study a new strategic approach was made to develop the complete bifunctional protein model. This includes: a) individual development of DHFR and TS models with the crystal structure coordinates using MODELLER[2]; b) development of complete model of Tg by using the coordinates of individual proteins of DHFR and TS generated by MODELLER. The generated bifunctional protein model was evaluated with PROCHECK; Verify 3D and PROSA. This model is further minimized for its low energy conformation and this conformation was used for docking studies to know the interactions of the protein with antifolates. The docking studies were performed by taking 179 existing antifolates, their activity expressed on Tg DHFR. Docking results showed better binding affinity towards the activesite. The information obtained from docking results was used to perform structure activity relationship studies between modeled protein and existing antifolates. Three dimensional quantitative structure activity relationship studies (3D-QSAR) on a wide variety of structurally diverse antifolates[3] having 2, 4-diamino pyrimidine as a pharmacophore (Figure-1) which is essential for the inhibition of DHFR. The 3D-QSAR studies showed good correlation between the structure and activity. The statistical values are provided in the table below.

	Atom based QSAR		**Receptor based QSAR**	
	CoMFA	**CoMSIA**	**CoMFA**	**CoMSIA**
Q^2	0.569	0.575	0.544	0.547
R^2	0.985	0.896	0.963	0.899
SEE	0.120	0.308	0.187	0.304

F	637.024	156.832	327.127	161.575
$\mathbf{R^2_{pred}}$	0.6088	0.5360	0.4911	0.5179

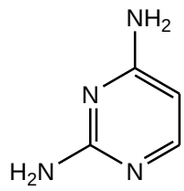

Figure-1 Pharmacophore

These results will enable us to design new drug molecules which satisfy the required pharmacodynamics for the inhibition of bifunctional protein enzymatic activity.

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P-48

Polyols effect on enzyme stability

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To understand the bimolecular interaction of polyhydric alcohols (polyols) on the enzyme thermal stability, we have monitored the differential scanning calorimetry (DSC), circular dichroism (CD), as a function of polyols concentrations. Our experimental results reveal that the associated structural changes of the α-chymotrypsin (CT), with polyols. All tested polyols (sucrose, sorbitol, trehalose and glycerol) are acted as enzyme stabilizers, with varying efficacies and efficiencies. The results of the folding screening could be interpreted by taking into account the effect of the studied polyhydric alcohols on protein aggregation, together with the systematic variations of their influence on the stability of native protein in solution. Our DSC results reveal that the enthalpy change (ΔH) and Gibbs free energy of change (ΔG_u) of CT in polyols increase linearly as osmolytes concentration increases. Evidently, we observed that naturally occurring osmolytes (polyols) play dominant contribution on stabilization of CT while not enhances its enzyme activity. Furthermore, our results reveal that trehalose exerts a powerful stabilizer and most effective compatible osmolyte, whereas sucrose is a weak stabilizer and least protective osmolyte. The CD spectra clearly showed the ability of polyols to compact the native structural conformation of enzyme, preventing the usual thermal unfolding which occurs in other media.

P-49

Synthesis and antileukemic activity of 1-(*(S)*-2-amino-4,5,6,7-tetrahydrobenzo[d]thiazol-6-yl)-3-(substituted phenyl) urea/thiourea derivatives: A Structure Activity Relationship Study

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Heterocyclic urea and thiourea derivatives play an important role as anticancer agents because of their good inhibitory activity against receptor tyrosine kinases (RTKs), raf kinases, protein tyrosine kinases (PTKs), and NADH oxidase, which play critical roles in many aspects of tumorigenesis. Benzothiazole moiety constitutes an important scaffold of drugs, possessing several pharmacological functions, mainly the anti-cancer activity. Based on these interesting properties of benzothiazoles with urea and thiourea moiety and to obtain new biologically active agents, we synthesised a series of novel 1-(*(S)*-2-amino-4,5,6,7-tetrahydrobenzo[d]thiazol-6-yl)-3-(substituted phenyl) urea and thiourea derivatives and evaluated for their efficacy as antileukemic agents against two human leukemic cell lines (K562 and Reh). These compounds showed good cytotoxic effect to cancer cell lines tested. Structure activity relationship

suggests that compounds with thiourea moiety showed good activity. Further, compounds with electron withdrawing dichloro substitution on phenyl ring of the aryl urea/thiourea showed significant activity. When we compare the effect of compounds containing dichlorophenyl urea and thiourea group, the effect of urea group was limited. Further, Flow cytometric analysis of annexin V-FITC/ propidium iodide (PI) double staining and DNA fragmentation suggest that compound with thiourea linking can induce apoptosis in better way than the compound with urea linkage.

P-50

Synthesis And Antibacterial Activity Of Quinazolinone Derivatives

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Taking lead from naturally occurring quinazolinone derivatives, a number of novel quinazolinone derivatives were developed and evaluated for antibacterial activity. In the present work the desired quinazolinone derivatives (DK-1, DK-2, DK-3, DK-4, DK-5, DK-6 & DK-7) were synthesized by treating 2-Chloro-N-(4-oxo-2- phenylquinazolin-3(4H)-yl)acetamide **(I-1)** with the different substituted phenols in presence of anhydrous potassium carbonate & catalytic amount of potassium iodide in dry acetone. The structures of the newly synthesized compounds have been established on the basis of their m.p., TLC, IR and 1HNMR data. All the newly synthesized quinazolinone derivatives were evaluated for their antibacterial activity by cup plate method by measuring inhibition zone. Ampicillin was used as standard drug. The comparison data revealed that the synthesized compounds exhibited mild to excellent antibacterial activity and the compound DK-2 showed more potent antibacterial activity than the standard drug ampicillin at a concentration of 100 µg/ ml.

P-51

Synthesis, Characterization And Evaluation Of Anti-Bacterial Activity Of Some Novel Pyrazoline Derivatives

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Several substituted 3-(2-pyridine) pyrazoline derivatives have been prepared by treating different chalcones 1C, 2C and 3C with Phenyl hydrazine, thiosemicarbazide respectively. Chalcones 1C, 2C and 3C were synthesized by Claisen-Schmidt Condensation reactions. The the structure of the synthesized compounds were characterized by IR Spectra and Mass spectral data and the purity of the compounds were tested by TLC and melting point method. Their anti-bacterial activity was investigated against Escherichia coli (MTCC 1573), Staphylococcus aureus (MTCC 1430) by cup-plate agar diffusion method at the 50,100, 200, 400, 600, 800, 1200, 1600 and 2000 µg/ml concentrations. A significant level of activity was observed by most of the synthesized compounds. Standard drug used for anti-bacterial activity is Ciprofloxacin. All bacteria were procured from MTCC (Microbial type culture collection) Chandigarh.

P-52

Predicting Caco-2 cell Permeation Coefficient of Hydroxymate TACE Inhibitors by QSAR Analysis

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Estimation of human oral bioavailability is an important step during lead optimisation program and drug development process. Caco-2 cells have many morphological and functional properties of in vivo intestinal epithelial cell barrier; therefore it is used as in vitro model of drug absorption [1]. Due to time and cost

involved in this model, use of Quantative Structure Properties Relationship (QSPR) is an attractive alternate to experimental measurements of Caco-2 permeability coefficient (Log P_{app}). TNF-alpha convertase enzyme (TACE) is responsible releasing soluble form of TNF-alpha, a main inflammatory mediator. TACE is found to have significant role in progress of Rheumatoid arthritis. Hydroxymate TACE inhibitors are found to have significant beneficial effect in RA. But poor absorption makes these compounds unsuitable for further studies [2]. So we have developed a QSPR model to predict bioavailability of Hydroxymate TACE inhibitors. A training set of 35 Hydroxymate TACE inhibitors reported in literature [3,4] was used to construct QSPR model of Caco-2 cell permeation. Various types of molecular descriptors were employed such as polar surface area, Hydrogen Bond Acceptors, Hydrogen Bond Donors, Mol. Wt., LogP and LogD. Among these descriptors, LogP was found to have high impact on diffusion through Caco-2 cell. Derived model may be a good tool for faster screening of Log P_{app} of new TACE inhibitors. The model also provides some insight into physicochemical processes of absorption. In summary, QSPR technique appears to have significant value in predicting passive permeability for congeneric series of molecule.

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P-53

Synthesis of novel succinate and phthalate derivatives of chitosan as carrier for colon targeted delivery of therapeutic active candidate.

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In the current scenario numbers of polymer have been use as drug carrier. These are used in the target delivery in order to produce the safe and effective therapeutic response . Chitosen has gained lots of attention toward using it as an excipents and drug carrier in the development of conventional and novel drug delivery system. Chitosan usually soluble in the pH < 6.5. In the study solubility window of the polymer was modified with the substitution in the position of reactive amino group of the polymer. Succinct and phthalate derivative under mild condition were substituted in the chitosan in order to modify solubility behaviour of the polymer. The derivatives of the polymer were characterize with FTIR analysis. Tetracycline was use as model drug for the evaluation of drug release from these polymers. Microparetic les of tetracycline formulated with use of these derivatives polymer. Dissolution of the microparticle was study in USP dissolution apparatus I (USP 24) and phosphate buffer 7.5 pH used as dissolution medium. *In vitro* drug release from the microparticle batchs were compared with the reference chitosen tetracycline microparticle and its shows significant difference in the release rate of the drug. The drug release from the polymer derivatives microparticle batches demonstrated sustained release for 8 h, and best fitted in the Peppas model with $n < 0.45$ suggesting a diffusion based mechanism of drug release from the microparticle.

P-54

Synthesis And Antimicrobial Activity Of Some Fused Bicyclic Heterocycles

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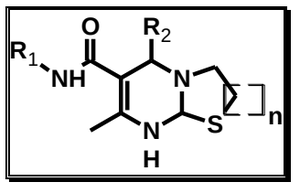
Dihydropyrimidine (DHPM) derivatives exhibit various pharmacological activities. This precursor is important not only as it exhibit biological activities but various fused bicyclic systems can be generated from the particular. Bo'szing and co-workers [1] reported DHPM are now known for calcium channel blockers property. Adam et. al. [2] filed US patent of phenyl substituted thiazole pyrimidines derivatives synthesized form DHPM. These compounds are cpable of high affinity binding to group II mGlu α

receptors, adenosine α3 receptor antagonism also as metabotropic glutamate receptor antagonists. The present investigation deals with rapid microwave synthesis containing fused bicyclic systems under different conditions to observe change in the % yield of the products.[3] Dihydropyrimidine obtained via a microwave-assisted Biginelli reaction were treated with dibromo alkanes under different microwave conditions to yield thiazolo-pyrimidine and pyrimido-thiazine systems. The usefulness of this method lies in carrying out the reaction without a catalyst and solvent in a shorter time. The Antimicrobial Activity of these compounds against under various strains such as *S.coccus Pypgens A77, S.aureus SG511, S.aureus E710, E.Coccus Faecalis, M.smegmatis (MY-1), M.smegmatis (MY-1)* was performed. The preliminary results were encouraging.



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P-55

Synthesis, Anti-Tubercular Activity And 3d Qsar Analysis Of Coumarin-4-Acetic Acid Benzylidene Hydrazides Derivatives

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The synthesis, screening and 3D-QSAR analysis of coumarin-4-acetic acid benzylidene hydrazides were carried out. A set of 25 compounds were synthesized and evaluated for their anti-tubercular activity using BACTEC 460 system against mycobacterium tuberculosis $H_{37}Rv$ strain. In order to establish relationship between structure and biological activity, 3D-QSAR study has been carried out using comparative molecular field analysis (CoMFA) with two different strategies viz. database alignment and field fit alignment. Among several generated models, database alignment based model was the best in terms of overall statistics with correlation coefficient (r^2) of 0.983 and cross validated correlation coefficient (q^2) of 0.636.

P-56

Synthesis And Anti-Hiv Activity Of *N*-1, 3-Benzo [*D*]Thiazol -2-Yl-2-(2-Oxo-2*h*-Chromen-4-Yl) Acetamides

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HIV (Human Immunodeficiency Virus) attacks the body's immune system. Normally, the immune system produces white blood cells and antibodies that attack viruses and bacteria. The infection fighting cells are

called T-cell lymphocytes. Months to years after a person is infected with HIV, the virus destroys all the T-cell lymphocytes. This disables the immune system to defend the body against diseases and tumors.
Coumarins (2-oxo-2*H*-chromen) have been found to exhibit a wide range of biological and controlled therapeutic activities in view of their extensive occurrence in nature and wide range of toxicity. Many heterocyclic substituted and fused Coumarin derivatives are widely used in drugs. Similarly Benzothiazole containing five member heterocyclic compounds and several Benzothiazole derivatives show considerable biological activities.
In our efforts to discover novel anti-HIV agents, we have synthesized diversed N-1, 3-benzo[d]thiazol-2-yl-2-(2-oxo-2H-chromen-4-yl) acetamides. N-1, 3-benzo[d]thiazol-2-yl-2-(2-oxo-2H-chromen-4-yl) acetamides were prepared by the condensation of coumarin-4-acetic acids & respected benzothiazole. All the synthesized N-1, 3-benzo[d]thiazol-2-yl-2-(2-oxo-2H-chromen-4-yl) acetamides [1,2,3] were screened for their *in vitro* anti-HIV activity against various human HIV cell lines. These compounds required to achieve 50% protection of MT-4 cells from the HIV-1-induced cytopathogenicity, as determined by the MTT method. Synthesis and anti-HIV activity of the heterocyclic compounds will be presented.

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P-57

Synthesis And Anticancer Screening Of Some Novel Dihydropyrimidine (Dhpm) With Carbamoyl Side Chain

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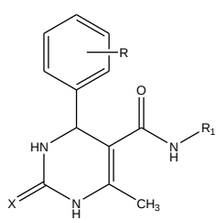
Over the past dacade, Dihydropyrimidine 2(1-H)one and their derivatives have attracted considerable attention in organic and medicinal chemistry as the DHPM scaffold displays wide range of activity such as calcium channel blocker, antihypertensive agents, antiviral and antitumor[1] etc.
Several novel DHPM derivatives having a carbamoyl moiety as a side arm were synthesized by the three component Biginelli[2] reaction between acetoacetanilide, aldehyde and urea under classical and microwave assisted method with the help of acid catalyst and all the compounds were characterized by the IR, ^{1}H-NMR, Mass Spectroscopy, Elemental analysis and XRD study[3].
Primary screening was carried out of all compounds. The anticancer activity of these compounds were evaluated against a series of cancer cell lines namely **A-549** (Epithelial), **MDA.MB.231** (Breast), **MiaPaCa-2** (Pancreas) and **ACHN** (Renal). The results are presented.



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P-58

Thiazolidinones As Potential Anti Tubercular Agents: Synthesis Of Some New Thiazolidine-4-Ones Using Benzimidazole Nucleus

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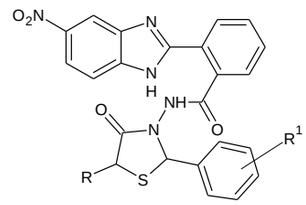
Despite the availability of highly potential antitubercular agents, tuberculosis remains primary cause of comparatively high mortality worldwide. The statistics shows that around three million people throughout the world die annually from tuberculosis and today more people die from tuberculosis than ever before. Therefore, the development of new drugs with activity against multi drug-resistant (MDR) TB, extensively drug-resistant (XDR) TB, and latent TB is a priority task [1]. Also new agents that will shorten the duration of current chemotherapy are also needed. A special interest has been focused on five member heterocyclic compounds like triazole, pyrrole, oxadiazole, especially thiazolidinone and other heterocyclic system derivatives have been reported [2, 3]. These studies involved the synthesis of 4-thiazolidinone derivatives using benzimidazole nucleus and screening for their antitubercular activity and antimicrobial activities. The obtained activity results seem to be interesting from the biological point of view.

R= H, CH_3
R1= -OCH_3, -OH, -Cl etc.



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P-59

Synthesis And Antimicrobial Evaluation Of 3(E) Benzylidene-1-Methylquinoline-2, 4-(1h, 3h)-Dione Against 17 Different Strains

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Quinolines constitute a very important class of heterocyclic moiety. Various substituted quinolines possess wide range of biological activities. 3-substituted quinolines have been found as antimicrobial, antitumor, anticonvulsant, antidepressant, antimalarial, antihistaminic agents. Moreover, N-methyl quinolines derivatives have been shown to possess unique antiadema and anti-inflammatory activities. Currently, to establish minimum structural requirement necessary for antimicrobial activity, a small library

of compounds were prepared and to evaluate them against various 17 gram +ve and gram –ve micro organisms namely *Escherichia coli ATCC 25922, Escherichia coli, Escherichia coli*, Enterobacter aerogenes, Proteus valgaris, Proteus valgaris*, Salmonella paratyphi B, Salmonella paratyphi B*, Pseudomonas aeruginosa ATCC 27853, Pseudomonas aeruginosa, Staphylococcus albus*, Staphylococcus aureus ATCC 25923, Staphylococcus citrus, Staphylococcus citrus*, Klebshiella pneumoniae* 1, Bacillus subtilis ATCC 6633, Klebshiella pneumoniae* 2 .*
The MIC values are determined and several "hits" were identified from this series. The activity data will be presented.

P-60

A high performance liquid chromatographic method for the simultaneous determination of atenolol and lercanidipine hydrochloride in commercial tablets.

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A simple, rapid, precise and accurate isocratic reversed phase stability indicating HPLC method was developed and validated for the simultaneous determination of atenolol (ATE) and lercanidipine hydrochloride (LER) in commercial tablets. The chromatographic separation was achieved on phenomenex Gemini C18 (250mm×4.6mm, 5µm) column using a mobile phase consisting of acetonitrile and buffer (20 mM potassium dihydrogen phosphate pH 3.5) in the ratio of 55:45 (v/v) at a flow rate of 1.0 mL/min and UV detection at 235 nm. The linearity of the proposed method was investigated in the range of 40-160 µg/mL (r=0.9995) for ATE and 8-32 µg/mL (r=0.9993) for LER. The LOD for ATE and LER were 0.02 and 0.05 µg/mL, respectively; the LOQ were 0.05 and 0.1 µg/mL, respectively. Degradation products produced as a result of stress studies did not interfere with the detection of ATE and LER and the assay can thus be considered stability-indicating.

P-61

Stability indicating HPLC method for Drotaverine Hydrochloride in Pharmaceutical Dosage Form and Tablet Dosage form

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Drotaverine is a well accepted non pharmacopeial drug used widely as antispasmodic**.** Present work describes a precise, accurate, reproducible and stability indicating high performance liquid chromatographic (RP-HPLC) method of analysis of Drotaverine Hydrochloride both as a bulk drug and in formulations. The formulation was subjected to ICH recommendation stress condition. Chromatography was carried out on C8 column using mobile phase of 0.2% formic acid(v/v) : methanol(55:45) at a flow rate of 1.0ml/min with UV detector at 300nm. The retention time of the Drotaverine Hydrochloride was about 5.2 mins. The detector response is linear from 40-180µg/ml of test concentration with a correlation coefficient of 0.9999 of Drotaverine Hydrochloride. The limit of detection and Limit of quantification was 0.01 µg/ml and 1 µg/ml. The method was validated to specificity, linearity, LOD & LOQ, precision, accuracy and robustness. The method was found specific against placebo interference and also during the force degradation. The specificity of the method was determined by assessing interference from the placebo and by stress testing of the drug (forced degradation).Intraday and interday system and method precision were determined. The proposed method is simple, fast, sensitive, linear, accurate, rugged and precise and hence can be applied for routine quality control of Drotaverine Hydrochloride in bulk and in tablet dosage form.

P-62

Synthesis, Characterization And Antimicrobial & Antiviral Study Of Some Trithiane Derivatives.

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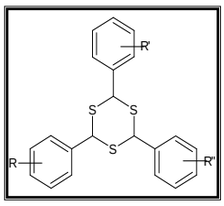
Trithianes have found their way into a variety of fields of applications like photopolymerization, pharmaceuticals, intermediate for many important chemical compounds, plastics and polymers. It also has very wide use in flavoring and taste-modifying agent in the aromatization of foodstuffs in general and imitation flavors for foodstuffs, animal feeds, pharmaceutical preparations and tobacco products.

Trithianes were prepared by one pot synthesis, passing hydrogen sulphide and hydrogen chloride gas in the soluntion of substituted aromatic aldehydes in methanol. All compounds were well characterized by IR, NMR and Mass spectral data. X-Ray crystallographic study of one of the series compounds proves the crystal structure of compound. Trithaianes compounds were carried out for anti microbial activity against Gram +Ve strain *Escherichia coli* and Gram -Ve strain *Staphylococus aureus*. They are also screened for their antiviral properties. Details of the work and activity data is discussed.



P-63

Crystal structure of DP-7: A new mdr reverting agent against tumor cells

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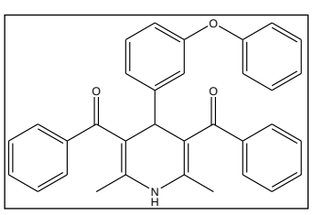
In the past few years, extensive studies have been performed with the aim of developing effective chemosensitizers to overcome MDR of human cancer cells. Among them Ca2+ channel blockers, such as Verapaml and some dihydropyridines related to Nifedipine, have been extensively investigated. They are endowed with inherent cardiovascular activity.

3,5-dibenzoyl-4-(3-phenoxyphenyl)-1,4-dihydro-2,6-dimethylpyridine (DP7), studied extensively in last few years and established as a novel MDR reverting agent. Several experiments to evaluate its biological profile were performed & reported (reference 1-7).

The synthesis of this dihydropyridine, DP7, bearing dibenzoyl groups at C(3) and C(5), respectively, has been achieved by applying the modified Hantzsch-type condensation. The product obtained was characterized by spectroscopic techniques.

In order to correlate structure activity relationship, the X-ray crystallographic study of DP-7 has been carried out by developing a single crystal by thin layer evaporation method. The details of the study related to X-ray data & ORTEP diagram will be presented.



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P-64

Development and Validation of Stability-Indicating RP-HPLC Method for Assay of Rosuvastatin calcium in Tablets and for Determination of Content Uniformity

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A simple, precise, and accurate isocratic reversed-phase (RP) stability indicating high-performance liquid chromatographic (HPLC) method has been developed and validated for assay of rosuvastatin calcium in tablets and for determination of content uniformity. Reversed-phase liquid chromatographic separation was achieved by use of acetonitrile and water (pH 3.5 adjusted with phosphoric acid) in the ratio of (40:60, v/v) as mobile phase. The method was validated for specificity, linearity, precision, accuracy, robustness, and solution stability. The specificity of the method was determined by assessing interference from the placebo and by stress testing of the drug (forced degradation). Response was a linear function of drug concentration in the range 20-80 µg/mL (r= 0.9984). Intraday and interday system and method precision were determined. Accuracy (recovery) was between 99.3 and 101.9%. The method was found to be robust, and was suitable for assay of rosuvastatin calcium in a tablet formulation and for determination of content uniformity.

P-65

A Chromatographic Determination Of Ntipsychotic Drug By Hplc And Uplc: A Comparative Validation Study

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A simple, precise, and accurate isocratic reversed-phase (RP) stability-indicating column high-performance liquid chromatographic (HPLC) assay method was developed and validated for determination of Aripiprazole in bulk & solid pharmaceutical dosage forms and the technology is transfer to the UPLC under the same chromatographic condition which is more accurate, faster and reliable .Isocratic separation was achieved on a Phenominex Luna C_{18} column (250 mm X 4.6 mm id, 5 µm particle size) using mobile phase composed of acetonitrile: 20 mM Ammonium Acetate buffer (90:10,v/v) at a flow rate of 1.0 mL/min, and detection was performed at 240 nm using a photodiode array detector while by UPLC

the column was Acquity BEH C18(50 mm X 2.1 mm id, 1.7 µm particle size).The drug has subjected to oxidation, hydrolysis, photolysis, and heat to apply stress conditions. The method has validated for specificity, linearity, precision, accuracy, robustness, and solution stability. The method was linear in the drug concentration range of 40-180 µg/mL with a correlation coefficient of 0.998 by HPLC & 0.999 by UPLC. The repeatability relative standard deviation (RSD) for 6 samples was 0.373% for HPLC and 0.21% for UPLC and the intermediate precision (RSD) for 6 samples was 0.412% for HPLC and 0.1% for UPLC, the accuracy (recovery) was between 98.0 and 100.0%. Degradation products produced as a result of stress studies did not interfere with detection of aripiprazole, and the assay can thus be considered stability--indicating.

P-66

Synthesis Of Hybrid Structures: Thiazole Linked Coumarin Derivatives

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When 2-Amino thiazole ring system is a useful structural element in medicinal chemistry having application in drug development for the treatment of allergies, hypertension, inflammation, schizophrenia, bacterial and HIV infections.[1] Aminothiazoles are known to be ligands of estrogen receptors [2] as well as novel class of adenosine receptor antagonists.[3] Coumarin and its derivatives shows various pharmacological effects.Coumarin and thiazole derivatives have been associated with diverse pharmacological activities such as antibiotics, antibiotics,anti-inflammatory,antidiabatics,antimicrobial and fungicidal properties. Some important findings are obtained in our laboratories for the antiviral properties of coumarin derivatives of such hybrid structures linked by CH_2-CO-NH- spacer combining of two moieties with thiazole units. The promising results have encouraged us for the further derivatization of the compounds.

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P-67

Synthesis And Anticoagulant Activity Of Dimeric 4-Hydroxycoumarins Having Indole And Chromone As Central Linkers

Shrey Parekh and Shailesh Thakrar

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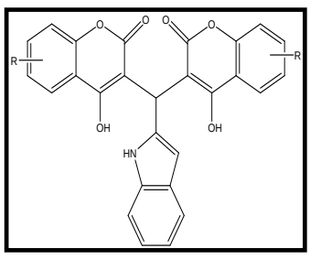
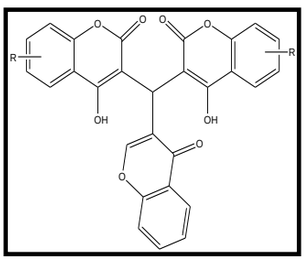
The mode of action of the coumarin anticoagulants involve blocking the regeneration of reduced Vit-K and induce state of functional Vit-K deficiency, thus interfering with the blood clotting mechanism. Several new coumarin derivatives were synthesized in order to evaluate the role of central part of dimeric coumarin which are structurally Symmetrical to dicoumarons but have slight distortion in Centro symmetrical position. Our first task was to check the anticoagulant activity against human whole blood and if the compound is proven to be an anticoagulant, it will be used for the determination of prolongation of prothrombin time (P.T.) Anticoagulant activity was assessed by measuring the prothrombin time plasma (100µl) mixed with saline (100µl) or saline solution of the compound and incubated for 5minutes at 37^0C. Coagulation was started with 1:1 mixture of rabbit brain thromboplastin (DIAGEN) and 0.025M calcium chloride (200 µl).

The Anticoagulant data of two series will be presented.





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P-68

In Vitro Cytotoxicity Evaluation Of Modified Diverse Coumarin Skeleton

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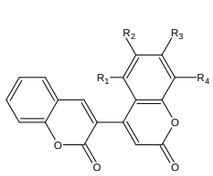
Coumarin derivatives exhibit diverse biological functions including anti-bacterial, anti-cancer, anti-psorratic, anti-tubercular, anti-fungal etc.

In the present study, three series of Coumarin derivatives namely, 3-(2-oxo-5,6,7,8-tetra substituted-2H-chromen-4-yl)-2H-chromen-2-ones-I,3-(5-(2-oxo-2H-chromen-4-ylamino)-1,3,4-thaidiazol-2-yl)-2H-chromen-2-ones-II and 6,7,8,9-tetrasubstituted-3-methyl-4H-chromeno[3,4-*d*]isoxazol-11-ones-III were synthesized. These were characterized by IR, NMR, Mass spectra and Elemental Analysis

Screening of these compounds on the panel of cell lines representing various cancer types was carried out. The cytotoxicity data of these series of compounds was evaluated against a series of cancer cell lines namely **SW 620** (Colon), **MDA.MB.453MCF-7** (Breast), **L132** (Lung), **ECV.304** (Endothelial), **MiaPaCa** (Pancreas), **HuTu80** (Stomach) and **G401** (Renal). Anticancer activity data will be presented.



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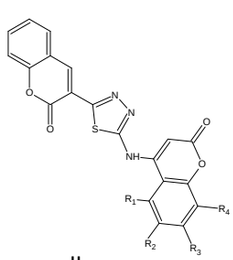

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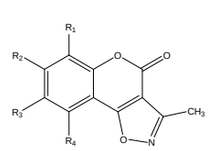

III

P-69

Potassiuim bromate oxidation of Glycine and Iso-leucine using Osmium tetra oxide in its microamount as homogeneous catalyst : A kinetic and mechanistic study

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The kinetics of Os(VIII) catalyzed oxidation of Glycine and Isoleucine by Potassium bromate in alkaline medium at 298 K has been investigated. The oxidation products are formaldehyde and 2-methyl butyric acid in case of Glycine and Isoleucine respectively. The stiochiometric analysis reveals the ratio of [Glycine] :[$KBrO_3$] as well as [Isoleucine] : [$KBrO_3$] = 1:1. The reaction shows first order kinetics in [Os(VIII)] and [$KBrO_3$] for the oxidation of both amino acids. Negative effect of [OH^-] was observed in the oxidation of both Glycine and Isoleucine. Variation of the ionic strength (μ) and dielectric constant of the medium and addition of [$Hg(OAc)_2$] (used as Br^- scavenger) has an insignificant effect on the rate of reaction. Activation parameters have also been calculated and reported. A suitable mechanism consistent with the observed kinetic result has been suggested and the related rate law deduced.

P-70

Design And Synthesis Of Chalcone Analogues As Vegfr-2 Inhibitors For Tumor Anti-Angiogenesis Activity

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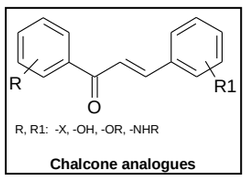
Identification of novel tyrosine kinase receptor inhibitors is an area of intense investigation in anti-tumor research. Inhibition of angiogenesis through blockade of vascular endothelial growth factor receptor (VEGFR-2) signaling pathway could starve developing cancer of required blood flow by limiting vasculature to growth site [1-3]. This study involves design and synthesis of chalcone analogues as VEGFR-2 inhibitors. Chalcones are reported to be angiogenesis inhibitors [4-5]. Hence, series of substituted chalcone analogues was designed. Crystal structure of VEGFR-2 was obtained from Protein Data Bank. Active site of receptor was studied for optimum binding with ligand. The designed analogues and known VEGFR-2 inhibitors were docked into active site of VEGFR-2 using *Glide* [Maestro® 7.5, Schrödinger, USA] docking module. ADME properties of designed molecules were predicted using QikProp (Schrödinger) module. Toxic properties of designed molecules were also predicted. Based on the scores of Glide and predicted ADMET properties, molecules were prioritized for synthesis.

Synthesis of chalcone analogues by aldol condensation of substituted ketones and aromatic aldehydes is in process.



Chalcone analogues

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P-71

A Novel Mucoadhesive Bio-Material From Fruit Pulp Of *Phoenix Dactylifera*

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The current aim of our research work is to isolate bio-polymer from the fruit pulp of *Phoenix dactylifera* and evaluate its mucoadhesivity. The bio- material was isolated by simple economical process. The isolated biomaterial was subjected for various physico- chemical tests like solubility, colour changing point, viscosity, surface tension & pH. The mucoadhesivity of the biomaterial was assessed by shear stress method and ex- vivo mucoadhesivity by rotating cylinder method using *Capra aegagrus* (goat) labium & intestine as a mucosal substrate. The result was compared with standard HPMC and sodium CMC.

Our experimental results revealed that the isolated biomaterial showed solubility in water. The color changing point is 230^0C and pH is 7.4. Its 1 to 5% concentration solution showed viscosity ranging from 1.1 to 1.72 cps and surface tension 76.38 to 67.91 dyne /cm. The shear stress study revealed that 5% concentration showed promising mucoadhesivity in comparison to standard HPMC and sodium CMC polymer. The *ex- vivo* release study with *Capra aegagrus* labial mucosa & intestinal mucosa revealed that the biomaterial is potentially mucoadhesively similar to HPMC and sodium CMC. Conclusion was drawn that the biomaterial can serve as a novel mucoadhesive agent.

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P-72

Synthesis Of Novel Hydroxypropyl Methylcellulose -Azo Polymer For Colon Specificity

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The current aim of our research work is to synthesize a novel azo polymeric complex by using HPMC and phenylalanine for colon targeting. HPMC was subjected for synthesizing its azo derivative by using phenylalanine, sodium nitrite, methanol and conc. hydrochloric acid. Methyl ester hydrochloride of phenylalanine was prepared by adding thionyl chloride to methanol and then refluxing with phenylalanine at 60-70^{o}C for 4 hours. It was diazotized by reacting with sodium nitrite and hydrochloric acid at 0-5^{0}C in ice bath. The diazotized salt was coupled with HPMC polymer in 2M sodium hydroxide under cold conditions by maintaining alkaline & cold environment throughout the reaction. The prepared azo derivative was separated, dried & recrystalized using methanol. It was evaluated for its physical properties like color, pH, solubility, colour changing point, viscosity and compared with hydroxypropyl methylcellulose. The *in-vitro* azoreductase effect on synthesized azo polymer was evaluated in rat fecal matter using Shimadzu 1800 UV spectrophotometer.

Our experimental results reveal that the novel HPMC- azo derivative showed modified solubility, physical appearance and colour changing point in comparison with hydroxypropyl methylcellulose. It also showed promising colon specificity. Finally, conclusion was drawn that the synthesized hydroxypropyl methylcellulose azo derivative can serve as a potential colon targeting polymer and it can be used as an excipient for formulating colon targeted drug delivery systems.

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P-73

Synthesis Of Some Suitably Substituted Pyrimidines For Their Antifungal Potential

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Azole derivatives (fluconazole, clotrimazole, econazole, ketoconazole, butoconazole, itraconazole, terconazole, miconazole and voriconazole) have displayed broad spectrum of antifungal activity and occupy a significant role in the antifungal chemotherapy. The pyrimidine, an enlarged ring size of imidazole by one carbon atom is not extensively exploited as antifungal agents. The antimicotic activity of azoles, encouraged us and we envisioned our approach toward to the synthesis of various 2-substitutedthio-4-chloro pyrimidine derivatives, to the study their antifungal activity and to explore their therapeutic potential as antifungal agents. 6- (3-Pyridyl) -2- thioxo-4- oxo-1*H,* 3*H*- pyrimidine-5-carbonitrile **(1)** was synthesized by the condensation of the equimolar ratio of ethyl cyanoacetate, thiourea and 3-pyridinecarboxaldehyde under basic condition. Compound **1** was then subjected to alkylation with alkyl/aryl halide at 0ºC to afford a series of 6-(3-pyridyl)-2- substitutedthio-4-oxo-3*H*-pyrimidine-5-carbonitriles **(2a-e).** Compounds **(2a-e)** were then converted into corresponding halocompounds, 2- substitutedthio-4-chloro-6-(3-pyridyl) pyrimidine-5-carbonitriles (3a-e) by refluxing with $POCl_3$. The structure of the synythesized compounds were confirmed an the basis of elemental and spectral data analysis. The synthetic procedure, characterization of the synthesized compounds and chemistry of these reactions will be the matter of our presentation.

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P-74

Synthesis and pharmacological evaluation of novel triazole containing Benzothiazole moiety

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The triazole analoues were obtained from multistep synthesis, initiated with ethyl nicotinoate (3) which converted to nicotinoyl hydrazide (4), which intermolecular cyclisation of (4) with 4-methylbenzoic acid in presence of phosphorous oxy chloride afforded 2-(3-pyridyl)-5-(4-methylphenyl)-1,3,4-oxadiazole (5) further condensed with various substituted 2-hydrazino benzothiazole 2a-j furnished 3-(3-pyridyl)-5-(4-methylphenyl)-4-(*N*-substituted-1,3-benzothiazol-2-amino)-4*H*-1,2,4-triazole 6a-j analogues. All the synthesized compounds have been established by elemental analysis, IR, NMR and Mass spectral data and have been screened for antifungal, antibacterial activities and antitubercular activity.

P-75

Sustainability Of Environmental Management Strategies Of Groundwater Pollution

Beena Rani*[1], Raaz Maheshwari*[2], Upma Singh[3], K K Jhankal[4]

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The block printing textiles from Sanganer & Bagru (Jaipur) have adorned the European markets from the time of the East India Company. But sofar, little initiative by the state government has been taken to check effluents contaminating the groundwater or ensure a sustainable future for the state's growing economy. The area has witnessed so many deaths and several persons being hospitalised in the past few years allegedly after consuming contaminated groundwater. Each stage in textile production produces waste that requires proper management. Especially the wet processes like dying emit VOCs. When these compounds percolate into water sources, becomes very harmful to the environment and health of the local and surrounding community as well. The textile wastescontaining organic pollutants and several indestructible inorganic toxicants viz. heavy metals such as Cu, Zn, Pb, Cr, Hg, metalloid as, even in small dose can disrupt the body's metabolic activities and get deposited in the kidneys, liver and some skeletal tissues. Oncedischarged into the pond/ lake, these effluents percolate to the surrounding soil, deteriorate the quality, texture and mineral content, and disturb the biological balance of the organisms, and impose lethal effect on the plant growth, development and productivity.Treatment processes for different types of effluents should ensure elimination or recuperation of the pollutant in order to reach the strict authorised levels for discharge of these effluents. Reduction,if not elimination of such pollutants can be achieved through a combination of resource management, process modification, and some end-of-pipe treatment. The established technologies are based on various processes viz. Oxidation (e.g. electrochemical, photochemical, biological and wet processes), evaporation, adsorption, coagulation, flocculation, and filtration, air/steam stripping, incineration, reverse-osmosis, capacitive-deionisation, electro-dialysis, and ion-exchange methodologies. The reaction rates are limited in the oxidation strategies. Recent R&D works indicate that rate limitations may be rectified and the cost of operation can be lowered if conventional oxidants are replaced by combination of oxidants and UV radiation. These processes are known as advanced oxidation processes [AOPs (-in principle, AOPs are characterized by high oxidation rates, flexibility small dimension of equipment and easy adaptability to water recycling process. For substrates that are biodegradable, biological treatmentcan be effective and inexpensive. The wisdom of using expensive chemical oxidants viz. KMnO4, O3/ H2O2,
to accomplish something which microbe could perform cheaper isquestionable. For a complex effluent containing degradable components, the possibility of only partially oxidizing the organics to enhance the biodegradability should be considered. This could be especially important for an industry with many waste streams of different compositions. Selectively treating waste streams to partially oxidize toxicants

followed by biological treatment of combined effluents could be an effective strategy. Some of the more commonly applied forms of this technology include: UV/O3, UV/H2O2, UV/TiO2 catalyst, and various forms of Green Fenton's chemistry)]. Oxidation at mild conditions by reactive species, such as .OH radicals (which attack most part of the organic molecules with little selectivity) generated by UV radiation in presence of oxidants such as O3 and/or H2O2 constitutes the basic idea of AOPs.
The conventional physical, chemical and biological methods are generally employed for wastewater treatment. Existing conventional treatment procedures suffer from some inherent drawbacks. For one, these methods don't destroy the organic pollutants but simply transfer the pollutant from one form to another. For example adsorption technique transfers the pollutant from liquid phase to solid phase without destroying them. Likewise, incineration converts water pollution problems to an air pollution problem. These methods may be employed to recover reusable or valuable components of wastewater at higher concentration levels, but are uneconomical at low concentration levels. Merits and demerits of other conventional methods have also been discussed in this manuscript. Various oxidation processes for environmental management, in general and photo-chemical oxidation (PCO), the latest method in the genre of advanced oxidation technologies having use of semiconductors, in particular, have been delineated.

P-76

Characterization of Novel Transfersomes, and their effectiveness against Resistant and Sensitive Clinical isolates of V. Leishmaniasis

D. Singodia, [1] G. K. Gupta,[1] V.Singh,[1] P. Shukla,[1] P.Misra,[2] S. Sundar,[3] A. Dube,[2] and P.R. Mishra[1, *]

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Aim of present study is to determine the in-vitro sensitivity of Leishmania donovani isolates (Antimony sensitive -2001 and resistant strain-2039) from Bihar VL patients with AmB bearing transferosomes (TF 3) in comparision to Ambisome and free AmB and also to evaluate transdermal efficacy of transferosomes in comparison to liposomes through in vitro franz diffusion cell. The flux value of transferosome [TF3] formulation was found to be 1.5 times compared to L1 formulation which could be ascribed to fluidized behaviour of TF3 imparted due to presence of SDC which facilitates penetration through skin and better partitioning in the skin layers. When formulations tested against *L. donovani* intramacrophagic amastigotes it has been observed that TF3 showed IC_{50} value of 0.22µg/ml while AMB solution (F-1) and Ambisome (F-2) formulation exhibited 0.45 and 0.3µg/ml respectively. It is evident that the activity of TF3 formulation was two times and 1.5 times compared to F-1 and F-2 respectively against sensitive strain. The IC50 value of TF3, F-1 and F-2 against resistant strain was found to be 0.26, 0.50 and 0.33 µg/ml respectively. It is interesting to note that TF3 formulation is more effective than F1 and F-2 formulation against both sensitive and resistant strain. Even in case of resistant strain the TF3 formulation is able to kill 50% of parasites at almost half of the concentration compared to F-1 formulation while when compared to marketed Ambisome® formulation the TF3 can kill the same population at 4/5th concentration of AmB. Result obtained in vitro point towards interest in Amphotericin B encapsulated in transferosomes in the chemotherapeutic control of leishmaniasis.

P-77

Escalating Groundwater Contamination Clinical Manefestations, Remediation Measures & Preventive Strtegies For Sustainable Future

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[1]Principal, Poornima College of Engineering, RIICO-Institutional Area(ISI-2), Goner Road, Sitapura, Jaipur
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Rapid industrialization, urbanization and domestic, agricultural, and traffic activities have lead to increased disposal of effluents and toxic solid wastes into the environment which in turn degrading aquatic ecosystem, terrestrial biota, and have become a matter of concern all over globe. Lakes, rivers

and oceans are being overwhelmed with indestructible inorganic, organic pollutants and pathogenic microbes. Toxicants viz. Heavy metals such as Cu, Zn, Pb, Cr, Hg, metalloid As, non metallic moieties e.g. fluorides, nitrates & pesticides, even in small dose can disrupt the body's metabolic activities and get deposited in the kidneys, liver and some skeletal tissues. The majority of the environmentalists, in the past were unable to bring enough to meet the solution for the contaminants perceived by the soil through percolating water carrying microbes and toxic substances. Soil receives large quantities of hazardous waste from different sources, and gets polluted. Soil pollutants deteriorate the quality, texture and mineral content of the soil, and disturb the biological balance of the organisms in it and have lethal impact on the plant growth and development. Besides the dumping of industrial wastes, urban wastes, agricultural practices, volatile organic compounds (VOCs), and radioactive wastes pollute the soil to a large extent. With increasing use of fertilizers, pesticides, herbicides and soil conditioning agents to increase crop yield, the soil contaminants have also increased. Fertilizes contaminate the soil with impurities which come from raw materials during their manufacture. For example As, Pb, and Cd present in rock phosphate mineral get transferred to super phosphate fertilizers. Some ions such as Co2+, Zn2+, Ni2+, Mn2+ etc are added to the soil as macronutrients, which in excessive amount accumulate far above the toxic levels. Unhealthy soil management methods have chronically threatened soil quality and increased polluted runoff into lakes, and streams. When toxicants enter lakes, streams, rivers, and other water bodies, they get dissolved or lie suspended in water or get on the bed, resulting in the pollution of water affecting aquatic ecosystem. The industrial wastes containing organic pollutants and several heavy metals in their effluents discharged into the pond/ lake percolate to the surrounding soil, affecting quality and productivity.

Treatment processes for different types of effluents should ensure elimination or recuperation of the pollutant in order to reach the strict authorised levels for discharge of these effluents.Reduction, if not elimination of such pollutants can be achieved through a combination of resource management, process modification, and some end-of-pipe treatment. The established technologies are based on various processes viz. Oxidation (e.g. electrochemical, photochemical, biological and wet processes), evaporation, adsorption, coagulation, flocculation, and filtration, air/steam stripping, incineration, reverse-osmosis, capacitive-deionisation, electro-dialysis, and ion-exchange methodologies. The reaction rates are limited in the oxidation strategies. Recent R&D works indicate that rate limitations may be rectified and the cost of operation can be lowered if conventional oxidants are replaced by combination of oxidants and UV radiation. These processes are known as advanced oxidation processes (AOPs). Oxidation at mild conditions by reactive species, such as .OH radicals (which attack most part of the organic molecules with little selectivity) generated by UV radiation in presence of oxidants such as O3 and/or H2O2 constitutes the basic idea of AOPs. The conventional physical, chemical and biological methods are generally employed for wastewater treatment. Existing conventional treatment procedures suffer from some inherent drawbacks. For one, these methods don't destroy the organic pollutants but simply transfer the pollutant from one form to another. For example adsorption technique transfers the pollutant from liquid phase to solid phase without destroying them. Likewise, incineration converts water pollution problems to an air pollution problem. These methods may be employed to recover reusable or valuable components of wastewater at higher concentration levels, but are uneconomical at low concentration levels. Merits and demerits of other conventional methods have also been discussed in this manuscript. Various oxidation processes for environmental management, in general and photo-chemical oxidation (PCO), the latest method in the genre of advanced oxidation technologies having use of semiconductors, in particular, have been delineated. In principle, AOPs are characterized by high oxidation rates, flexibility small dimension of equipment and easy adaptability to water recycling process. For substrates that are biodegradable, biological treatment can be effective and inexpensive. The wisdom of using expensive chemical oxidants viz. KMnO4, O3/ H2O2, to accomplish something which microbe could perform cheaper is questionable. For a complex effluent containing biodegradable components, the possibility of only partially oxidizing the organics to enhance the biodegradability should be considered. This could be especially important for an industry with many waste streams of different compositions. Selectively treating waste streams to partially oxidize toxicants followed by biological treatment of combined effluents could be an effective strategy. Some of the more commonly applied forms of this technology include: UV/O3, UV/H2O2, UV/TiO2 catalyst, and various forms of Green Fenton's Chemistry. Waste management includes recycle and reduction of waste at the point of its origin (waste minimization) and environmentally-friendly dispose of non recyclable wastes. Waste minimization or source reduction is

usually placed at the conventional waste management hierarchy. Source reduction affects the volume and to some extent the nature of the waste. There has been a tremendous growth in water consumption for industrial purposes in the past century. The steady growth in the water consumption, typically for most developed nations, has resulted from rapid industrialization. Growth in water usages by industries represents a growth in industrial production rather than the development of more water intensive technologies. Hence, water is being progressively polluted by the increasing industrial activities. Industrial wastewater treatment is one of the most challenging pollution related problems. Organic and inorganic toxicants present in wastewater though are present in very small amounts but are either not easily biodegradable or they possess a biocide character (e.g. C2H5OH and its derivatives). Therefore degradation of these compounds is a great concern.

P-78

Mapping of Fluoride Endemic Areas in Rae Bareli District

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The prevalence of fluorosis is mainly due to the consumption of more fluoride through drinking water. It is necessary to find out the fluoride endemic areas to adopt remedial measures to the people on the risk of fluorosis[1,2]. The objectives of this study are to mapping of fluoride endemic areas of some block of Raebareli district .The fluoride level in drinking water is estimated through SPADNS method. Google earth and isopleths technique were used for mapping of fluoride endemic areas[3,4]. From the study, it was observed that Dalmau and Amawa block of Rae Bareli district in Uttar Pradesh is highly fluoride endemic. About 80% of villages in these blocks have fluoride level more than the prescribed permissible limit in drinking water. Health risks due to fluorosis to the people in Amawa and Dalmau blocks have become evident. From the results, the people in Dalmau and Amawa blocks are advised to consume drinking water with fluoride level less than 1 mg/l. It has been recommended to the government authorities to take serious steps to supply drinking water with low fluoride concern for the fluorosis affected villages.

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P-79

Antinociceptive potential of *Saussurea lappa*

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The ethanolic extracts of the root of *Saussurea lappa*, was prepared and evaluated for their Antinociceptive potential. Both the chemical and thermal methods were used for the evaluation of

antinociceptive activity in swiss albino mice. The ethanolic extract of the root exhibited significant antinociceptive potential in both the test.

P-80

Synthesis of Previledged N-hetrocyclic Compounds through Novel Bridged Annulation

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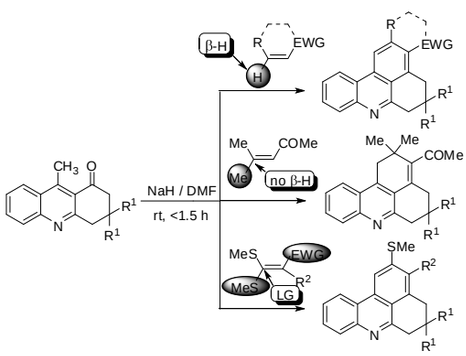
Quinoline, acridine and related *N*-heterocyclic systems like phenanthridine are key structural motifs found in a large number of biologically important natural alkaloids isolated from plant and marine sources and represent privileged scaffolds in medicinal chemistry.[1] Among them, those bearing an acridine moiety display a wide range of pharmacological activities such as antiviral, antimalarial, antihelmintic, antifugal, antitumor, and stimulative and other activities.[2,3]



In this presentation, we will present a general and novel 'bridged annulation' methodology for the synthesis of N-hetrocyclic Compounds such as 5,6-dihydro-4*H*-benzo[kl]acridines via Michael-Aldol reactions on 9-methyl-3,4-dihydroacridin-1(2*H*)-one with various cyclic or acyclic unsaturated carbonyl/nitrile compounds under mild conditions at room temperature in a short time[4].

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P-81

Electroorganic synthesis of some 2-amino-5-substituted-1,3,4-oxadiazoles at the platinum electrode

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The electroorganic synthesis of 2-amino-5-substituted-1,3,4-oxadiazoles have been synthesized by the electrochemical oxidation of semicarbazone at platinum anode at room temperature under controlled potential electrolysis in an undivided cell assembly. The electrolysis were carried out in non-aqueous medium acetic acid and lithium perchlorate was used as a supporting electrolyte This method is convenient and has a large benefit due to its broad applicability ease and safe handling of reagents

because of use of only simple solvent and electrolyte and there is no environmental hazards. This is an environmentally benign method in the field of electroorganic systhesis and a part of green chemistry.

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P-82

A simple method for the spectophotometric determination of Cefixime in pharmaceuticals using variamine blue

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A simple specrtophotometric method for the determination of Cefixime with variamine blue is presented. The determination is based on the hydrolysis of β-lactum ring of Cefixime with sodium hydroxide which subsequently reacts with iodate to liberate iodine in acidic medium. The liberated iodine oxidizes variamine blue to violet colored species of maximum absorption at 572 nm. Beer's law is obeyed in the range pH range of 0.5-5.8 µg/mL for Cefixime. The analytical parameter was optimized and the method is successfully applied for the determination of Cefixime.

P-83

Self Organizing Molecular Field Analysis towards Antitumor Activity of Hydroxamic Acids in Vitro: 3D-QSAR Approach

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Hydroxamic acids a group of very weak organic acids of general formula $R_1NOH{\cdot}R_2C(=O)$, where R_1 and R_2 are phenyl or substituted phenyl groups, are associated with diverse biological activities including antibacterial, antifungal and antitumor profiles.

Self organizing molecular field analysis (SOMFA), is used to generate three-dimensional quantitative structure-activity relationship (3D-QSAR) models for log $1/IC_{50}$ values of hydroxamic acids against human adenocarinoma cells A431 in vitro. The best SOMFA model obtained with cross-validation q^2 (0.658) and non cross validation r^2 (0.859), shows a good predictive ability. The analysis of SOMFA contour maps provided insight into the possible modification of the molecules for better activity.

P-84

Antioxidant Activity Of Some Novel 2-Substituted-4, 5-Diphenyl Imidazole

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There is an increased evidence for the participation of free radicals in the etiology of various diseases like cancer, diabetes, cardiovascular diseases, autoimmune disorders, neurodegenerative diseases, aging, etc. An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules which scavenge the free radicals and prevent the damage caused by them. Imidazole derivatives having wide

range of biological activities including analgesic and anti-inflammatory, antiparasitic, antitubercular, antiviral, anticonvulsant and insecticidal agents [1]. In view of such reports, the present work is designed for synthesis of various 2-substituted-4, 5- diphenyl imidazoles and evaluates their antioxidant activity.

Here 2-substituted-4, 5-diphenyl imidazoles were prepared by refluxing benzil with substituted aromatic aldehyde in presence of ammonium acetate and glacial acetic acid and recrystallized by ethanol [2]. The structures of the synthesized compounds were confirmed on the basis of IR, ^{1}H NMR and mass spectral data. The antioxidant activity of the synthesized compounds (**1a-d**) was evaluated using DPPH method. All the prepared compounds have been diluted in absolute ethanol to get 250, 100, 50 and 10 µg/mL concentrations. DPPH solution (2 µ mol) has been prepared by absolute ethanol. Then 0.5 ml of DPPH solution (freshly prepared) were added 0.5 mL of DPPH solution and 0.5 mL of absolute ethanol were used as control. Ascorbic acid was used as reference standard. All the compounds showed antioxidant activity, among them 2-(2-methoxyphenyl)-4, 5-diphenyl imidazole (**1b**) and 2-(3-chlorophenyl)-4, 5-diphenyl imidazole (**1c**) showed excellent activity when compared with reference standard, Ascorbic acid.

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P-85

Bioanalytical Method Validation: A Tool For Pharmacokinetic Studies

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Pharmacokinetic studies invariably begin with the development of an analytical method for the quantitative determination of drugs and their metabolites in biological samples. The most widely employed bioanalytical techniques include, but are not limited to, conventional chromatographic-based methods (such as GC and HPLC), mass spectrometry-based methods (such as GC-MS and LC-MS), and ligand-based assays (such as radioimmunoassay [RIA] and enzyme-linked immunosorbent assay [ELISA]). It is therefore important to validate the analytical method in biological fluids as the method must generate reproducible and reliable data in order to permit valid interpretation of the studies they support.

There are two distinct phases of bioanalytical method validation (1) analytical method development (pre-study validation), where the appropriate bioanalytical method with its various parameters is developed, and the assay is defined; and (2) application of the bioanalytical method to actual analysis of samples from bioavailability, bioequivalence, and pharmacokinetic studies. Many of the principles, procedures, and requirements for quantitative bioanalytical method validation are common to all types of analytical methodologies. Bioanalytical method validation includes all of the procedures that demonstrate that a particular method used for quantitative measurement of analytes in a given biological matrix, such as blood, plasma, serum, or urine, is reliable and reproducible for the intended use (FDA 2001; Shah 2007; Vishwanathan 2007). In general, the parameters evaluated for quantitative procedures are selectivity, calibration model, stability, accuracy (bias, precision) and limit of quantification. Additional parameters which might have to be evaluated include limit of detection, recovery, reproducibility and ruggedness (robustness). Current pre-study acceptance criteria for bioanalytical methods require the observed mean concentration from the quality control (QC) samples to be within ±15% of the nominal value and the observed precision to be ≤15% coefficient of variation, though these limits are both 20% at the lower limit of quantification. The current in-study acceptance criteria for monitoring require that at least four of every six QC samples must be within 15% of their respective nominal concentration (FDA 2001). Analytical runs failing this criterion must be rejected. Therefore, it is essential to employ well-characterized and fully validated analytical methods to yield reliable results that can be satisfactorily interpreted. The details will be presented.

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P-86

Survey Of Dispensing Prescription Drugs Without A Prescription In Four Community Pharmacies Of Dehradun District Of Uttarakhand

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Three months study was carried out in four community pharmacies of the Dehradun to determine the dispensing pattern of schedule H drugs and reasons for dispensing such drugs with out a prescription and to determine whether the drugs are dispensed as per prescription issued by the doctor .The study was carried out by viewing the customers for three months in each of the community pharmacies. And the customers who visited the community pharmacies without a prescription were interviewed and data were documented in a prepared proforma. It was noted that in all the community pharmacies drugs were being dispensed without a prescription and more number of schedule H drugs were dispensed with out a prescription as compared to over the counter drugs at a ratio of 3.29:1 (553:168). The major influencing factors contributing for purchase of schedule H drugs was the previous prescription issued by the doctor. The study reveals that the drugs belonging to the category of schedule H were more dispensed without a prescription in all the community pharmacies and the factors that influence such dispensing lies on part of pharmacist and hence such unethical practice can be prevented by the pharmacist and the Government drug control authorities can also play an important role by enforcing strict rules in India. These efforts will definitely help in promoting rational dispensing practice and will minimize the harmful effects of the drugs.

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P-87

A Simple and Efficient Green Approach to Dihydro-1,3-oxazines.

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Dihydro-1,3-oxazines have occupied an unique place in medicinal and material chemistry because of their valuable pharmaceutical and material properties. These molecules are known to exhibit various pharmacological properties such as antitumor [1], anti-HIV [2], antimicrobial activities [3,4] and potent non-steroidal progesterone receptor agonist [5]. In addition, dihydro-1,3-benzoxazines have been very useful in making polybenzoxazines, which display remunerative properties ranging from small shrinkage in curing, low water absorption, good thermal stability, no release of volatile materials during cure, no need of catalyst and inexpensive raw materials [6]. The synthetic development for the preparation of these molecules began in the middle of 19th century, when Burke and co workers reported the one-pot three-component synthetic protocol for the preparation of these molecules, by reacting phenols or naphthols with formaldehyde and primary amines [7,8]. Later, various synthetic procedures have been developed by several investigators including reaction under neat conditions [9]. However, many of these methodologies are associated with several drawbacks such as prolonged reaction time, use of volatile and highly inflammable organic solvents and alkaline media. Thus the development of simple and environmentally benign synthetic methodology for the synthesis of these molecules is highly desirable. In continuation of our efforts to devise a simple and economical synthetic protocol for the construction of biologically important molecules, we have successfully developed an eco-friendly synthetic strategy [10] for the

synthesis of various dihydro-1,3-oxazine derivatives in aqueous media. The synthesis and characterization of these compounds will be discussed in the poster.

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P-88

Synthesis And Anticancer Activity Of Novel 4-(3′-Indolyl)Oxazoles

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Oxazole heterocycle is a basic building block for many of the natural products and biologically important compounds [1]. In particular, indolyl azoles have received significant attention during the last decade due to their diverse biological activities [2]. Many natural products containing 5-(3′-indolyl)oxazole ring system such as pimprinine, pimprinethine, pimprinaphine have been isolated and identified as potent anticonvulsant agents. Recently reported 5-(3′-indolyl)oxazoles such as Laboradorin 1 and Laboradorin 2 were isolated from Pseudomonas *syringae pv. Coronafaciens* and found to exhibit cytotoxicity against cancer cell lines [3]. Our interest to design small molecules as anticancer agents, recently we have reported indolyl-1,3,4-oxadiazoles and 1,2,4-oxadiazoles as potent anticancer agents [4, 5]. In view of interesting anticancer activities of 5-(3′-indolyl)oxazoles, we have prepared a series of isomeric 4-(3′-indolyl)oxazoles and studied for their cytotoxicity against six different cancer cell lines. Our facile synthesis for the preparation of 4-(3′-indolyl)oxazoles involve the microwave-accelerated neat reaction of 3-tosyloxyacetyl-1-benzenesulfonylindole with amides followed by deprotection of sulphonyl group using NaOH in refluxing ethanol. Details of this synthetic protocol and anti-cancer activity will be discussed in the presentation.

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P-89

A One-Pot Facile And Expeditious Synthesis Of 1,4-Diaryl-1,2,3-Triazoles

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With increasing stringent regulatory considerations, the development of environmentally benign, efficient and economical methods is vital and challenging in organic synthesis. From this perspective, multicomponent reactions (MCRs) in benign media are particularly worthwhile due to their atom economic, high convergence, and less laborious process [1]. Click chemistry has been explored as a newer approach for the synthesis of drug-like molecules that can accelerate the drug discovery process by utilizing a few practical and reliable reactions [2]. In our efforts [3] to develop environmentally benign and sustainable protocols for the synthesis of 1,4-diaryl-1,2,3-triazoles using click approach, we have achieved a new sequential one pot reaction of diaryliodonium salts, sodium azide and terminal alkynes in the

presence of Cu(I) as a catalyst by *in situ* generation of aryl azides followed by coupling with terminal alkynes. More information about this work will be detailed in the poster presentation.

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P-90

3,5-Disubstituted-1,2,4-Oxadiazoles As Potential And Selective Anticancer Agents

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Cancer is a fatal disease that has posed serious threat to human health. Many classes of anticancer drugs have been developed. However, most drugs cause undesirable side effects due to lack of tumor specificity and multidrug resistance. The development of safer and selective anticancer agents remains a major challenge. 1,2,4-oxadiazole scaffold attracted the attention of medicinal chemists to develop novel therapeutic agents because of its unique chemical structure and broad spectrum of biological activities. They are well documented in literature for tyrosine kinase inhibition, muscarinic agonism, histamine H_3 antagonism, antiinflammation, antitumor, and monoamine oxidase inhibition [1]. This important class of heterocycle also widely used as bioisosters of amide or ester and in the design of dipeptidomimetics as peptide building blocks [2]. In continuation of our efforts to search for an effective anticancer agent [3], we have synthesized a series of novel 1,2,4-oxadiazoles and screened them for their anticancer potential in various human cancer cell lines: prostate (PC3, DU145 and LnCaP), breast (MCF7 and MDA231), colon (HCT116), and pancreas (PaCa2). The screening results were very encouraging and the best compound exhibited significant activity against prostate cancer cell line, LnCaP (10 nM), with 450 fold selectivity [4] Among seven other cancer cell lines. Results will be discussed during paper presentation session.

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P-91

$Cu(Otf)_2$ Promototed Synthesis Of Bis(Furyl)Methanes Under Solvent Free Condition

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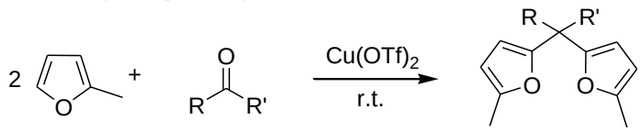
Bis(furyl)methanes are industrially important compounds and their synthesis is an important and challenging goal. Bis(furyl)methanes are used in food industry [1], dye chemistry and these are main component of a number of fungicides [2]. Bis(furyl)methanes are also used as an intermediate for the synthesis of tetaoxaquaterenes and other macromolecules which are used as a metal ion carriers. Furan ring is highly reactive towards electrophilic aromatic substitution and it produces polymers and unwanted decomposed materials under normal Lewis acid conditions. Metal triflates are reported to be unique and mild Lewis acids catalysts and promote various carbon–carbon and carbon-hetero atom bond forming reactions [3].

In continuation of our efforts towards development of greener reaction methodologies [4], we have developed an efficient and solvent free synthesis of bis(furyl)methanes in the presence of $Cu(OTf)_2$ (Scheme 1). It was found that 10 mol % of $Cu(OTf)_2$ was enough to accomplish the bis(furyl)methanes in 45-72 % yield at room temperature. It is expected that the reaction proceeds through the formation of furfuryl alcohol derivative followed by condensation with another molecule of carbonyl compound. The main advantages of the method are mild, clean and solvent-free reaction conditions, good to excellent yields and an environmentally benign catalyst.



Scheme 1

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P-92

An Expeditious One-Pot Synthesis Of 3-Substitued Indoles Catalyzed By $Yb(Otf)_3$-Sio_2

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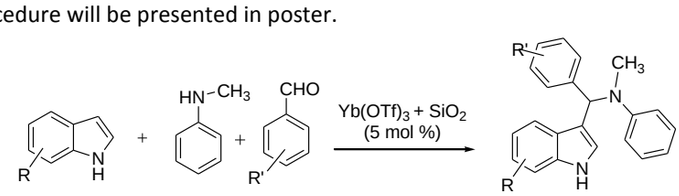
Multicomponent reactions have been playing a powerful role in preparation of industrial and medicinal scaffolds. They are powerful tools for producing diverse array of compounds in one step and high yields. Substituted indoles are important in drug discovery because of their diverse biological properties [1]. They have been shown to possess anti-cancer and kinase inhibition activities. Due to their importance in drug discovery many synthetic routes have been reported for their synthesis [2]. However, most of these methods are associated with one or more problem from environmental point of view such as relatively long reaction time, harsh reaction conditions and toxic aqueous waste resulting from the catalyst. Thus, development of mild, simpler and more efficient methods are still desirable for the sysnthesis of 3-substituted indoles.

In continuation of our efforts towards the development of environmentally friendly organic transformations catalyzed by metal triflates, we have developed an expeditious one pot synthesis of 3-substitued indoles by three component condensation catalyzed by $Yb(OTf)_3$-SiO_2 (Scheme 1) under solvent free conditions. Various metal triflates were screened for this transformation and 5 mol % ytterbium triflate absorbed on silica gel was found to give best yield. Details of the reaction conditions and experimental procedure will be presented in poster.



Scheme 1

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P-93

Facile Synthesis Of Substituted Pyridines From Unsaturated Ketones

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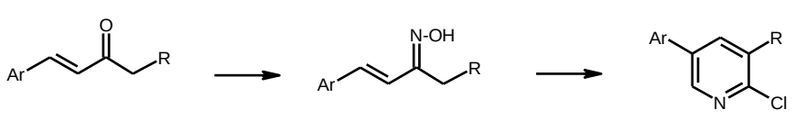
Pyridines are of great interests because of the occurrence of their saturated and partially saturated derivatives in biologically active compounds and natural products. Moreover, synthetically obtained pyridine molecules also received a great deal of attentions due to their therapeutic importance [1]. Literature reveals the existence of some benzopyrano[2,3-b]pyridine scaffolds of synthetic origin, which possess cancer chemopreventive, antibacterial, hypotensive, anti-rheumatic and anti-asthmatic activities [2]. Some biologically active pyridine molecules, as for example amlexanox inherits anti-allergic activity, 2-substituted arylimidazo[4,5-b]pyridines possess anti-bacterial property, 6-substituted-2,4-dimethyl-3-pyridinols possess antioxidant activities and imidacloprid exhibits insecticidal activity [3]. Due to biological importance of substituted pyridines, significant work has been carried for the development of newer synthetic strategies. Earlier, we have developed novel strategies for the synthesis of steroidal and non-steroidal pyridines from beta formyl enamides using inverse electron demand Diels-Alder reaction, Henry reaction and microwave promoted Knoevenagel condensation reactions [4-6]. We have recently reported a microwave promoted and Lewis acid catalysed synthesis of 2,4,6-triarylpyridines using urea as benign source of ammonia [7]. In continuation of our interests on development of novel synthetic methods for substituted pyridines, we report herein a facile two-step synthesis of 2-chloro-3-alkyl-5-arylpyridine from conjugated ketones in high yields.



R = Me, Et, i-propyl
Ar = Ph, p-tolyl

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P-94

Microwave assisted Synthesis and Evaluation of Carboxymethylated Sago starch for Pharmaceutical Application

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In the present work, carboxymethylated sago starch (CSS) was synthesized using native Sago starch (SS) and monochloroacetic acid (MCA) with sodium hydroxide in microwave radiation environment.FT-IR analysis of the sample confirmed the carboxymethylation by showing absorption peak at 1425 cm^{-1} and 1622.1 cm^{-1}. CSS with degree of substitution (DS) of 0.21 was formed and, it was further evaluated as disintegrant in Ondasetron based tablets. Ondasetron tablets were prepared with 2, 4, 6 and 8% w/w of CSS as disintegrant and were comparatively evaluated with established Sodium starch glycolate (SSG) in

same concentration. The results revealed that CSS could be used as superdisintegrant in tablet formulation in concentration dependant manner.

P-95

Anthelmintic Activity Of The Roots Of *Rotula Aquatica Lour*.

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Rotula aquatica Lour belongs to family borogenaceae known in Ayurveda as pashanbed.it was collected from the ganges of river Netravati Manglore District authenticated and dried under sun ,powdered and extracted with various solvents by successive soxhlet hot extraction process with increasing order of polarity on phytochemical investigation , the petroleum ether extract and alcoholic extracts has shown alkaloids and flavone glycosides so the drug is screened for anthelmintic activity on adult earth worms pheritma posthuma, using albendazole as standarded drug.Both petroleum ether and alcoholic extract has shown significant anthelmintic activity compared to standared drug albendazole.

P-96

Targeting Aniline Mustard Across Brain By Reversible Redox Drug Deliver

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Central Nervous Disorder (CNS) disorders are major causes of mortality and disability and are predicted to become the major medical need of the 21st century according to WHO. The worldwide market for therapies for central nervous system disorder is worth more than $ 50 billion and represents the fastest growing segment of the total pharmaceutical market[1]. Brain tumour is one of the major classes of CNS disorder. Brain tumour is:

1. Second most common malignancy of childhood, most common solid tumour.
2. Second leading cause of cancer related deaths in males age 20-40.
3. Fifth leading cause of cancer related deaths in women age 20-40.

Objective:

Aniline mustard has been recognized for its experimental antitumour activity and has also shown useful clinical results. But it is too polar to cross the highly lipophilic Blood Brain Barrier. Due to its necessarily high chemical reactivity, it is preferentially toxic to proliferating normal cells outside the brain such as those in the intestine, the bone marrow, and the mucosa and cause undesired side-effects2. So it was aimed to target the aniline mustard specifically to brain by dihydropyridine↔pyridinium salt redox system3 for the specific delivery and sustained release of a bis-(2-chloroethyl)amine as anticancer moiety to the brain as the initial effort in a search for agents that may prove effective as CNS antitumour agent.

Method: The cytotoxic moiety aniline mustard instead of direct coupling with nicotinic acid is synthesized in series of reactions to form the final desired compound 1-methyl-3-[4-[N,N-Bis(2-chloroethyl)amino]carbamoyl]-1,4 dihydropyridine (5), by four steps. The p-chloroamino-nicotinamide (2), obtained by reaction of p-chloroaniline with nicotinic acid in the presence of DCC, which was converted in quantitative yield to [4-[N,N-Bis(2-chloroethyl)amino]carbamoyl pyridine (3). The compound (3) was converted into 1-methyl-3-[4-[N,N-Bis(2-chloroethyl)amino]carbamoyl]-1,4-dihydropyridiniumiodide (4) on treatment with methyl iodide in acetone. Reduction of the latter with sodium dithionite gave the final compound, (5). Structures of all the synthesized compounds were confirmed by U.V., I.R., and 1H N.M.R. techniques.

Result: T he in vitro chemical oxidation studies with silver nitrate showed that target drug (5) could be oxidized into their corresponding quaternary compounds (4) at an adequate rate, which ensure the release of the carried

anticancer drug. The in vivo studies by reverse phase HPLC studies on temporarily restrained male wister rats showed that compound (5) was able to cross the BBB at detectable concentration. The study of some physicochemical properties calculated by online software such as lipophilicity, rule of five, number of NH or OH hydrogen bond donors, and nON value also indicates that it can be a potential candidate for targeted and sustained delivery of anticancer agent to the brain for the treatment of brain tumor

Conclusion: Conclusively, the studies demonstrated successful targeting of alkylating anticancer agent, aniline mustard, to brain as a novel strategy to treat brain tumour.

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P-97

Polymer-Supported Lewis Acid as a Convenient and Efficient Catalyst for Synthesis of 1,5-Benzodiazepine

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Benzodiazepines and their derivatives continue to attract considerable attention of medicinal/organic chemist because of their medicinal properties [1], and industrial use [2]. Moreover, 1,5-benzodiazepines are valuable synthons used for the preparation of other fused ring compounds such as triazolo, oxazino, and furano-benzodiazepines. Thus, the synthesis of these heterocyclic nuclei is still of much interest. The use of catalysts provide easy and faster way of synthesis and different metal salts have been exploited as Lewis acid catalyst in variety of organic transformation from this laboratory [3].

We herein report synthesis of 1,5-benzodiazepine derivatives using catalytic amount of polymer supported Lewis acid (10 mol%) in good to excellent yields at room temperature in the presence and absence of solvent. The reaction proceeds well with versatile substrates and bearing heteroaromatic moieties to form highly functionalised 1,5-benzodizepine.

The advantages of this protocol includes (i) the use of air-stable, recyclable catalyst, (ii) operational simplicity, (iii) short reaction times and (iv) high yields of the product providing means towards the fulfillment of the 'triple bottom line philosophy' of the green chemistry [4].

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P-98

Facile and Efficient Synthesis of Functionalised Pyridines Catalysed by Recyclable Protic Acids on Solid Support

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Functionalised pyridines are well known for their potent biological properties such as topoisomerase I & II inhibitors [1], serine/threonine kinase Akt inhibitors [2], cyclooxygenase inhibitors [3] and anti-tumour activity [1] etc. These, necessitates the development of new catalytic procedure for convenient synthesis of 2,3,6-trisubstituted pyridine. The heterogeneous catalysts are leading contenders for green synthesis [4] due to the potential benefits as they can be reused and easily separated from the end products by filtration. Continuous efforts have been directed from this laboratory for the use of clays as

heterogeneous catalysts for various organic transformation useful in the preparation of drugs and drug intermediates [5]. Supported protic acids constitute a new class of heterogeneous catalysts systems. These laboratory has discovered two novel catalysts systems [6] e.g., $HClO_4$-SiO_2 and HBF_4-SiO_2 that are being used for variety of organic reactions [7]. Herein we wish to describe a highly efficient multi-component procedure for the synthesis of 2,3,6-trisubstituted pyridines catalysed by supported protic acids having the following distinct advantages: (i) use of a cheap, non corrosive and reusable catalyst, (ii) operational simplicity: ease of catalyst preparation/handling, product isolation/purification, (iii) solvent free and short reaction times, (iv) multi-component reaction affording the product formation in one pot, and (v) high yields that offer promise for the fulfill the requirement of the 'triple bottom line philosophy' of the green chemistry [8].

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Design and Synthesis of New Pyranone-Derived Antihyperglycemic Agents

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In current scenario, the treatment of type 2 diabetes has been revolutionized with the advent of thiazolidinedione (TZD) class of drugs (rosiglitazone, pioglitazone) that ameliorate insulin resistance and thereby normalize elevated blood glucose levels,[1] but these drugs are associated with risk of hepatotoxicity, weight gain, and edema.[2] The alarming situation emphasized the need to discover new antihyperglycemic agents with reduced or no hepatotoxicity. One such alternative is to explore antidiabetic leads from traditional sources, identify a pharmacophore-based scaffold, which not only retain blood sugar lowering activity but are also known as hepatoprotectants.

Thus, we envisaged that the simulation of natural**/**synthetic hepatoprotective agents with pharmacophoric moieties of known antidiabetic drugs would be an interesting scaffold to examine the antihyperglycemic activity.[3] On the basis of information available on various active PPARs ligands, we designed and synthesized new pyranone based antihyperglycemic agents. Some of the new synthesized compound showed good activity in *in vitro* adipocyte differentiation assay and significant antihyperglycemic activity in *in vivo* models.

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P-100

DNA Microarray Technology in Drug Development

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On the contrary to slow and non specific traditional drug discovery methods, DNA microarray technology could accelerate the identification of potential drugs for treating diseases like cancer, HIV and provide fruitful results in the drug discovery. Microarray analysis allows scientists to understand the molecular mechanisms underlying normal and dysfunctional biological processes. It has provided scientists with a tool to investigate the structure and activity of genes on a wide scale. The technique provides efficient automation and maximum flexibility to the researchers and can test thousand compounds at a time. DNA microarray can be useful in disease diagnosis, monitoring desired and adverse outcomes of therapeutic interventions, as well as, in the selection, assessment and quality control of the potential drugs. In the current scenario, where new pathogens for example human mutant of the bird-flu virus, H5N1, are expected every year, DNA microarray promises as an efficient technology to detect new organisms in a short time. Classification of carcinomas at the molecular level and prediction of how various types of tumor respond to different therapeutic agents can be made possible with the use of microarray analysis. Also, microarray technique can prove instrumental in personalized medicines development by providing

microarray data of a patient which could be used for identifying diseases, treatment specific to individual and trailing disease prognosis. Microarray analysis could be beneficial in the area of molecular medicines for analysis of genetic variations and functions of genes in normal individuals and diseased conditions. The technique can give satisfactory results in single nucleotide polymorphism (SNP) analysis and pharmacogenomics studies i.e. correlation between therapeutic responses to drugs and genetic profiles of the patients. The challenges that arise with the technology are high degree of variability in data obtained, frequent upgradation of methods and machines and lack of trained manpower. Despite this, DNA microarray promises to be the next generation sequencer which could explain how organisms evolve and adapt looking at the whole genome. The present paper focuses on DNA microarray technology as an automated process for screening of compound targets, diagnostic and drug development with improved efficiency, quality and reliability of data, helping to reduce overall cost of research and development.

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P-101

Challenges Associated With Nanotech In Medicines

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Nanomedicines will usher human beings in a new area in health care that will be highly accurate, less painful, less toxic and with fewer side effects than their current counterpart.

Application of nanotechnology in medicines currently being developed employing nano-particles to deliver drugs, heat, light or other substances to specific cells in the human body. These nanomedicines allow detection and treatment of diseases and injuries within the targeted cells, thereby minimizing the damage to healthy cells in the body. Despite the enormous promises of nanomedicines, there are serious considerations regarding the health and safety aspects of nanotech in medicines. There is a fine line between medical and nonmedical uses of nanotech for diagnostic, therapeutic and preventive purposes. The sensitivity associated with the use of nanomedicines can be observed in making intentional changes in the body, creation or improvement of bodily parts that were undamaged. This gives rise to a debatable topic of Transhumanism and many related unethical issues. Possible dangers that can arise with development in nanomedicines are 'bioweapons' which can be used as untraceable weapon of mass destruction. Nanoscopic robots repairing the human body autonomously, the same medical nanobots could be turned into nanoviruses, spreading uncontrollably and there is no way to protect against them. Nanomedicines have captured the scenario along with their unintended adverse effects. Major risks associated with nanomedicines include mesothelioma, cancer, asbestosis, thallidomide and bovine spongiform encephalopathy. Some recently developed nanomedicines might have unpredictable consequences like destruction of beneficial bacteria in body, increase in biomarkers for inflammation and stress response and serious lung disorders. Other than obvious potential risks to patients, there are other toxicological Risks associated with nanomedicines. There are also valid concerns over the disposal of nanowaste and environmental contamination from the manufacture of nanomedical devices.

Therefore with bigger opportunities come the greater responsibilities. Hence wise, careful and judicious implementation of nanomedicines is essential to safeguard the hazards that popped up with the development of nanotech in medicines.

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P-101

Microwave Assisted Synthesis Of [5-Chloro-3-Methyl-7-Aryl-7*h*-Furo [3,2-*G*]Chromen-2-Yl](Phenyl) Methanones And Their Antibacterial Activity

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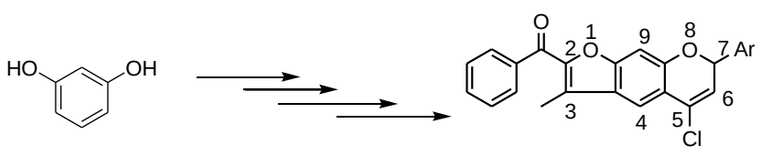
Heterocyclic compounds play a vital role in biological systems. Many natural products like vitamins, antibiotics, amino acids, plants pigments, nucleic acids, drugs contain heterocyclic moiety. Chromenes and fused chromenes are biologically potential compounds with antibacterial, antifungal, antitumor, antiviral activities. A number of benzofuran derivatives have been reported to possess a wide variety of biological activities such as antiinflammatory, antifungal, antibacterial, antiallergic, estrogenic and antiimplantation properties. In recent years microwave assisted organic synthesis (MAOS) has gained popularity as an environmental benign technology. In view of the potential bioactivity of chromene and benzofuran moieties, we have taken up the microwave assisted synthesis of some new [5-Chloro-3-methyl-7-aryl-7*H*-furo [3, 2-*g*] chromen-2-yl] (phenyl) methanones. All the compounds were screened for their antibacterial activity.

Scheme:



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Green Chemistry Techniques In Organic Synthesis

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Organic Chemistry is *the* heart of our societies as it provides a multitude of consumer goods without which modern life would not have been possible. Organic compounds display a wide variety of biological properties, many of which can be exploited for medicinal purposes and are also essential for the human well-being. Therefore methods for the synthesis of such systems are of significant interest. The environmental protection has become a global concern and the synthetic organic chemists are searching the ways of developing and applying more efficiently and environmentally benign strategies for future sustainable growth. One of the thrust areas for achieving this target is use of **Green Chemistry Techniques in Organic Synthesis.** In recent years, Microwave Assisted Organic Synthesis (MAOS), Ultrasound Assisted Organic Synthesis (UAOS), Ring Closing Metathesis (RCM), Aqueous Phase Organic Synthesis (APOS), Solvent Free Organic Synthesis (SFOS), Enzyme Catalyzed Organic Synthesis (ECOS) attracted the attention of organic chemists**.** The salient features of these methodologies are enhanced reaction rate, easy workup, high yields, operational simplicity, greater selectivity and experimental ease of manipulation, low cost and economy. In view of these advantages of the above environmental benign approaches and as a part of our ongoing research programme towards the non traditional methods, the concept of Green synthesis has been adapted for the rapid and efficient synthesis of some novel heterocycles of biological interest. All the compounds screened for anti-bacterial and anti-feedant activities.

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Brand Name Designing Of Pharmaceutical Companies

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The main objective of this study is to find out the brand name designing of pharmaceutical companies and to study the brand elements. Brand is name, term, sign, symbol, intended to identify goods and service of one seller and differentiate them from those of competitors. Top 40 internationally successful pharmaceutical brands were selected for the study. Brand name was analyzed against its designing based on the parameters of drug name, company name, disease, uniqueness; simplicity of the brand. Collected information was converted into data. Results were derived by using Percentage method. Now days designing brand name is crucial and contributes in the success of drug. To stay in competition pharmaceutical companies working heavily to keep brand name of their product. The brand is also providing differentiating factor from their competitors. This study reveals that 43.0% of the multinational companies keep unique brand name of their drugs i.e. they are not keeping brand name of drug based on either Mechanism based or Drug name based or Disease name or combination of drug name, company name and disease name. It is also evident that near about 32.0% of companies keeping drug name as the brand name. The trend of keeping either mechanism based brand name is 10.0%or disease based brand name is 9.5%. At the same time near about 2.5% of companies keeping drug name and company name or drug name and disease name.

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P-104

Ipr Issues Related To Microbes And Microbial Processes In India

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Patenting of microorganisms and their related processes and products deliberates that whether the term microorganism should be defined in a generic manner or not. The technical complexity involved in the patenting of microorganisms confines to not only patent documents and claims but also R&D and trade. Detailing of requirements for the deposition and the rules for accessing microorganisms from depositories are distinct according to the legal practices of the developing and developed countries (1). The Budapest Treaty identifies the regulatory guidelines to build an internationally recognized depository for facilitating patenting of microorganisms and microbiological inventions. These International Depository Authorities accept patent deposits of bacteria, virus, fungi, protozoa, algae, plant and animal virus etc. and also takes care of the biosafety aspect (2, 3). The biosafety requirements signify a key aspect in processes patenting in respect of microbiological inventions involving GMOs (Genetically Modified Organisms) (3). In a developing country like India microorganisms and genes do not have any protection through patents in spite of its dependence on agriculture. Hence it becomes essential for implementing a criterion of novelty and inventiveness of the microbial wealth substantiated by an integrated approach of scientists, technologists, legal professionals, science managers and policy makers. The present paper endeavors to create awareness among scientists and technologists in the area of biotechnology and the urgent need for training patent examiners and attorneys to entail modern and complex scientific concepts and methodologies which decides our R&D goals and corporate objectives in attaining IPR.

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P-105

Modified Nucleic Acids: Drug Targets For Complex Diseases

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Modified nucleic acids elucidate a widespread mechanism for coordinated regulation of gene expression in case of a variety of diseases such as cancer, obesity, diabetes, vascular diseases, inflammation, angiogenesis, schizophrenia and control and self renewal of stem cells. Pharmacogenomic aspects like miRNAs, siRNAs, natural antisense interactors (antisense oligonucleotides & anti-mRNA oligonucleotides), locked nucleic acids, antagomirs, viral vectors expressing miRNA genes, etc. are tools deciphering the role of specific genes which act as critical players in functional metabolic pathways (3). The gene regulated expression links with viral disease, neurodevelopment and cancer as in case of chronic lymphocytic leukemia, colonic adeno carcinoma and Burkiff lymphoma. These expressed genes function as oncogenes and/or tumor suppressors. Potential gene-targeted drugs such as Thioacetamide nucleic acids (TANA) target complementary DNA and RNA sequences in thermal stability studies. The high binding affinity of TANA with RNA also blocks protein expression of specific genes in melanoma metastasis (1). Targeting chromosomal sites with locked **nucleic** acid-**modified** triplex-forming oligonucleotides (TFO) is another example in which sequence-selective compounds target chromosomal DNA modulating gene structure and function in living systems (2). Modified nucleic acids are potential gene-targeted drugs which along with aids like microarrays, PCR treatment, Genome Analyzer, etc. project an accurate insight into disease processes. The present paper focuses on the role of nucleic acids as a concise set of biomarkers which could expedite the discovery of useful targets for diagnostics, target validation and modulation of gene structure for complex diseases.

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P-106

Carbohydrate Building Block In The Ugi 3cc Reaction: The First Annulation Of Iminosugars On Imidazoles

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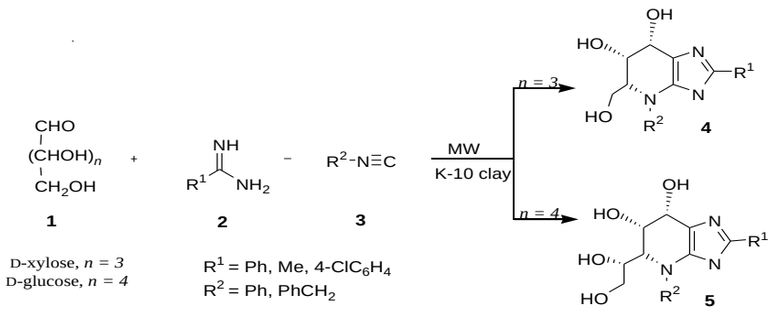
Iminosugars are arousing a great interest as potential therapeutic agents against HIV infection, cancer, diabetes and other genetic and metabolic disorders due to their powerful interference with glycosidases as well as glycotransferases.[1-3] Moreover, several drugs incorporating imidazo[1,2-*a*]pyridine systems are presently in clinical use, *e.g.*, zolimidine (an antiulcer drug), zolpidem (a hypnotic drug), and alpidem (a nonsedative anxiolytic drug).[4] One of the most reported multi-component reaction (MCR) that offers convenient access to a variety of novel molecular scaffolds is the Ugi reaction.

For the first time, in 1998, Blackburn, Bienaymé, and Groebke reported an elegant variation of this isocyanide-based MCR which enabled the ready synthesis of imidazo[1,2-*a*]azines.[5] Many synthetic routes are well documented for the formation of imidazo[1,2-*a*]pyridines, but in all these cases, the synthesis of imidazo[1,2-*a*]pyridines involves 2-aminopyrimidine and aromatic aldehyde building blocks along with isocyanide in the Ugi three component coupling (3cc) reaction. Herein, we present an unprecedented

version of the Ugi 3cc reaction using unprotected aldoses as a biorenewable aldehyde component for an expeditious synthesis of iminosugars-annulated imidazoles of pharmacological potential.
The present optimized synthesis was accomplished using MW irradiation of an equimolar intimate solvent-free mixture of D-glucose/D-xylose **1**, amidines **2** and isocyanides **3** with K-10 clay (particle size 32.7 nm), at 90 ^{o}C for 12-15 minutes in a Chemical Laboratory Microwave Oven, 230 volt, 50 Hz power input. Isolation and purification by recrystallization from ethanol afforded the iminosugars annulated pyridines **4** and **5** in excellent yields (86-95%).



Scheme. Synthesis of Imidazo[1,2-*a*]pyridines **4** and **5**.

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P-107

QSAR Studies on a Series of Biphenylsulfonamide Endothelin Receptor Antagonists, as a New Class of Potent ET_A Antagonists

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Endothelins (ET-1, ET-2, and ET-3) constitute a family of 21- amino acid peptides. Endothelin receptor antagonists by blocking vasoconstrictor effects of ET-1, produces vasodilation. QSAR studies have been performed on a series of Biphenylsulfonamide endothelin receptor antagonists, using physico-chemical parameters like substituent hydrophobicity constant ($\pi_{R'}$), molar refractivity ($MR_{R'}$), field effect ($F_{R'}$), resonance effect ($R_{R'}$) and indicator parameter (Ix) for substituents R' and R respectively. Endothelin receptor antagonistic activity of Biphenylsulfonamide derivatives was found to have strong correlation with indicator parameter (Ix), molar refractivity ($MR_{R'}$), field effect ($F_{R'}$) and resonance effect ($R_{R'}$).
It is inferred that an oxazole ring at R position and a substituent with large value of molar refractivity, field effect and highly negative value of resonance effect at R' position will remarkably enhance the endothelin receptor antagonistic activity.

P-108

Design and synthesis of small molecule inhibitors of DPP-IV

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Diabetes mellitus is one of the most common endocrine disorder, currently affecting over 170 million people world-wide and prospectively over 365 million in the year 2030 [1]. Diabetes mellitus results from a combination of defects: resistance to insulin-mediated suppression of hepatic glucose output and

resistance to insulin-mediated glucose uptake by muscle and adipose tissues, together with deterioration of beta-cell function. There are several other health related risk factors and chronic complications associated with the disease. Many attempts have been made to get near normal glycemic control and various kinds of drugs are being developed. Majority of the drugs currently in the market for this chronic disease have led to weight gain and many side effects. Therefore there is a great need for a safe drug. Currently there is much focus on the glucagon-like peptide-1 (GLP-1) peptide hormone as the basis for a potential new treatment paradigm for type 2 diabetes. GLP-1 stimulates insulin secretion and biosynthesis and inhibits glucagon release. GLP-1 is rapidly degraded *in vivo* through the action of dipeptidyl peptidase IV (DPP-IV), to give its inactive form [2]. Inhibitors of GLP-1 degrading enzyme DPP-IV have been shown to be effective for the treatment of type 2 diabetes in animal models and in human subjects [3]. These inhibitors that couple durable glycemic control with reductions in body weight are under development. This novel class of agents is known as DPP-IV inhibitors or 'gliptins'. We have designed and synthesized some small molecules as DPP-IV inhibitors. The details of the study will be presented.

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P-109

Beckmann Rearrangment In Synthesis Of Benzoxazepine And Benzoxazocine Derivative

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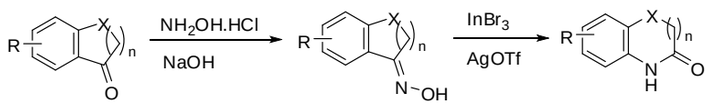
During recent years new reagents have been developed for synthesis of lactams by Beckmann rearrangement viz. $BF_3.Et_2O$ [1], super critical water [2], metaboric acid [3]. We have used a new combination of reagents for the synthesis of benzoxazepine and benzoxazocine from corresponding oximes using Indium bromide and Silver triflate as catalyst in good to excellent yields.



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P-110

Pharamacognostical Evaluation On The Root Of *Rotula Aquatica Lour.*

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The root of *Rotula aquatica* is also called as pashanbed, belonging to the family Borogenaceae. It is widely distributed in India from kumaun to Assam and western to southern India.The medicinal values of plant lie in their component phytochemicals such as alkaloids, flavonoids, phenolic compounds and other nutrients like as amino acid, proteins, which produce a definite physiological action on the human body.

The present study attempts pharmacognostic studies of root, extraction, identification of chemical constituents from the crude extracts, and anthelmintic activity studies of different extracts of *Rotula aquatica.*Macroscopic as well as microscopic studies of any crude drug are the primary steps to establish its botanical quality control before going to other studies.

Hence pharmacognostic studies of crude drug play a very important role in identifying the purity and quality of crude drugs. The present investigation reveals pharmacognostic characters which include morphology, T.S, Powder microscopy, extraction, phytochemical screening, and further isolation and identification of phytoconstituents from ethanolic extract of *Rotula aquatica*

Our experimental results reveal that the novel HPMC- azo derivative showed modified solubility, physical appearance and colour changing point in comparison with hydroxypropyl methylcellulose. It also showed promising colon specificity. Finally, conclusion was drawn that the synthesized hydroxypropyl methylcellulose azo derivative can serve as a potential colon targeting polymer and it can be used as an excipient for formulating colon targeted drug delivery systems.

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P-111

Chiron Approach Synthesis of Muricatacin

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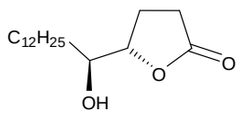
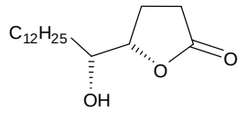
Muricatacin, a naturally occurring □-butenolide was isolated in 1991 from the seeds of *Annona muricata.* It shows cytotoxic activity on tumor cell line (with A-549, lung carcinoma, ED_{50} = 23.3 μg/mL).

Because of its simple structure and potent biological activity it has garnered much attention from several groups and there are a number of total syntheses of this natural product or its analogues. Synthesis of the title natural product and its stereoisomers reported in the literature and our own Chiron approach synthesis will be discussed.



(+)-Muricatacin



(+)-5-*epi*-Muricatacin

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P-112

A Convenient Synthesis Of Steroidal Dienamide Under Microwave Irradiation

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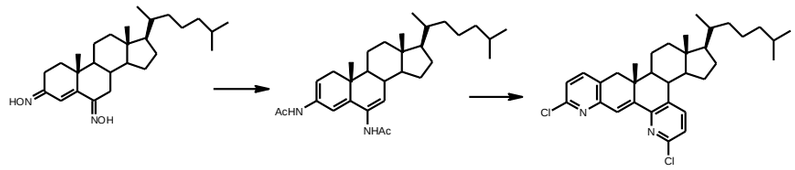
Enamides are very important organic intermediates as precursor of optically active amines by their demonstrated use in asymmetric hydrogenation reaction. They also find application in numerous other areas of organic synthesis [1]. Enamides are considered as tuneable enamines which participate in a number of interesting transformations with electrophiles. The first enantioselective use of enamides as nucleophiles in reactions with aldehydes under copper catalysis has been reported by Kobayashi et al [2].

Because of their importance as synthetic intermediates, several reports are available in the literature for the preparation of enamides from ketones. The A-ring annelated steroidal enamides have been prepared from steroidal 3-ketoxime using Barton's procedure, wherein, the ketoxime was treated with refluxing acetic anhydride in pyridine followed by radical reaction [3]. The preparation of steroidal-2-en-3-acetamide has also been reported by us from 3-ketosteroid by acetylation and rearrangement reaction using iron and acetic anhydride-acetic acid [4]. However, most of the procedures involve stringent reaction condition under thermal condition. Herein, we report a fast and convenient synthesis of steroidal dienamide from diketoxime using nickel powder and acetic anhydride-acetic acid under microwave irradiation in high yield. The steroidal dienamide has been employed as nucleophile for synthesis of A/B annulated heterosteroid using chloromethylene iminium salt.



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P-113

Dual Activation Catalysis: Green Protocol for an Efficient Stereoselective Olefination

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Stereoselective olefination is a much demanded organic transformation due to the wide range of pharmaceutical importance of stereodefined olefinic compounds such as xanthine oxidase inhibitor[1[a]], anti-tumour[1[b]], anti-oxidant, neuroprotective, anti-diabetic[1[c]], cyclo-oxigenase-1 inhibitor[1[d]], anti-leishmaniasis[1[e]] etc. While useful methodologies have been reported for this purpose, the numerous disadvantages associated with these procedures warrants the need of improved and comprehensive protocol especially in the context of the requirement of greener method [2]. The strategy of 'ambiphilic (electrophile-nucleophile) activation' has been found to be a newer approach for sustainable chemistry development [3]. Novel green chemistry approaches have been adopted in this laboratory devising stoichiometric [4] and catalytic [5] 'dual activation' strategy. Herein we would like to describe our findings on 'dual activation catalysis' for stereoselective olefination that constitutes a novel green protocol of the targeted compounds.

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P-114

2-[4-(Methylsulfonylamino)phenyl]propionamide Analogues as Potent TRPV1 Antagonists and Analgesics

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The TRPV1 (Vanilloid receptor 1 or VR1) is a member of the transient receptor potential (TRP) superfamily. Since TRPV1 functions as a non-selective cation channel with high Ca^{2+} permeability, its activation by endogenous ligands leads to an increase in intracellular Ca^{2+} that results in excitation of primary sensory neurons and ultimately in the central perception of pain. The blocking of this receptor activation, by desensitization or antagonism, would have considerable therapeutic utility.

We have previously reported that isosteric replacement of the phenolic hydroxyl group in potent TRPV1 agonists with the alkylsulfonamido group provided a series of compounds which were effective antagonists to the action of capsaicin on rat TRPV1. Further optimization provided novel chiral *N*-(2-benzyl-3-pivaloyloxypropyl) 2-[4-(methylsulfonylamino) phenyl]propionamide analogues which were characterized as highly potent and stereospecific rTRPV1 antagonists.[1] Their high binding affinities and potent antagonisms are comparable or more potent than those of 5-iodoRTX under the same assay conditions.

On the basis of our findings, a series of TRPV1 antagonists having 4-(methylsulfonylamino)phenyl as an A-region and alpha-methyl amide as a B-region have been investigated extensively and finally KMJ-372, *N*-(4-*tert*-butylbenzyl)-2-[3-fluoro-4-(methylsulfonylamino)phenyl]propionamide, was selected for further examination as a drug candidate. KMJ-372 showed selective and potent antagonism against capsaicin, pH, heat and NADA in rat and human TRPV1 and also displayed excellent analgesic profiles in inflammatory and neuropathic pain models.

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P-115

Mode of action of ionophores as antibiotics

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Ab initio molecular orbital calculations at the Hartree Fock level have been performed on some selected transport antibiotics like Valinomycin, Tetranactin to understand their mode of action. Conformational aspects together with electrostatic interactions play a role in determining efficient transport properties of these compounds. Our results indicate that cytotoxicity of nactins may be related to their highly reorganized ionophore in presence of ion leading to tightly bound ion that cannot be delivered at site of action. On the other hand Valinomycin shows little reorganization and efficient ion delivery at site leading to its clinical usage as antibiotic. Understanding of mechanistic aspects will enable efficient designing of compounds with more drug like features and prospective usage as antibiotics.

P-116

Inhibitors of Memapsin 2 and their conformationally controlled mechanistic aspects

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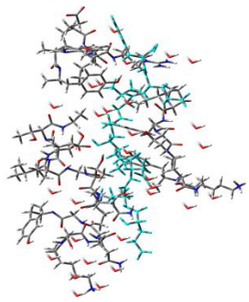
Ab initio Hartree Fock molecular orbital calculations have been performed on selected peptidic inhibitors of memapsin 2. Different conformations of these inhibitors were docked in active site of memapsin 2. Their interactions with catalytic motif and active site residues were evaluated accurately at the

microscopic level utilizing state of the art quantum mechanical calculations. Results obtained indicate the importance of conformational aspects over electrostatic in determining potency of these inhibitors. Our results suggest a possible explanation for failures encountered in earlier designing attempts. Target structure based designing attempts will be discussed.



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P-117

Effect of Metformin on Differentiation of $3T_3$-L_1 preadipocytes and obesity in high-fat diet fed rats.

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The present study examined the anti-obesity effect of metformin in $3T_3$-L_1 preadipocytes and in vivo studies. Metformin are used to reduce the degree of insulin resistance in type 2 diabetes. Metformin treatment suppressed both GAPDH and PPAR in cultured $3T_3$-L_1 adipocytes. To investigate the effect of metformin on obesity in rats fed high-fat diet, four type of diet which include normal diet (ND), high-fat diet (HFD), ND + Metformin and HFD + Metformin diet, were fed to rats adlibidum for 6 weeks. The metformin supplement significantly decreased body weight gain and visceral fat mass compared to the HFD group. The total cholesterol, triglyceride, and leptin levels in the plasma were significantly reduced by metformin supplement compared that of the HFD group.

In conclusion, metformin treatment suppressed differentiation of $3T_3$-L_1 adipocytes, in part by down-regulation expression of leptin , adiponectin, PPARγ mRNA, and reduced adipose tissue mass and hyperlipidemia in obese rats fed HFD. Therefore, metformin may be considered for use in therapy to control obesity also.

P-118

Study on phytochemicals, nutraceuticals and antifungal activities of *Piper pedicellatum C.DC.* of Arunachal Pradesh, India

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Phytochemicals and nutraceuticals were evaluated in the leaf of *Piper pedicellatum C.DC.* The ethno medicinal plant is used as traditional medicine as well as wild vegetable by the tribal people of Arunachal Pradesh. The plant has very high demand in the local market. The tribal people use the leave of the plant for removal of internal body pain, join pain etc. The essential oil was extracted from fresh leaf. Total eleven nos. of chemical constituents were evaluated in essential oil of the plant. *Nerolidol* was found major constituent followed by *Germacrene-D and Caryophyllene.* Nutraceuticals of the leaf of the plant was determined by standard method. The macronutrients, micronutrients and heavy elements like nitrogen, sodium, potassium, calcium, phosphorus, magnesium, iron, copper, zinc, lead and molybdenum were estimated. The calcium (0.63±0.009%), magnesium (0.95±0.006%), phosphorus (1.08±0.001%) iron (33.0±0.02ppm) content were quite significant. The crude fibre, protein, total sugar, fat and vitamin C content of the plant were estimated. The antifungal activity was evaluated of the oil samples. The result showed that the leaf of *Piper Pedicellatum C.DC* is a potential source of nutritive and antifungal agent.

P-119

Cloning and Expression of *Brugia malayi* Glucose-6-phosphate dehydrogenase

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Filariasis (elephantiasis) caused by *Wuchereria bancrofti* and *Brugia malayi* is endemic in tropical and subtropical countries and annually affects about 120 million people worldwide. The filarial parasites mainly depend upon carbohydrate for their energy requirements. Pentose phosphate pathway (PPP) is an important metabolic pathway for yielding reducing power in the form of NADPH and production of pentose sugar needed for nucleic acid synthesis. Glucose-6-phosphate dehydrogenase (G6PD) is the first enzyme of the pentose phosphate pathway that converts α-D-glucose-6-phospate into D-glucono-1,5-lactone-6-phosphate and is involved in the generation of NADPH. RNA from *Brugia malayi* was isolated and cDNA was synthesized. G6PD gene was PCR amplified from cDNA using specific primers and was cloned in pGEM®-T Easy cloning vector. The positive clones were confirmed by restriction digestion and sequencing of the clones. These clones were sub cloned in the pTriEx-4 expression vector. Recombinant G6PD clone was transformed in *E. coli* Rosetta (DE3) cells for expression of protein. Recombinant protein was purified by Ni-NTA affinity column and expression was confirmed by the western blotting. Kinetic properties of the purified protein showed significant differences as compared to enzyme from other parasites.

P-120

Green Synthesis of synthesis of 8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one derivatives.

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Xanthenes and its derivatives has received significant attention in recent years because of their pharmacological properties. Thus, devising newer synthetic methodologies of xanthene derivatives is currently of much importance. However, the increasing influence of green chemistry on medicinal chemistry research [1] has induced a renaissance in the discovery chemistry phase of drug development. In the context of sustainable chemistry development organic reactions in aqueous medium has gained momentum [2] because of its inherited benefits and that it also plays a decisive role in formation of highly

selective and desired product otherwise not possible in conventional organic solvents. Recognising the additional advantages of multi component reactions (MCR) [3] in green synthesis, herein we wish to present an extremely efficient MCR protocol for synthesis of tetrahydrobenzo[*a*]xanthen-11-one derivatives in water.

The advantages includes (i) high selectivity; (ii) fast, highly efficient, and environmentally benign; (iii) operational simplicity, (v) high product yields that fulfill the requirement of the 'triple bottom line philosophy' of the green chemistry [4].

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P-121

Purification and characterization of Adenosine Deaminase of *Plasmodium yoelii*

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Malaria still remains the leading cause of morbidity and mortality in tropics. In view of wide spread development of resistance in parasites against commonly used drugs, identification of new drug targets and pharmachophores is required. Adenosine Deaminase (ADA) is one of the important enzyme of purine salvage pathway catalyzing the conversion of adenosine to inosine in the malarial parsites. The enzyme serves as important chemotherapeutic target for the development of new antimalarial compounds. The enzyme from *Plasmodium yoelii* was purified using anion exchange and gel exclusion chromatography and its kinetic properties were studied. The enzyme exhibited activity at broad pH and temperature range showing maximum activity at pH 7.4 and 37ºC respectively. The Km value for inosine was found to be 41µM. The EHNA [Erythro-9-(2-hydroxy-3-nonyl)adenine] showed the significant inhibitory effect on the parasitic enzyme. The enzyme was inhibited by thiol group inhibitors viz. PHMB and NEM showing the presence of cysteine in the protein. The antimalarial drugs exerted significant inhibitory effect on the malarial enzyme. The immunogenesity of the purified enzyme was checked by raising the antisera against it in rabbit. The specificity of the antisera was confirmed by western blot.

P-122

Antidyslipidemic Activity of *Aloe-vera* & *Allium sativum* in Hyperlipidemic as well as Streptozotocin induced Diabetic Rats

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The antidyslipidemic action of ***Allium Sativum*** and ***Aloe-vera*** extract has been studied in triton and cholesterol fed rats. Serum lipids were found to be lowered by ***Allium sativum*** and ***Aloe-vera*** (10 ml/kg and 5 ml/kg b.w.) in triton induced hyperlipidemic rats. Chronic feeding of these extracts (2.5g/ml of ***Aloe-vera*** and 5g/ml of ***Allium sativum*** for 15 consecutive days) in animals simultaneously fed with cholesterol (25 mg/kg b.w.) for 15 days, caused lowering in lipid and protein levels of □-lipoproteins followed by an increase in high density lipoprotein. Cholesterol level in drug treated rats (also fed with high fat diet) was compared with the cholesterol fed control groups. These extracts altered lipolytic activities in the blood plasma and livers of high fat diet fed hyperlipidemic as well as streptozotocin induced dyslipidemic rats. *In vitro* experiments with extracts (2.5g/ml of ***Aloe-vera*** and 5g/ml of ***Allium sativum***) concentrations inhibited the oxidative degradation of lipids in rat's low-density lipoprotein and liver microsomes. These

extracts when tested against generation of oxygen free radicals, counteracted the formation of superoxide anions and hydroxyl radicals in enzymatic test systems. The present study indicates the efficacy of ***Allium sativum*** and ***Aloe-vera's*** *extract* as antidyslipidemic as well as antioxidative agent.

P-123

Pharmacognostical And Pytochemical Investigation Of Leaves Of *Murraya koenigii (LINN)*

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The plant, Murraya koenigii (L.) Spreng is belongs to the family Rutaceae. It is commonly found in forests, often as gregarious under-growth. It is much cultivated for its aromatic leaf and for ornament throughout India. The leaves are commonly used as spice and also used as a condiment in the preparation of curry powder, pickle, chutney, sausages and seasonings. The leaves, root and bark of the plant are found to be medicinally active. In the present study, the histological, physicochemical, powder characteristics and preliminary phytochemical investigations were carried out on the leaves of Murraya koenigii (L) successfully. Histologicaly- epidermis is single layer, trichomes are unicellular non glandular, vascular bundles have contains calcium oxalate crystals. Physicochemical parameters were observed as total ash value-14.19%, water soluble ash value-2.68%, acid insoluble ash value-2.15%, alcoholic extractive value-51.05%, water extractive value-59.18% and moisture content were found 6.06%. Phytochemical parameters were observed as carbohydrates, alkaloids, glycosides (saponin and flavones), flavanoids tannin and phenolic compounds in water and alcoholic extract both but alcoholic extract have more constituents than water extract.

P-124

Altered expression of *Brugia malayi* proteome pattern and the host inflammatory immune reactions in response to prolonged tetracycline treatment

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Parasitic nematodes responsible for causing lymphatic filariasis are reliant for survival, growth and fertility on *Wolbachia* the alpha-proteobacterial endosymbiont thereby presenting it *to be a potential target for filariasis* control. Integration of wolbachial proteins with filarial proteins is bound to be there and this implies that killing of *Wolbachia* by tetracycline antibiotic treatment may play an important role not only in alteration of filarial proteome pattern but also in modulation of host immune responses. Present study deals with tetracycline treatment of *Brugia malayi* infected rodent host and proteomic analysis of parasite proteins, immune response of the host to bacteria depleted and intact brugian extracts including tissue inflammatory reactions. Proteomic analysis of the filarial nematode proteins revealed 100 protein spots followed by CBB staining of 2-D gel and all were included for comparative analysis. Of these, 54 showed differential expressions, while two new protein spots emerged (of 90.3 and 64.4 kDa). These proteins were subjected to further analysis by MALDI-TOF for their identification using *Brugia* coding sequence database composed of both genomic and EST sequences. *Wolbachia* depletion also resulted into the reversal of impaired T cell immunosuppression and $CD4^+$ T lymphocyte subpopulation and marked reduction in oxidative stress as observed by flow Cytometric studies. The number and intensity of cells in the inflammatory cellular aggregate around Sepharose beads coated with *Wolbachia* depleted adult *B. malayi* antigen was also found to be significantly reduced in lung emboli in comparison to those coated with *Wolbachia* intact antigen. These findings extend our knowledge towards the symbiont–parasite interaction by representing the altered proteins to be essential for parasite survival and active involvement of *Wolbachia* derived molecules in host immune / inflammatory reactions.

P-125

Study of Corrosion Inhibition of Iron by Alcoholic Extracts of Naturally Occurring Plant *Cordia dicotoma* in Acidic Media

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The inhibition of iron Corrosion in different concentration of acid solutions at 299 ± 2°c was studied by mass loss method and thermometric method in absence and presence of alcoholic extracts of dry fruits, leaves and stem of plant *Cordia dicotoma* . In the present paper the role of natural green inhibitors on the corrosion inhibition in presence of different acid concentration is discussed. The extracts of *Cordia dicotoma* shows very good corrosion inhibition efficacy. On the basis of the result it is concluded that the dry fruit extract of *plant Cordia dicotoma* shows maximum corrosion inhibition efficiency up to 97%.

P-126

2-Azetidinone and 4-Thiazolidinone derivatives of Isoniazid and their screening for antimicrobial activity

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2-Azetidinone and 4-Thiazolidinone scaffolds are synthetically important and possesses wide range of promising biological activities. The synthesis and pharmacological activity of N-(4-aryl-2-oxoazetidine) isonicotinamides and isonicotinoyl thiazolidinones are described. The Schiff's bases of isoniazid were synthesized by stirring and were further utilized for synthesis of 2-azetidinone and 4-thiazolidinone analogues. The conventional method for synthesis of 2-azetidinones and 4-thiazolidinones require long reflux times (12-48 hrs) with high energy consumption and formation of undesirable side products. Condensation reactions reported also involves the use of Dean-stark water separator for the removal of water formed during the reaction. Herein, we have reported the synthesis of 2-azetidinones and 4-thiazolidinones of isoniazid by stirring in shorter reaction times (60-180 min) with improved yields as compared to the conventional methods. The synthesized analogues were characterized by UV, IR, ^{1}H NMR and MS studies.

The synthesized 2-Azetidinones and 4-thiazolidinones were screened for their antimicrobial activity against various strains of bacteria (Gram positive and Gram negative) and fungi. Salicylidene, 4- hydroxy benzylidene, p-Cl benzylidene, p-NO_2 benzylidene, p- dimethoxy benzylidene isonicotinoyl azetidinones exhibited antimicrobial activity. However, the 2,5-dimethoxy benzylidene isonicotinoyl azetidinone derivative showed most promising activity against all bacterial and fungal strains. Also the benzylidene, p-chloro benzylidene and p-nitro benzylidene isonicotinoyl thiazolidinone derivatives showed potent activity against the bacterial strains; *S. aureus* and *E. coli*. Furfurylidene, p-chloro benzylidene, p-nitro benzylidene isonicotinoyl thiazolidinones showed potent activity against the fungus *A. niger.* The antimicrobial studies suggested that the synthesized azetidinones and thiazolidinones exhibit significant antimicrobial activity and can be further investigated for the development of potent anti-microbial agents.

P-127

Synthesis, Characterization and Catalytic Application of Transition Metal Complexes with Ionic Liquid Tagged Schiff Bases

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In the past few years recovery and reuse of catalysts has attracted growing interest for environment friendly and cost–effective reaction processes. The use of organic salts which are liquid at ambient temperature (ionic liquid) have emerged as alternative solvents and catalytic transformations have been carried out successfully in them. These solvents provide many advantages over conventional solvents in

terms of activity, stability and reusability of catalyst or solvent–catalyst system [1, 2, 3]. The interest in the synthesis and characterization of transition metal complexes containing Schiff bases lies in the catalytic and biological activity [4]. We have synthesized Schiff base ligands containing ionic liquids and then complexed them with different transition metals **(Scheme 1)**. These metal complexes have been characterized on the basis of different spectral studies and screened for catalytic applications.

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Enamides are very important organic intermediates as precursor of optically active amines by their demonstrated use in asymmetric hydrogenation reaction. They also find application in numerous other areas of organic synthesis [1]. Enamides are considered as tuneable enamines which participate in a number of interesting transformations with electrophiles. The first enantioselective use of enamides as nucleophiles in reactions with aldehydes under copper catalysis has been reported by Kobayashi et al [2]. Because of their importance as synthetic intermediates, several reports are available in the literature for the preparation of enamides from ketones. The A-ring annelated steroidal enamides have been prepared from steroidal 3-ketoxime using Barton's procedure, wherein, the ketoxime was treated with refluxing acetic anhydride in pyridine followed by radical reaction [3]. The preparation of steroidal-2-en-3-acetamide has also been reported by us from 3-ketosteroid by acetylation and rearrangement reaction using iron and acetic anhydride-acetic acid [4]. However, most of the procedures involve stringent reaction condition under thermal condition. Herein, we report a fast and convenient synthesis of steroidal dienamide from diketoxime using nickel powder and acetic anhydride-acetic acid under microwave irradiation in high yield. The steroidal dienamide has been employed as nucleophile for synthesis of A/B annulated heterosteroid using chloromethylene iminium salt.

P-128

Synthesis of 3, 4-dihydropyrimidinone derivatives and screening for antidepressant activity

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Pyrimidinones and their derivatives exhibit a wide range of biological activities such as anti-tumor, antihypertensive, antibacterial, antifungal, or antiviral activity. The original Biginelli synthesis of substituted 3,4 dihydropyrimidin-2-(1H)one has undergone various modifications, with respect to the use of different substituted aldehydes, Urea/thiourea with the use of some Lewis acids, metal catalysts, ionic liquids etc. over the period of time.

An attempt was done to synthesize dihydropyrimidinone derivatives (DHPM) using an inorganic acid like Sulfamic acid as a catalyst which is non metal containing, inorganic acid. The reaction was carried out by microwave irradiation at 140W under solvent free conditions. Substituted aldehydes were treated with ethyl acetoacetate and urea and reactions monitored by TLC and products characterized by physicochemical parameters and screened for antidepressant activity. The derivatives showed significant antidepressant activity at higher dose of synthesized compounds compared with standard drug. Order of anti-depressant activity of dihydropyrimidinone derivatives in the tail suspension test and forced swim

test at the dose of 400 mg is m-nitro> p-chloro>p-hydroxy> 4-hydroxy- 3-methoxy derivative of DHPM. when compared with the standard drug Imipramine (30mg/kg.,i.p.).

P-129

Pharamacognostical Evaluation On The Root Of *Rotula Aquatica Lour.*

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The root of *Rotula aquatica* is also called as pashanbed, belonging to the family Borogenaceae. It is widely distributed in India from kumaun to Assam and western to southern India.The medicinal values of plant lie in their component phytochemicals such as alkaloids, flavonoids, phenolic compounds and other nutrients like as amino acid, proteins, which produce a definite physiological action on the human body.

The present study attempts pharmacognostic studies of root, extraction, identification of chemical constituents from the crude extracts, and anthelmintic activity studies of different extracts of *Rotula aquatica.*Macroscopic as well as microscopic studies of any crude drug are the primary steps to establish its botanical quality control before going to other studies.

Hence pharmacognostic studies of crude drug play a very important role in identifying the purity and quality of crude drugs. The present investigation reveals pharmacognostic characters which include morphology, T.S, Powder microscopy, extraction, phytochemical screening, and further isolation and identification of phytoconstituents from ethanolic extract of *Rotula aquatica*

P-130

Luffa cylindrica fruit juice as a source of peroxidase

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Peroxidases [EC.1.11.1.7] are heme containing enzymes found in plants, in some animal tissues and in microorganism[1]. They perform a variety of physiological functions like lignification of cell wall and in defense mechanism against pathogenic attacks[2]. Some of the peroxidases play crucial roles in deglignification of lignocellulosic materials[3] and in degradation of recalcitrants organic polutants[4]. Recent studies have revealed that not all peroxidases are similar in their structures and functions[2,5]. Ligniperoxidase differs from horseradish peroxidase in the sense that ligninperoxidase directly oxidises veratryl alcohol whereas horseradish peroxidase can not[7]. Soyabean peroxidase[7] has liginperoxidase type activity but it is more stable at acidic pH and at higher temperatures than the ligninperoxidase. These studies have indicated that peroxidases from different sources should be studied to find their biocatalytic potential[12]. Keeping this point in view, we have analysed the *Luffa cylindrica* fruit juice for peroxidase activity and have found that it is a good source of peroxidase. The K_m values of this peroxidase for the substrates guaiacal and hydrogen peroxidase are 1.5 mM and 148 µM respectively. The pH and temperature optima are 6.5 & 60 ^{0}C respectively. Like other peroxidases, it follows double displacement type mechanism.

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P-131

Synthesis, Characterization And Anti-Microbial Screenings Of 10-[3'-(1'-(Substituted) Malonyl-5'-Phenyl)-Pyrazolinyl] Phenothiazines

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The pursuit of **"Heterocyclic Chemistry"** is an established culture among the community of chemists across the globe. Several classes of organic compounds such as nucleic acid, alkaloids, vitamins, flavonoids, coumarins, antibiotics, synthetic drugs, agrochemicals etc, which are intimately connected to life are heterocyclic in nature and have attracted attention of chemists, scientists and researchers since decade. The synthesis of heterocycles is of continuing interest to chemists as the heterocyclic compounds (synthetic as well as natural) have been extensively explored for their application in the field of medicinal, agricultural and industrial chemistry. Development of new synthetic routes in heterocycles has been fascinating, challenging and exciting area in medicinal chemistry. A broad spectrum of biological activity associated with heterocyclic compounds has attracted interest in drug discovery research all over the world. The chemistry of nitrogen-sulfur heteroatom containing aromatic compounds is becoming more popular as an area of research. Phenothiazines and related compounds have shown diverse biological activities including as tranquilizers, anti-inflammatory, anti-malarial, anti-psychotropic, anti-microbial, anti-tubercular, anti-tumour and stimulation of the penetration of anti-cancer agents *via* the blood-brain barrier. They bind to physiological targets or receptors, producing many possible mechanisms of actions. However, solid cancers of the brain and stomach are generally resistant to chemotherapeutic agents. Phenothiazines are inexpensive and widely available, and therefore have been examined as anti-cancer drugs. These properties prompted us to synthesize some novel phenothiazines. The synthesis, characterization and anti-microbial screenings of the synthesized phenothiazines will be presented.

P-132

Synthesis And Anti-Microbial Activity Of 1-(Substituted Aniline Malonyl)-3,5-Dimethyl-4-(Substituted Phenyl Azo) Pyrazoles

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Development of new synthetic routes in heterocycles has been fascinating, challenging and exciting area in medicinal chemistry. A broad spectrum of biological activity associated with heterocyclic compounds has attracted interest in drug discovery research. As evident from literature, both synthetic as well as natural oxygen and nitrogen containing heterocyclic molecules possesses significant antimicrobial activities and a large number have been made up to clinics for health care world wide. A diverse range of biological activities is endowed with pyrazoles. Pyrazoles and their derivatives are widely used as pharmaceutical and agrochemical agents and consequently a large number of synthetic routes to pyrazoles have been reported. Several pyrazoles have been prepared in an attempt to enhance hypoglycaemic activity. Due to the property of reducing blood sugar by pyrazoles it has resulted in the synthesis of their several congeners. According to literature some pyrazole derivatives have been mentioned to possess anti-cancer properties.
In our present study, we have synthesized set of these pyrazoles by the subsequent cyclization of the appropriate aryl hydrazones of 1,2,3-triketones with substituted hydrazides to yield the final product
The purity was determined using TLC and melting points and structural elucidations were carried out by spectral studies. Details of experiments, spectral data and anti-microbial screenings will be presented during conference.

P-133

Synthesis and characterization of amino acid based copper complexes and their DNA cleavage properties

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Much of the literature on phosphodiester degradation by small molecules has focused on either hydrolysis of activated substrates or oxidative degradation of DNA. The oxidative cleavage agents require addition of an external agent (eg., light or H_2O_2) to initiate cleavage and also these processes are radical based and deliver products lacking 3'-or5'-phosphate groups that are not amenable for further enzymatic manipulation and their applications are limited in molecular biology. Hydrolytic cleavage agents do not suffer these drawbacks and the cleaved products religated enzymatically. Therefore, the development of reagents which hydrolytically cleave nucleic acids under mild conditions is currently attracting great interest in the field of artificial metallonucleases since they promote the DNA and RNA hydrolysis in a non-degradative manner and with high levels of selectivity for a site, sequence or structure.

Keeping this in view, the ternary [Cu(II)(ala)(L)(H_2O)] ClO_4 complexes (**1**,**2**), where ala is the L-alanine and L is N,N donor heterocyclic base like 1,10-phenathroline (phen; **1**) 2,2' bipyridine (bpy; **2**) were synthesized and characterized and their nuclease properties were probed. The complexes **1** and **2** convert the supercoiled plasmid DNA (SC-DNA) into its nicked circular (NC) form. At 250µM complex concentration 100% cleavage was achieved by **1** and 52% by **2** at physiological conditions in the absence of any agents like light or reducing agents. The rates of conversion of the SC form to NC form in the presence of Cu(II) complexes are found to be 1.20 and 0.58 $h^{-1}$for **1** and **2** respectively, which amounts 2.15-3.90 x10^7 fold rate enhancement compared to non-catalyzed ds DNA.

P-134

Purification and Characterization of Extracellular Laccase secreted by *Gloephyllum stratum* MTCC-1117

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Laccase (E.C. 1.10.3.2) is a dimeric or tetrameric glycoprotein which contains four copper atoms per monomer distributed in three redox sites. This enzyme catalyses the oxidation of ortho and para diphenols, aminophenols, polyphenols, polyamines, lignins and arylamines as well as some inorganic ions coupled to the reduction of molecule dioxygen to water Sergio et al. [1]. The substrate range of laccase can be extended to nonphenolic subunits of lignin by inclusion of mediators such as 2,2'-Azino-bis- (3-ethylbenzthiazoline-6-Sulphonic acid) Ammonium (ABTS), 3-hydroxyanthranilic acid, 1-hydroxybenzotriazole (HBT) & phenothiazines.

This enzyme is industrially importance due to its applications Luisa et al. [2] pulp and paper industry, Textile industry, food industry, Bioremediation, organic synthesis, Nanobiotechnology, Pharmaceutcal sector. Keeping in view, the biotechnological applcaions of this enzyme, we have initiated studies on laccases of indigenous fungal strain Sahay et al. [3] *Gloephyllum stratum* MTCC-1117. Recently we have purified and characterized a laccase from the culture filtrate of *Gloephyllum stratum* MTCC-1117.

The enzymatic characterisitics like K_m, *p*H and temperature optimum using DMP (2,6-dimethoxyphenol) as a substrate have been determined and found to be 1.2 mM, 4.5 and 37 °C respectively. The results of our studies will be presented in the form of a poster.

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P-135

Microwave Irradiation synthesis of various substituted chalcones using various heterogenous catalyst under solvent – free conditions and their biological evalution.

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Synthesis of thirteen substituted chalcones using various heterogenouos catalysts using mont. K10, anhydrous K_2CO_3, anhydrous $ZnCl_2$ and $Ba(OH)_2$ under MWI was carried out for improved Claisen – Schmidt condensation reaction. A comparative aspect of different compounds in respect of different catalysts , time taken and per cent yield has been discussed. The advantages of this process is to design and develop new synthetic routes to various bioactive chalcone which is environmentally desirable and economically viable. The structures of all the compounds have been established by analytical and spectral (IR, ^{1}H NMR, & mass) data. The synthesized compounds were also used for various biological screening .

P-136

Green chemical synthesis and biological evaluation of a series of different substituted chalcones

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A facile synthesis of twenty chalcones via Claisen-Schmidt condensation of aromatic aldehydes and acetophenones in presence of heterogeneous catalysts anhy. K_2CO_3, fused $Ba(OH)_2$ and KF-Al_2O_3 by using microwave and ultrasound assisted methods is described. A comparative study of synthetic methods and the catalytic behavior of different heterogeneous catalysts used are also discussed. A substantial enhancing effect in yield was observed under microwave and ultrasound activities in comparison to conventional method. Apart from experimental simplicity, the advantages of this methodology are the rapid, environmentally benign and less expensive process, which will contribute to the progress of green chemistry. The structures of all the compounds have been established by analytical and spectral (IR, ^{1}H NMR, ^{13}C NMR & mass) data. A representative number of synthesized compounds have also been screened for their antibacterial, anti-inflammatory, cytotoxicity, antiviral and anti-HIV assay.

P-137

Design and synthesis of new 4-aminoquinoline-based isatin derivatives as antimalarial agents

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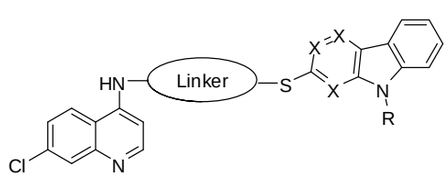
Among the neglected tropical diseases, malaria is one of the most lethal disease that affects about 250 million people world-wide and cause nearly one million deaths every year [1]. The main problem with antimalarial chemotherapy is increase in the resistance of the *Plasmodium falciparum* against classical treatment. Design and synthesis of hybrid molecule can be a good strategy to overcome this problem [2]. The quinoline anti-malarials inhibit β-haematin formation in the parasite and subsequently lead to formation of toxic haem that kills the parasites [3]. While the isatin unit is natural pharmacophore, its derivatives cover a broad spectrum of antibacterial, antifungal, antiparasitic and anticancer activities [4]. We have synthesized one such series of 4-aminoquinoline-based isatin derivatives with the aim of generating new antimalarials against resistant strain of *P. falciparum*



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P-138

DNA-Directed Alkylating Agents. Synthesis and Biological activity of Phenyl N-Mustard-Quinoline Conjugates Having a Urea or Hydrazinecarboximide Linker

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Designing DNA-directed alkylating agents by linking alkylating N-mustard pharmacophore to DNA-affinic molecules is one of promising strategy to overcome the general drawbacks of alkylating agents probably by increasing sequence-specific drug/DNA interaction. Recently, we have synthesized a series N-mustard-9-anilinoacridine conjugates via a urea or carbamate linker and demonstrated potent antitumor activity against human tumor xenografts both in vitro and in vivo. To continue our research on developing new DNA-directed alkylating agents as potential anticancer agents, we have synthesized a series of phenyl N-mustards linked to DNA minor groove binder quinolines through a urea and hydrazine-carboxamide linker for antitumor evaluation. The result revealed that these agents exhibit potent antiproliferative activity against human leukemia (CCRF-CEM) and various solid tumors cell growths in vitro. The structure-activity relationship studies showed that compounds having a hydrazinecarboxamide linker are more cytotoxic than the corresponding derivatives bearing a urea linker. Several conjugates were selected and subjected to evaluate their therapeutic efficacy in nude mice bearing human tumor xenografts. Complete tumor remission of human breast carcinoma MX-1 xenograft and significant suppression of various solid tumors were observed in animal model when treated with these derivatives. Studies on the mechanism of action of these agents revealed that DNA interstrand cross-linking is their main mechanism of action. Moreover, we found that these agents have long half-life in rat plasma indicating that the urea or hydrazinecarboxamide linkers are able to stabilize the reactivity of reactive N-mustard pharmacophore. The chemical synthesis as well as antitumor activity of these conjugates will be presented.

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Evaluation Of Flower Of *Barleria Prionitis* For Anti-Inflammatory And Anti-Nociceptive Activity

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Traditionally aerial parts of *Barleria prionitis* Linn. has been used in the inflammation, fever & toothache. The present study was undertaken to evaluate the anti-inflammatory and anti-nociceptive activity of 50% ethenolic extract from flower of *B. prionitis* (BPF) against different model in experimental animals. The BPF in doses of 50, 100 and 200 mg/kg caused a dose-dependent inhibition of swelling caused by carrageenin equivalent to 17.8–48.6% protection (P>0.05–P<0.001) and in cotton pellet granuloma, 15.32–36.4% protection (P<0.01-P<0.001) was observed from inflammation. There was a significant increase in analgesio meter force induced pain in mice equivalent to 26.3–48.23% protection (P<0.01-

P<0.001) & 5.24 - 34.6 % (*P*<0.05–*P*<0.001) protection against Acetic acid induced writhing. Our results shows that flower of *B. prionitis* possess significant anti-inflammatory and anti-nociceptive activity.

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Total Synthesis of Integerrimide B – A Cyclopeptide of Natural Origin

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A natural cyclic heptapeptide - Integerrimide B, previously isolated from latex of *Jatropha integerrima* (Euphorbiaceae), was synthesized employing solution-phase technique. The cyclopeptide molecule was split into three dipeptide units Boc-L-ala-L-leu-OMe, Boc-L-leu-L-val-OMe, Boc-L-ser-L-pro-OMe and a single amino acid unit Trp-OMe.HCl. In order to obtain dipeptides, Boc-protected amino acids viz. Boc-L-ala-OH, Boc-L-leu-OH and Boc-L-ser-OH were coupled with amino acid methyl ester hydrochlorides L-leu-OMe.HCl, L-val-OMe.HCl and L-pro-OMe.HCl employing different carbodiimides as coupling agents. Ester group of dipeptide unit Boc-L-ala-L-leu-OMe was removed using LiOH and Boc group of Boc-L-leu-L-val-OMe was removed using TFA. Deprotected dipeptide units were coupled to get tetrapeptide Boc-L-ala-L-leu-L-leu-L-val-OMe. Similarly, Boc-L-ser-L-pro-OMe after deprotection at carboxyl end was coupled with L-Trp-OMe.HCl to get tripeptide Boc-L-ser-L-pro-L-trp-OMe. After suitable deprotections, tetra and tripeptide units were coupled together to get linear heptapeptide Boc-L-ala-L-leu-L-leu-L-val-L-ser-L-pro-L-trp-OMe which was coupled with PFP after hydrolysis. Boc group of resulting unit was removed using TFA and finally, deprotected linear fragment was cyclized in presence of catalytic amount of bases to get cyclic product. Structure of cycloheptapeptide was confirmed by spectral and elemental analysis. Synthesized cyclopeptide exhibited potent cytotoxic activity against DLA and EAC cells, and good antihelmintic activity against *Eudrilus sp.* and *M. konkanensis*.

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Unexpected deviation from diene behaviour of Uracil Amidine leading to formation of Pyrido[2,3-*d*]pyrimidine derivatives

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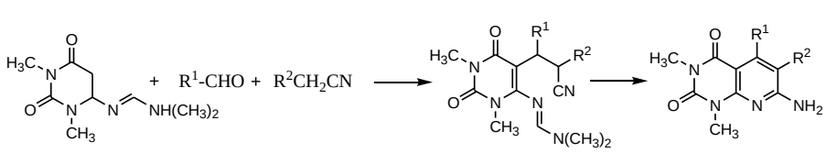
Uracil derivatives have long been used as versatile synthons by chemists for preparation of nitrogen-containing heteroaromatic species of biological significance. Pyrimidopyrimidines, pyrazolopyrimidines, pyridopyrimidines, and xanthine derivatives have all been prepared by functionalization of these important heterocyclic building blocks.[1] Of these, the synthesis, reactions and biological activities of pyridine containing molecules stands as an ever expanding area of research in heteroaromatic chemistry as this structural motif appears in a large number of pharmaceutical agents and natural products. Several patents have been granted for the preparation of these fused heterocycles, derivatives of which are useful as bronchodilators, vasodilators, antiallergic, antihypertensive and anticancer agents.[2-4]

The behaviour of uracil amidine as a reactive diene has been studied and well documented by our group.[5] Exploitation of the diene nature of this molecule in various Diels-Alder reactions is an interesting field in view of a great variety of potential products. We have observed the first deviation from diene behavior of uracil amidine molecule in a reaction between uracil amidine, aldehyde and active methylene compound. In this reaction, Michael addition products are initially generated, which are efficiently and selectively catalyzed by silica gel to the corresponding pyrido[2,3-*d*]pyrimidine derivatives inside a chromatographic column in excellent yields.



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A novel biopolymer from the seeds of *Glycine max*

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The current aim of our research work is to isolate biomaterial from the seeds of *glycine max* (family-fabaceae) and to evaluate its pharmaceutical applications by formulating films. The seeds of *glycine max* were collected and the biomaterial was separated by simplified economical process. The biomaterial was screened for its physicochemical properties like colour, solubility and colour changind point. Three different films were prepared by using biomaterial as film former, sodium CMC as a co-filmformer agent along with suitable co-processnats by casting method. The prepared films were subjected for different evaluation parameters like texture analysis, ex-vivo mucoadhesitivity by Park and Robinson and Rotating cylinder method, ex-vivo mucoretentability, folding endurance and surface pH. Our results revealed that the film F3 containing four parts of biomaterial and two parts of co-film former displayed promising filmability, smooth texture, significant folding endurance, mucoadhesitivity and mucoretentability properties in comparision with film1 and film 2. The conclusion was drawn that biopolymer can serve as a film forming agent for formulating various Tran mucosal drug delivery system.

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An α-L-rhamnosidase from *Aspergillus clavato-nanicus* MTCC- 9611.

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α -L-rhamnosidase[E.C. 3.2.1.40] catalyses the hydrolysis of terminal α - L- rhamnose[1, 2]of natural and synthetic glycosides.

This enzyme has turned out to be of great biotechnological potential due to its industrial applications in debittering of citrus fruit juices[3], elimination of hersperidin crystals from orange juices[4], in enhancement of wine aromas[5] ,in the manufacture of prunin from naringin and in the manufacture of L-rhamnose by hydrolysis of natural glycosides. Moreover, α-L-rhamnosidase can be used to prepare diosgenin[9] (a precursor of clinically useful steroids drugs) from the fenugreek seeds.

Keeping the above point in view, we have initiated studies on the α-L-rhamnosidases of indigenous fungi. Recently we have isolated a fungal strain which has been identified as *Aspergillus clavato-nanicus* MTCC-9611 and produces an α-L-rhamnosidases which has pH optimum in the alkaline range. The enzyme has been purified to homogeneity from the culture filtrate of the fungal strain using concentration by ultrafiltration and ion exchange chromatography on CM cellulose. The molecular weight of the protein estimated by SDS-polyacrylamide gel electrophoresis analysis was 82.0 kDa. The K_m value of the enzyme for p-nitrophenyl α-L-rhamnopyranoside and naringin were 0.65mM and 0.95mM respectively. The enzyme was optimally active at pH 10.0 and 50ºC. The enzyme transforms naringin to pruning at pH 10.0

and further hydrolysis of prunin to naringenin does not occur under these reaction conditions. The result of these studies will be presented in the form of a poster.

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Method Development and Validation of Nobiletin in Rat Plasma

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A simple and specific HPLC method has been developed and validated for the estimation of nobiletin in rat plasma, using Coumarin as internal standard (IS). Protein precipitation method was used for extraction of Nobiletin and Coumarin (IS). The recovery at LQC, MQC, HQC of Nobiletin and IS (Coumarin) in rat plasma were 112.47%, 99.9%, 91.72% and 83.15%, 84.07%, 79.26% respectively using methanol as extraction solvent. The resolution of peaks was achieved with the mobile phase consisting 0.04 M Dihydrogen Phosphate buffer (pH 5.5):Acetonitrile::50:50 (v/v) on a LiChroCART, RP-18 column. The total chromatographic run time was 10 min. Specificity was determined and found that method was specific and there was no significant matrix effect. The method was proved to be accurate and precise at linearity range of 50–10000 ng/mL with a correlation coefficient (r) of ≥0.997. The intra- and inter-day assay precision ranged from 4.82 to 6.20% and 3.10 to 9.78%, respectively; and intra- and inter-day assay accuracy was between 95.27–98.95% and 91.73%-102.83%, respectively. Nobiletin was found stable in the battery of stability studies viz., bench-top, auto-sampler, freeze/thaw cycles and long term storage in a freezer at -80 ^{0}C.

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Evaluation of free Radical Scavanging Activity of *Cordia macleodii* Bark. (HOOK.F.& THOMSON)

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Antioxidant activity has been assessed by *in vitro* method for phytochemical fraction of plant, viz. methanolic extract of ***Cordia macleodii*** bark. This investigation was under taken to evaluate methanolic extract of ***Cordia macleodii*** bark for possible potential. The extracts were evaluated for their phenolic content & Antioxidant activity. Phenolic content was measured using Folin-ciocalte reagent & was calculated as Gallic acid equivalents. Antiradical activity of methanolic extract was measured by 1,1, diphenyl-2, picrylhydrazyl (DPPH) assay & was compared to ascorbic acid and Ferric reducing power of the extract was also evaluated by OYAIZU method. In the present study three method used for evalution of Antioxidant activity. The first two methods were for direct measurement of radical scavenging activity & remaining one method evaluated the reducing power. The present study revealed the ***cordia macleodii*** bark has significant radical scavenging activity.

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A novel Bis-isoflavone from the roots of *Chlorophytum tuberosum*

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Chlorophytum tuberosum is commonly known as “Safed Musli” and belongs to the family liliaceae. In present time ***Chlorophytum tuberosum*** (Roxb.) is one of the most popular medicinal plant. It has been

one of the chief ingredient in Ayurveda and for other local medicines for ages. It is a bulbed plant and the bulb roots (which are known as bulb or fingers) lies in ground, up to 10 inches. In "Indian Materia Medica" The name of this plants is described as ***Chlorophytum arundinaceum***. This plant is found in forests of India in different regions in natural forms, mainly found in the forests of Madhya Pradesh and Rajasthan. Medicinal properties of plants are due to the presence of some bioactive chemical constituents. By isolation and characterization of medicinally active chemical constituents from plants increases their versatile therapeutic uses into modern system of medicine. The present paper deals with the isolation and structural elucidation of a novel isoflavonoid having remarkable antifungal and antibacterial activities. The ethyl acetate soluble fraction of the air-dried roots afforded the isoflavonoid component on chromatographic resolution over silica-gel and sephadex LH-20. The phytochemical study obtained as brown amorphous substance, m.p. 240-245^{o}C was analysed for $C_{50}H_{54}O_{24}$ $[M+H]^{+}$ at m/z 1039. Detailed spectroscopic as well as chemical studies enabled to characterize the novel isoflavonoid as Bis (6, 3', 4', 5', - tetra methoxy–7-O-β-D-glucopyranoside) I-5, II-5 biisoflavone. The spectroscopic studies of the biisoflavone includes UV (with various shift reagents), IR, ^{1}H NMR, ^{13}C NMR, 2D NMR and mass spectra.

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Phytochemical And Pharmacognostic Studies Of Roots And Flowers Of Cassia Auriculata Linn.

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Cassia auriculata Linn. is a member of genus *Cassia* and locally named as Aawali. Various parts like flowers, leaves, root, bark, and seeds are used as medicine to cure various diseases; Asolkar *et al.* [1], Jayaweera *et al.* [2]. In the present study we have used floweres and roots for phytochemical and pharmacognostic investigation. Total ash, acid insoluble ash and water-soluble ash of flowers were found to be 5.7%, 0.8% and 1.1% and that of roots were 4.5%, 0.5% and 0.8% respectively; Khandelwal [3], Vogel H *et.al*. [4]. Soluble extractive values of water, ethanol, ether, chloroform and ethyl acetate of flowers were obverse to be 20.40%,26.20%,3.90%,4.20% and 8.80% respectively Khandelwal [3]. The extraction was done by cold maceration method; The Pharmacopoeia of India [5]. The loss on drying (LOD) of the flowers and roots powdered found to be 10.50% and 9.50% respectively ; The Ayurvedic Pharmacopoeia of India. Qualitative investigation of flowers and roots for various inorganic compounds and elements in total ash revealed the presence of Calcium, Potassium, Magnesium, Sodium and Phosphates. Qualitative preliminary phytochemistry over aqueous and 80% methanolic extract of flowers and roots showed the presence of glycosides, alkaloids, carbohydrates, flavonoids and proteins; Harborne. The extraction of total carbohydrates of flowers and roots was done according to method phenol-sulphuric acid respectively method. The methanolic extract of flowers and roots showed anti – inflammatory activity in rat and results were compared with literature.

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Cooperative Hydrogen Bonded Clusters: Untangling the Mysteries of the Ionic Liquid Catalysis

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The increasing influence of sustainable chemistry presses the need for convenient and high yielding synthetic methods addressing environmental issues such as minimisation of waste and avoidance of auxiliary substances (e.g., solvents, additional reagents) for the timely supply of the designed new chemical entities for biological evaluation [1]. The room temperature ionic liquids (RTILs) are projected as future green solvents [2] expected to be a major driver for sustainable develo pment in organic transformations [3], but the cytotoxicity [4] of some of the RTILs raises concern for their use in large quantities. Therefore, the catalytic use of RTILs is in focus to exploit their unique prpoerty in accelerating reaction rates. But mysteries remain in "how"?

The present study will focuss on the molecular level understanding of the mechanism of IL catalysed organic transformation [5, 6] that would provide rational for their further applications.

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Stereoselective synthesis of functionalized 2,3-dihydrobenzofurans, 1-benzopyrans and 1-benzoxepines by phenoxide ion-mediated carbocyclization

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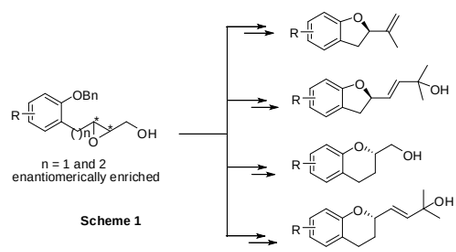
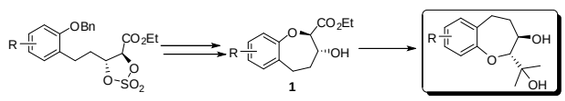
2,3-Dihydrobenzofuran, 1-benzopyran and 1-Benzoxepine derivatives are ubiquitous in natural products as well as large number of unnatural molecules. Owing to their wide range of biological properties demonstrated, they have attracted considerable attention of organic and medicinal chemists.

We have developed an efficient asymmetric synthesis of 2,3-dihydrobenzofurans, 2-substituted-1-benzopyran scaffolds (**Scheme 1**)[1] utilizing Sharpless asymmetric epoxidation followed by phenoxide ion-mediated intramolecular epoxide ring opening reactions. Further a new asymmetric synthesis of 2,3-disubstituted-1-benzoxepines(**1**) utilizing Sharpless asymmetric dihydroxylation followed by phenoxide ion-mediated intramolecular 7-*endo*-*tet* S_N2 carbocyclization of *syn*-2,3-dihydroxy ester-derived cyclic sulphates (**Scheme 2**) as the key step has been achieved[2].This strategy was utilized efficiently to access Heliannuol-like structural framework (**2)**.





Scheme 2

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Inclination towards Green Chemistry: Delve into Acquiring Seven Membered Heterocyclic Scaffold

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The broad spectrum of biological activity such as anticonvulsant, Ca^{+2} channel antagonist, anti-HIV, etc. [1] of compounds bearing the 2,3-dihydro-1,5 benzothiazepines moiety has stimulated interest in developing new synthetic protocols for their synthesis [2]. Solemn drawbacks of reported methodologies like the use of high boiling solvents, excess amounts of acid or base, special apparatus, corrosive and hazardous reagents etc. received our attention to develop improved methods of synthesis of such compounds [3].

The increasing concern about the maintenance of greenness in synthetic pathways [4] encouraged us towards sustainable development of synthetic methodologies for which the improvement of reaction medium appears to be a major driver. In this context we demonstrated an improved synthesis of the titled compounds in aqueous medium [5]. Ionic liquids (ILs) are also leading contender of innocuous reaction medium [6]. However, the issues pertaining to combustibility, toxicity and lack of biodegradability of ILs are not encouraging to carry forward with the green solvent image and the use of ILs as organo-catalyst add a new dimension [7,8]. The present investigation deals with the highly convenient synthesis of 2, 3-dihydro-1, 5 benzothiazepines at milder conditions. In view of its inherent properties like environmental compatibility, greater selectivity, operational simplicity, non corrosiveness, ease of handling, short reaction times and high yields fulfill the requirement of the 'triple bottom line philosophy' of the green chemistry [9].

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Densities, Viscosities and Ultrasound Velocities for Binary Mixtures of Isopropylethanoate and Non-polar Hydrocarbon Solvents

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Densities (ρ_{12}), viscosities (η_{12}), and ultrasound velocities(u_{12}) for binary mixtures of isopropylethanoate and non-polar hydrocarbon solvents viz cyclohexane,benzene,1,4-dimethylbenzene and 1,3,5-trimethylbenzene have been measured at 308.15K.Adiabatic compressibilities($\beta_{ad})_{12,}$ available volume(V_a) and acoustical impedance(Z_{12}) for the binary mixtures are evaluated from the ultrasound velocity and density data. Deviations in viscosity ($\Delta\eta$), in ultrasound velocity (Δu) and in compressibility ($\Delta\beta_{ad}$) from their additive values for all the systems studied are evaluated from the experimental values for the mixtures and their components at experimental temperature. $\Delta\eta$ and Δu values are negative and $\Delta\beta_{ad}$ are positive for isopropylethanoateate + cyclohexane binary mixture. Several models for mixture viscosity are analysed. The strength of interactions are discussed in terms of Grunberg and Nissan interaction parameter (d). Hind – McLaughlin –Ubbelohde viscosity equation is found to be most suitable for the viscosities of the binary mixtures studied. Results are discussed in terms of interactions between components of the mixtures.

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Aromatization of Hantzsch 1,4-dihydropyridines and synthesis of 5-benzylated barbituric acids *via* a microwave-assisted three-components reaction in solvent-free conditions

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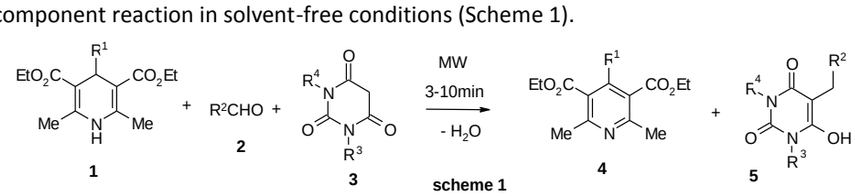
Hantzsch 1,4-dihydropyridines (1,4-DHP) are an important class of drugs for the treatment of cardiovascular disease such as hypertension and angina pectoris [1]. Some commercial representatives such as amamodipine, felodipine, nifedipine and nicardipine are among the best selling DHP drugs used in the treatment of cardiovascular diseases. In the human body these compounds are oxidized to pyridine derivatives, by the action of cytochrome P-450 in the liver [2]. The oxidation of 1,4-DHPs to the corresponding pyridine derivatives constitutes the principal metabolic route in biological systems, as well as a facile access to the corresponding pyridine derivatives, which show anti-hypoxic and anti-ischmic activities,[6] from easily available DHPs. In order to understand these biological process, as well as to develop a useful synthetic approach to poly substituted pyridines, the oxidative aromatization of 1,4-DHP derivatives has received considerable attention from synthetic chemists. A variety of reagents have been developed for the aromatization of DHPs. These include the use of stoichiometric or excess amount of inorganic oxidants or organic oxidants. However, all these methods have some limitations and drawbacks. Therefore development of more efficient method for the oxidation of 1,4-DHPs is still sought after.

5-Alkylated barbituric acids are an important class of compounds of medicinal importance. A number of clinically used hypnotic drugs of barbiturates class, for example veronal, seconal, phenobarbital, sodium pentothal etc, are simply 5-alkylated derivatives of barbituric acid [3]. Bucolome is an antiinflamatary drug. Moreover, 5-Benzyl barbituric acids are an important class of HIV-1 and HIV-2 protease inhibitors.

The development of resource and eco-friendly process in terms of sustainable chemistry has become a focal point of chemical research in recent years. In the present world of green chemistry, chemical processes with high atom economy have received a growing interest from the scientific community.

In our continued interest [4] in the development of highly expedient methods for the synthesis of diverse heterocyclic compounds of biological importance, we report here a novel and green oxidative aromatization of 1,4-DHP and synthesis 5-benzylated barbituric acids *via* a micro-wave (MW) assisted one-pot three-component reaction in solvent-free conditions (Scheme 1).



1 + R^2CHO + **2** → **3** → **4** + **5**

scheme 1

The details of the work will be presented.

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P-153

Solvent Free Synthesis Of Some Chalcones And Pyrazoline Derivatives Under Microwave Irradiation

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1, 5-substituted diphenyl-1, 4-pentadiene-3-one chalcones were prepared by Claisen-Schmidt reaction of different aromatic aldehydes with acetone under microwave irradiation in presence of some solid support. A dry media synthesis of nitrogen containing five membered heterocyclic compounds was carried out via cyclization to give Pyrazoline derivatives. The heterocyclic compounds were synthesized using solvent free approach and under microwave irradiation. The newly synthesized compounds were characterized by elemental analysis and spectral data. On comparing with the conventional methods it was found that the increased yield of products was obtained in shorter time period. All the compounds have been screened as antimicrobial agents.

P-154

Ecofriendly Synthesis, Antibacterial And Herbicidal Activities Of Some New 3-[4'-(4''-Nitrophenoxy)-Phenyl]-5-Substituted Phenyl-2-Pyrazolines And 2-Isoxazolines

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Microwave assisted synthesis of 1-(4'-(4"-Nitrophenoxyaryl)-3-substituted phenyl-2-propene-1-ones chalcones was carried out. The treatment of these chalcones with hydrazine hydrate in presence of acetic acid resulted in the formation of 3-[4'-(4"-nitrophenoxy)-phenyl]-5-substituted phenyl-2-pyrazolines while treatment with hydroxylamine hydrochloride gave 3-[4'-(4"-nitrophenoxy)-phenyl]-5-substituted phenyl-2-isoxazolines. The heterocyclic compounds were synthesized using solvent free approach and under microwave irradiation. The structures of synthesized compounds were established by elemental analysis and IR, PMR and Mass spectral data. All the compounds have been evaluated for their antibacterial and herbicidal activities.

P-155

Free Radical scavenging activity of *Cassia fistula* (Linn.) flowers

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Cassia fistula L., a semi-wild Indian Labernum, is widely cultivated in Mauritius as an ornamental tree for its beautiful bunches of yellow flowers and also used in traditional medicine for several indications.A selection of medicinal plant *Cassia fistula,* was screened for their in vitro antioxidant activity. flower parts of selected plants were dried at room temperature, and powdered. Then, the extractions were performed with methanol. The extracts than qualitatively screened for their free radical scavenging activity. Protective Role of *Cassia fistula* flower in Antioxidant activity by DPPH(2,2-diphenyl-1-picrylhydrazyl radical) method, OYAIZU (FRP) method, and total phenolic content was investigated. extracted plant was evaluated for their phenolic & antioxidant activity. Phenolic content was measured using Folin-ciocalte reagent & was calculated as Gallic acid equivalents.Antiradical activity of methanolic extract was measured by DPPH (2,2-diphenyl-1-picrylhydrazyl radical) assay & was compared to ascorbic acid,and Ferric reducing power of the extract was also evaluated by OYAIZU method. In the present study three methods used for evolution of Antioxidant activity. The first two methods were for direct measurement of radical scavenging activity & remaining one method evaluated the reducing power. The present study revealed the *Cassia fistula* flower has significant radical scavenging activity. In this study, *Cassia fistula* was identified as potentially novel soureces of free radical scavenging compound.

P-156

The recombinant Trehalose phosphate phosphatase (TPP) of *Brugia malay*i provides protection against infective larval challenge in rodent via mixed Th1/Th2 response

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Lymphatic filariasis is caused by nematodes *Wuchereria bancrofti, Brugia malayi* and *B. timori.* Presently available drugs Diethyl carbamazine, Ivermectin have no effect on adults. The alternative strategy remains to be is identify new drug target and vaccine molecules.In trehalose biosynthesis; trehalose phosphate phosphatase (TPP, EC 5.4.2.1) catalyzes the hydrolysis of trehalose phosphate to trehalose and phosphate . No homologues of TPP have been found in mammals. We have successfully cloned and expressed recombinant *Brugia malayi* TPP (~60kDa) in *E.coli*. The recombinant protein strongly reacted with endemic normal bancroftian serum. Vaccination of mastomys with BmA-TPP (+FCA) resulted into a significant reduction in microfilarial burden (56.9%) and adult worm establishment (60%), along with (62-74%) sterility of female worms in immunized group. The recombinant protein elicited high IgG antibody level in addition to increased oxidative burst (ROS) and Nitric oxide (NO) production. The resistant serum caused *in vitro* adherence of peritoneal cells (ADCC) to the surface of microfilariae (mf) and infective larvae (L3) of *B. malayi* causing cytotoxicity and their immobility and death. The rTPP vaccine induced the increased population of CD8+ cells and down-regulation of CD4+, CD45+ and CD30+ population. An expansion was also noticed in the Treg cell population. The recombinant protein generated a mixed Th1/Th2 helper immune response as revealed by an increase in the IgG1 and IgG2a and IgG2b levels. The findings reveal BmA-TPP to be a promising vaccine molecule and efforts to increase the vaccine efficiency by using human compatible adjuvants and vaccine delivery modes are underway.

P-157

Oligosaccharides present in mare's milk modulate the immunological responses of BALB/c mice

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Milk is an enormously rich source of bioactive oligosaccharides which are not easily digested in the small intestine and provide "soluble" fiber, that allows them to bind pathogens (bacteria, fungi and viruses) and

stimulate body's immune system, thus may be viewed as a `natural' way of protecting neonates against infections. The oligosaccharide fractions isolated from Mare's milk during colostral, transitional, mature and involutional (lactation) period were evaluated for their effect on immunological response of Balb/c mice. The immune parameters (oxidative burst, T/B cell surface CD antigens and Th1/ Th2 cytokines) were assessed in BALB/c mice after oral administration of the each oligosaccharide fraction at various doses (3, 1.0 and 0.3 mg/ kg) for 14 consecutive days. All the oligosaccharide fractions were found to stimulate the immune cells at various doses with highest stimulation being exerted at 3 mg/ kg, as represented by an expansion in the CD4+/ CD8+ T cell and CD19+ B cell population, and increased level of reactive oxygen species as compared to that of Levamisole, which was used as a standard immunostimulant drug. In addition, there was significant increase in Th2 cytokine production (Il-4 and IL-10) and the findings reveal that the oligosaccharide fraction isolated from mare's milk at colostral phase was the most potent immunostimulant followed by the lactation phase and revealed efficacy superior to Levamisole. The immune-stimulation was predominantly Th2 type which may be used in several immunosuppressed conditions including those caused by various pathogens.

P-158

Status of Iron and Fluoride Pollution in some parts of District Rae Bareli, U.P., India

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Ground water is one of the most important sources for drinking water and is also used for other purposes, with the explosion in human population; the demand for ground water is on the increase. The suitability of ground water for potable purposes is judged, from the health standpoint, on the types of minerals dissolved in it. We report herein that the ground water sources in some parts of district Rae Bareli in U.P. contain iron and fluoride ions in Quantities which are outside the permissible limit.

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P-159

Survey Of Antibiotic Utilization In Pediatric Patients In Hospital In Dehradun District Of Uttarakhand

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Pediatrics is the branch of medicine that deals with the medical care of infants, children and adolescents. The upper age limit of such patients ranges from age 12 to 21, depending on the country. Pediatrics constitutes about 40% of India's population. Infants and children are affected more with the illness. Antibiotics are most frequently prescribed by the doctors and it consumes more budgets in pharmacies and hospitals. The objective of this study is to determine the utilization of antibiotics in pediatric patients in the hospital. The data was analyzed by using medical records, prescription, discharge sheet, and by visiting to pediatric patients for antibiotic use. Demographic data along with the length of the hospital stay from the interview with family members and also from the medical records were analyzed. Along with this the number of antibiotics prescribed, the category and dose, duration of each antibiotic prescribed was taken in to account and noted in a prescribed proforma. During the study, a total of 200 patients were surveyed and most of them were already having a single course of antibiotics during their hospitalization. It was found that more number of prescriptions was for the youngest age group of the study population, and 5 % were admitted to the intensive care units. The average length of stay in the hospital for children receiving antibiotics was 7 days. The antibiotics were mostly prescribed in case of bacterial infections, followed by the diagnoses of respiratory tract infections. So strict control is required to improve the prescription pattern of antibiotic in the hospital and vitamins should be prescribed along with the antibiotic therapy and there is a need of clinical pharmacist in India for further suggesting the medication needs for the well-being of the patient.

P-160

In Vitro cytotoxicity of a novel 2-quinolone derivative- N(1H)-7-(chloroacetamido)-4-methyl quinoline-2-(1H)-one [nJST]

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Tipifarnib, 3-Aryl-2-quinolone derivative acts as anticancer by farnesyl transferase inhibition and it is currently under clinical trial. Considering 2- quinolone derivatives as a potential moiety for antitumour activity, a new derivative have been synthesized and screened for its cytoxicity by MTT assay on 4 different cell lines and DNA fragmentation assay using MCF-7 cell line.

The standard MTT bioassay was used to screen all the synthesized compounds for *in vitro* cytotoxicity in human adenocarcinoma cells (MCF-7), colon cancer *cell line (*HCT- 15), murine melanoma cell line (B16f10), Human breast adenocarcinoma cell line (MDAMB) for 24 h, 48h, and 72h. Exponentially growing cells (10^4cells/well) seeded in 96 well plates and allowed to adhere for 24 hours. Cells were treated with different concentrations of test compound (0.1mM-2mM) for 24, 48 and 72h. Optical density was recorded at 540nm. DNA fragmentation studies were performed by exposing different concentration of nJST on MCF-7 cells. DNA was extracted from the treated and untreated samples using phenol chloroform extraction. Then DNA was studied with the help of ethidium bromide staining.

IC_{50} of nJST was found to be less than 10 micromole in all the cell lines treated after 24, 48 and 72 h. DNA damage was confirmed by fragmentation pattern of bands. In normal untreated group single clear band was observed which says DNA was intact.

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P-161

Cytotoxic And Genotoxic Effect Of Mercuric Chloride On Blood Cells Of *Channa Punctatus* (Bloch)

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The present study was aimed to evaluate the cytotoxicity and genotoxicity of mercuric chloride ($HgCl_2$) on cultured blood cells of freshwater fish *Channa punctatus* (Bloch) using micronucleus test. The fish specimens were collected and acclimatized in laboratory condition for two weeks prior to experimentation. Blood was collected from caudal vein using heparinized 1 ml syringe. Whole blood culture was set up with approximately 200 µl of blood, suspended in 5 ml of RPMI 1640 media supplemented with 15% fetal calf serum heparin (10 IU/ ml) and antibiotics for 72 h at 28 °C in BOD incubator. The blood cells were exposed to three different concentrations, viz. 0.5, 1.0 and 1.5 µg/ ml, of $HgCl_2$. The experiment was performed in triplicate along with positive control. The viability of cell was assessed by trypan blue extrusion test for assessment of cytotoxicity and micronucleus test was applied for genotoxicity evaluation. Sampling was done after 24, 48, and 72 h of exposures. The slides for micronucleus test were prepared and scored manually for various parameters such as cells morphology, number of cells with single, double nuclei, and multiple micronuclei. The percentage of viable cells was found in decreasing order with increase in concentration of the test chemical and exposure durations. The observations of this study indicated the substantial changes in morphology of the cells, cytoplasm content and size as well as shape of the nucleus. The concentration dependent increase in frequency of micronucleus was observed and the frequency of micronucleus was higher than the control even at lowest concentration of the test chemical.

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A Stereoselective One-Pot Synthetic Approach To Functionalized 1,3-Thiazetidines

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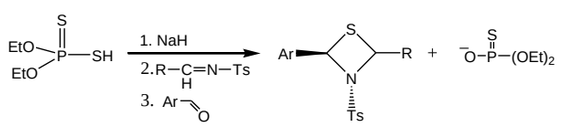
In the course of investigating transannular interactions between various combinations of functionalized groups, we wished to prepare certain cyclic models having sulfide and tertiary amino nitrogen in juxtaposition.[1-3] In view of this, the 1,3-thiazetidine system which is relatively rare and has been mainly accessed by cycloaddition and by eliminative cyclization are considered. Thiazetidine derivatives are particularly useful for their antibacterial activity and are thus useful for the treatment of bacterial infections both caused by gram-negative and by gram-positive bacteria. Because of their non-toxicity, they are useful for treating such infection in humans and animals. 1,3-Thiazetidines also underwent rearrangements to yield various interesting compounds.[4] Thus, a convenient synthesis of functionalized 1,3-thiazetidines is an interesting target of investigation from both chemical and pharmacological viewpoint.

Different approaches for the construction of 1,3-thiazetidine ring system have been reported in literature,[5] but here we report a facile and high yielding synthesis of 1,3-thiazetidines from readily and widely available starting material. The present synthetic protocol involve Michael addition of phosphorodithioate to aldimines followed by intramolecular cyclization of the in situ generated anion on treatment with aldehydes affording the desired 1,3-thiazetidines (Scheme 1).



Scheme 1

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P-163

Pharmacokinetics of An Arylpiperazine Derived SARM for Benign Prostatic Hyperplasia Management

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Benign prostatic hyperplasia (BPH), also called benign prostatic hypertrophy, or benign enlargement of the prostate (BEP), refers to the increase in size of the prostate in middle-aged and elderly men. In 40-50% of these patients, BPH becomes clinically significant. Recently, arylpiperazine derivatives have been reported as potent nonsteroidal AR antagonists [1-2] and the compound [(1-(4-Nitro-2-(trifluoromethyl) phenyl)-4-(-3-(trifluoromethyl) phenyl) piperazine)] showed higher decrease in the size of prostate in rat than finasteride. Therefore, the pharmacokinetic study of the compound was carried out in rats to develop it as a potential candidate drug.

Young and healthy male *Sprague Dawley* rats were administered a suspension formulation of the compound at 10 mg/kg oral dose. Blood and prostate were collected. An HPLC assay method was developed and validated and then applied for quantitative analyses of the compound in serum and prostate samples. Pharmacokinetic parameters were calculated from noncompartmental models using WinNonlin program, version 1.5 (Scientific Consulting Inc.).

The lower limit of quantification for the analytical method was 10 ng/ml of the compound in serum. Recovery of the compound from spiked control serum was more than 95% with the variations (accuracy and precision) within acceptable limits [3]. The animals tolerated the treatment as no peculiarities in the animals' behaviour were observed. It was observed that after oral dosing, its absorption was rapid with a peak concentration (C_{max}) at 0.5 h and could be monitored up to 8 h. However, the target organ (prostate) showed a very high C_{max} and AUC indicating that a significant amount of the compound reaches the target organ. The clearance (0.03 L/h/kg) was smaller than the hepatic blood flow (2.9 L/h/kg, [4]) of the rat, suggesting an insignificant amount of extrahepatic elimination of this compound. The details will be presented.

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P-164

High frequency plant regeneration through somatic embryogenesis in rice variety Swarna

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The regeneration protocol for rice plants from callus culture obtained from dehusked and sterilized whole rice seeds (caryopses) of a popular variety Swarna (MTU 7029). In the present study, callus induction, callus growth rate and indirect regeneration potentiality of the variety were examined. For callus

induction different ranges of 2,4-D (1-4 mg l^{-1}) were used and for somatic embryo formation and plantlets regeneration different combination of BAP (2-4 mg l^{-1}) and NAA (1 mg l^{-1}) were taken in consideration. For callus induction the best concentration was 4 mg l^{-1} 2,4-D, showed 96% callus induction efficacy. Whereas the high frequency of plantlets regenerated from embryogenic calli were observed in the combination of 4 mg l^{-1} BAP and 1 mg l^{-1} NAA; the embryogenic calli obtained from 2 mg l^{-1} 2,4-D concentration performed better in this media (4mg l^{-1} BAP and 1 mg l^{-1} NAA) than the other three used concentrations of 2,4-D. Physiological potentiality of 45 days old calli in terms of fresh and dry weights and proline content were examined in the present study. Highest used concentration of 2,4-D (4 mg l^{-1}) showed low regeneration capacity with higher proline content in plantlets.

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PCR based assessment of genotoxic effects pesticide profenofos in *Channa punctatus* (Bloch)

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Present study was aimed to evaluate the genotoxic potential of organophosphate pesticide, 'profenofos' to freshwater fish *Channa punctatus*, employing RAPD-PCR technique to detect the DNA damage. The 96 h LC_{50} value of commercial grade profenofos (EC 50) was determined as 2.313 ppb in a semi-static system. Live and apparently healthy specimens of *C. punctatus* (22 ± 3 g, 15 ± 2 cm) were exposed to three sub-lethal concentrations viz., sub-lethal 1 (1/4th of LC50 = 0.58 ppb), sub-lethal 2 (1/2nd of LC50 = 1.16 ppb) and sub-lethal 3 (3/4th of LC50 = 1.74 ppb) of the pesticide and the tissue sampling was done after 24 h, 48 h, 72 h, and 96 h, exposure for assessment of DNA damage. The genomic DNA was isolated from blood and RAPD-PCR was then carried out using a set of six selected Operon (OPA & OPB) primers for PCR amplification. The amplicons were resolved on 1.5% agarose gel and compared with the band profile of the control specimens. The appearance/ or disappearance of bands and /or intensity were evident in the RAPD profile of exposed as compared to the control fishes. Thus, the results indicated the utility of this technique for genotoxicity assessment of pesticides.

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Design and Synthesis of Thiazolidinones as Anti-Stroke Agents

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Ischemic stroke is the third leading cause of death in adults in industrialized countries [1]. It is accompanied by a robust inflammatory response, glutamate mediated excitotoxicity, release of reactive oxygen species and the initiation of apoptosis. This debilitating disease however, has limited treatment options and hence research continues to find effective anti– stroke agents. Thiazolidinediones (TZDs) have been recently reported to exhibit potent anti-inflammatory and anti-oxidant actions and also to inhibit both neural excitotoxicity and apoptosis, which has generated interest in their anti-stroke potential [2]. TZDs are agonists of peroxisome proliferator-activated receptor (PPAR)-□, a critical transcription factor in the regulation of adipocyte differentiation and these include the anti-diabetic drugs, troglitazone, pioglitazone (fig.1) and rosiglitazone. However, the major problem associated with this class of compounds is that they cause side effects like weight gain and edema [3]. Since the head group (tzd) has been reported to be responsible for binding to the ligand, several head group modifications have been done in order to obtain a better pharmacological profile. In this context, we have designed and synthesized compounds with a thiazolidinone head group (fig.2) in order to study its effect on PPAR □ and have tested their anti-stroke activity. Some of these compounds have shown interesting anti-stroke activity, with marked reduction in infarct size and elevation in endogenous stores of antioxidants. The details of the study will be presented.

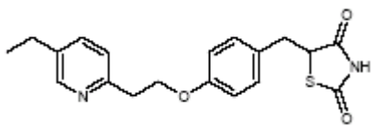

Fig.1:Pioglitazone

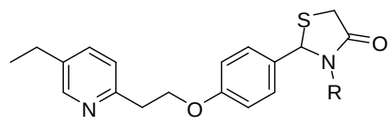

Fig.2: Thiazolidinone: general structure
R= H, alkyl, benzyl etc.

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P-167

Analysis of flower buds of *Eugenia caryyophyllata* using direct analysis in real time mass spectrometric techniques

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*Eugenia caryophyllata*_(clove) contains many compounds which have good medicinal value and good fragrance. Clove is known to be a traditional medicinal plant used as expectorant, antiemitic, stimulant antiflatulene and for the treatment of dyspepsia. The essential oil extracted from the dried flower buds of clove is used as topical application to relieve pain. The biological activity of *Eugenia caryophyllata* has been investigated on several microorganism and parasites. Including pathogenic bacteria herpes simplex and hepatitis c viruses. Different compounds of clove like eugenol have been used widely as herbal drug to treat dyspepsia, acute chronic gastritis and diarrhea. It was first component of an essential oil proved to be a significant germicide and sedative used in dentistry and today is still used.
Its other major components are β caryophyllenes, α humulene and humulene epoxide. These possesses antibacterial, anticarcinogenic, antifungal properties

The applicability of new mass spectrometric technique (DART) has been studied in analysis of compounds of Eugenia caryophyllata. Four fraction of ethanol extract of clove was analyzed by holding them in gap between the DART source and mass spectrometer for measurement. Volatile and nonvolatile compounds were identified by DART MS. The confirmation of structure of identified compounds was made through their accurate molecular formula determination. Characterization of these compounds has been done by different technique of mass. We used DART MS technique for this purpose. As we know mass spectrometry is one of the most powerful analytical methods available for structure identification of organic compounds. DART is new, more efficient method, which does not required investment of time (for sample preparation). Open air ionization method minimizes the sample and widens the range of mass spectrometry application. This method eliminates or significantly reduced the need for destructive sampling. Ionization in DART MS has traditionally been done within the vacuum system of MS. However using DART the sample is placed in stream of He that contains ionized atmospheric gases and water vapor and O2. Analyte in sample are ionized in open air of laboratory environment. This means that organic compounds in sample can be directly and in real time can determined without consuming analytical protocol and thus with high sample throughput.
DART can ionize not only low mass volatile compounds but also higher mass compounds that contains reactive functional group that can not be readily determined by GCMS.
Results and conclusion of above work will be discussed during the poster presentation.

P-168

Differentiation of *Tinospora cordifolia* plant type using direct analysis in real time mass spectrometric technique

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Species of the genus Tinospora are widely employed as medicinal plants throughout a large part of Asia and Africa.[1] Tinospora cordifolia Miers occurs throughout the plains of India. It has been used for several centuries in the Indian system of medicine for the treatment of jaundice, diabetes, skin diseases and anaemia.[2] The active principles of Tinospora cordifolia a traditional Indian plant were found to possess anticomplementary and immunomodulatory activities.[3]

Direct detection of chemicals on surface without sample preparation is ultimate goal in the field of mass spectrometry. Direct analysis in real time (DART) is a new ionization technique introduced by Cody et.al. DART is conducted in open air allowing for the direct analysis of almost variable type of sample with no previous sample preparation. Ion source of DART uses helium generated from an electrical discharge. This metastable helium ionizes atmospheric water generating protonated water cluster which can in turn ionizes molecules on the stream of helium therefore DART produces mass spectra consisting mainly of [M+H]+ molecular cation.

In this study we analyzed the stem of Tinospora cordifolia plant type (male plant and female plant) by using Direct Analysis in Real time mass spectrometry. More data and experimental part will discuss during the poster presentation.

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P-169

Block Copolymer Self-Assembled Micelles As Nanocarriers For Amphotericin B

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The continuous search for new drug delivery systems is driven by the ardour to maximize therapeutic activity while minimizing negative side effects. Particularly, much attention is now being paid to amphiphilic polymeric micelles as nanocarriers for drug delivering systems. Block copolymer micelles as drug carriers are able to provide highly desirable advantages. They are e.g. solubilization of poorly soluble drugs and thus increased bioavailability, reduced toxicity and other adverse effects, high loading capacity, nano-size, enhanced permeability across physiological barriers and they can also extend blood half life upon intravenous administration. In present study shown that the amphiphilic T r i -block copolymer Pluronic F-68 self–aggregated spontaneously into nano- sized micelles in aqueous solution. The nanocarriers for Amphotericin B was prepared from the functionalized block copolymer (Pluronic F-68) by dialysis and solvent evaporation method.It has a very low value of CMC (10^{-4}M) and CAC which indicates a good stability of the micelles. The drug entrapment efficiency of the micelles was satisfying and enhanced greatly upto the 33% with the dialysis method over the solvent evaporation method, and solubility of Amphotericin B was enhanced from 1000 to 1200 fold compared to its aqueous solubility. The particle size of about 99 nm of the loaded polymeric micelles of pluronic,was determined by Malvern Zetasizer and TEM photographs .Result has shown that very low concentration of micellization onset and the absence of toxic effects (haemolysis) represent promising characteristics for the development of a novel polymeric drug carrier. Current work was focussed to revealed that pluronic micelles are a feasible choice to enhance the solubility of hydrophobic drugs (i.e AmB) accompanied with reduction in haemolytic activity shown by aggregation behavior of polymeric micelles and hence can be a new approach in the struggle to find better carriers for drugs that are virtually insoluble in water.

P-171

KalmCold™, an extract of *Andrographis paniculata* alleviates symptoms of uncomplicated upper respiratory tract infection: A double blind placebo controlled clinical study

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KalmCold™, an extract of *Andrographis paniculata*, was evaluated for efficacy in patients with uncomplicated upper respiratory tract infection (URTI) in a randomized, double blind placebo controlled study. The subjects were allotted to either KalmCold™ (200 mg/day) or placebo groups. Symptoms of URTI viz., cough, expectoration, nasal discharge, headache, fever, sore throat, earache, malaise/fatigue and sleep disturbance were self evaluated by patients using Visual Analogue Scale. In both the groups, mean scores of all symptoms showed a decreasing trend from day 1 to day 3, but from day 3 to day 5 most of the symptoms in placebo group either remained unchanged or got worsened whereas in KalmCold™ group all symptoms showed a decreasing trend. Within groups, mean scores of symptoms in both the groups decreased significantly from day 1 to day 3 and day 5 while from day 3 to day 5 all symptoms except expectoration in placebo group did not improve considerably whereas in KalmCold™ group all symptoms improved significantly except earache. Comparing mean between both groups, all symptoms at day 1 and day 3 were found to be the same while at day 5 all symptoms except earache in KalmCold™ group improved significantly than placebo group. Similarly, within groups, overall scores of all symptoms in both the groups decreased significantly from day 1 to day 3 and day 5 while from day 3 to day 5 placebo groups did not improve significantly whereas KalmCold™ group exhibited remarkable improvement. On between groups analysis, KalmCold™ group revealed significant reduction in overall symptom scores as compared to placebo. The overall efficacy of KalmCold™ was 2.1 times better than the placebo. There were only few minor adverse effects in both placebo and KalmCold™ groups, with no significant difference in occurrence. Based on the findings of the present study, KalmCold™ was found to be effective in the management of URTI.

P-172

Identification of Cholecystokinin-B/Gastrin receptor on various cancer cell lines and effect of the quinazolinone derivatives on growth of pancreatic cancer cell line.

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Background: Cholecystokinin receptor, a type of GPCR, is a vital gastrointestinal hormone and one of the most abundant neurotransmitter peptides found in the brain [1]. Two types of CCK receptors- A and B have been distinguished on the basis of affinity to sulfated and non sulfated CCK analogs[2]. CCK-A receptor is responsible for gallbladder contraction, pancreatic exocrine secretion, gastrointestinal motility, satiety and glucose homeostasis [3], [4]. CCK-B receptor is involved in gastric acid secretion, anxiety regulation [5], [6]. The trophic actions of Gastrin/ CCK have been documented in gastric, pancreatic and colon cancer cells supporting the potential role for this regulatory peptide in the growth of these malignancies [7], [8]. Cell surface receptors over expressed in tumor tissues could act as targets for anticancer drugs attached to receptor ligands.

Aim: The aim of our study was to check the presence of CCK-B receptor on various cell lines and characterize quinazolinone derivatives as a non peptidic antagonist by MTT assay.

Results: Expression of CCK-B receptor was checked on twelve cancer cell lines such as ACHN, A-498, HCT-15, IMR-32, MDAMB-468 through RT-PCR and Western. CCK-B receptor was detected through RT-PCR and it was confirmed through western and sequence analysis. MiaPaCa-2, AR-42J and Jurkat were used as

positive control for the expression of CCK-B/Gastrin receptor. Toxicity of the synthesized derivatives in our lab was assessed by MTT assay in serum free media on MiaPaCa-2 cell line. It showed a maximum growth stimulating effect by Pentagastrin at concentration of 10^{-9} mol/ml. The stimulatory effect of Pentagastrin was braught down by the antagonists. The trophic effect of pentagastrin was diminished by CCK-B/Gastrin receptor antagonists.

Conclusion: The study revealed the presence of CCK-B/Gastrin receptor on the cell lines chosen which can be used as targets for the synthesized antagonists screened on positive control.

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P-173

LiBr as an efficient catalyst for one-pot synthesis of Hantzsch 1,4-dihydropyridines under mild conditions

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A simple, inexpensive and efficient one-pot synthesis of 1,4-dihydropyridines has been accomplished via lithium bromide-catalyzed Hantzsch three-component condensation reaction of an aldehyde, a *β*-ketoester and ammonium acetate in acetonitrile at room temperature in good to excellent yields. The present protocol is applicable to wide range of substrates including aliphatic, aromatic and heterocyclic aldehydes affording 1,4-dihydropyridines. Hantzsch 1,4-dihydropyridines (1,4-DHPs) and their derivatives have gained considerable importance in the field of organic and medicinal chemistry since they display a fascinating array of pharmacological properties.[1-3]

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P-174

Intellectual property-A strong determinant of Economic Growth

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The returns from almost all human endeavors can ultimately be translated into monetary gains. The past few years have seen increased attention to the strengthening of intellectual property rights due to globalization. The development of Intellectual property rights (IPR) over the years has invariably brought

an upsurge in the outlook of nations towards the aspect of societal and cultural growth, this being said with the preliminary assumption that economic growth has been the most affected realm and that it requires a separate spectrum of analysis. The artifacts between the IP regime and the national economy can be easily interpreted by the fact that India's independence had itself brought an era where the enactment of the national IP laws were considered to stand on the touchstone of the market economy. The aim of the present paper is to investigate the impact of strong IP regime in the economic development of a nation. Undoubtedly, IP systems must be developed so as to bring in socio-economic well-being. The fact that strong IPR actually provoke IPR infringements in many developing nations also seems to be an issue which needs to be analysed while understanding the need of the former. The trade-off between unfair competition laws and IP also assumes importance of high magnitude and hence needs to be particularly emphasized. With the growing recognition of IPR, the importance of world wide forums on IPR is realized. Companies, universities, and industries want to protect their IPR internationally. In order to reach this goal, countries have signed numerous agreements and treaties.

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P-175

HDP-A novel heme detoxification protein from *Plasmodium vinckei*

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Despite our best efforts malaria remains a disease of global significance with some 40% of the world's population at risk. Each year malaria kills up to 2.7 million people in Africa alone and global Gross Domestic Product (GDP) losses are estimated to be of the order of $20 billion.
During its intra-erythrocytic stage, *Plasmodium* ingests and degrades up to 75% of the host cell hemoglobin. The hydrolysis of hemoglobin makes amino acids available for parasite's development, while at the same time, this process liberates large amounts of heme, which is extremely toxic for the parasite. Malaria parasite utilizes a unique pathway of hemozoin formation to avoid heme toxicity. Therefore, along with a continuous degradation of hemoglobin, a concomitant detoxification of heme is necessary for an uninterrupted growth and proliferation of the parasite. Parasite effectively detoxifies heme, primarily by its conversion into an insoluble crystalline material called Hemozoin (Hz) which is mediated by heme detoxification protein (HDP). Our studies with laboratory derived arteether resistance strain of *P. vinckei* have shown that the hemozoin level at 10% parasitemia in resistant parasites are 15-20 fold lower as compared to the values in sensitive parasites. Here a study has been undertaken to clone and characterize HDP from *P. vinckei* sensitive and resistant parasites to elucidate its implication in resistance to artimisinin derivatives.

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Differential proteomic study revealed HPRT as a potential antimalarial drug target.

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Malaria has remained a major threat to public health and economic development in tropical and subtropical regions of the world with approximately 515 million cases each year. A better understanding of the biological processes that the parasite uses during its developmental cycle should lead to better therapeutics and amelioration of this devastating disease. The increasingly serious problem of malaria parasite resistance to currently used antimalarials has led to an urgent need to develop new and effective antimalarial molecules. This goal can be achieved in two ways: either by focusing on validated targets in order to generate new drug candidates; or by identifying new potential targets for malaria chemotherapy.
In order to identify potential drug targets, proteomic study was performed with parasite preparation from arteether resistant and sensitive strains of *Plasmodium vinckei* to compare the differential protein expression level. Gel patterns have shown that a specific 27kDa protein is expressed to a greater extent as

compared to that in resistant parasites. MALDI analysis of this specific band revealed it to be hypoxanthine phosphoribosyl transferase (HPRT). The cloning, overexpression and purification of this protein under native condition has been performed and further characterization of this protein is underway. As is well known, the enzyme HPRT is central to the salvage pathway for purine nucleotide biosynthesis in protozoans which lack *de novo* pathway, and hence is a potential antimalarial chemotherapeutic target.

P-177

An Efficient One Pot Synthesis of 4-Aroyl-2-pyrones: A New Class of Potential Estrogen Receptor Ligands

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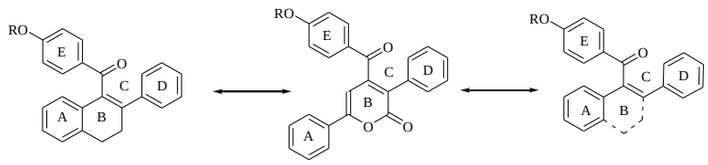
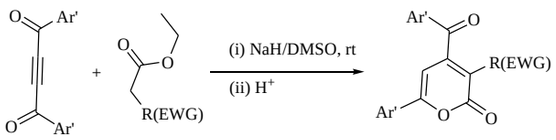
The 2-pyrone motif is found in many naturally occurring compounds, which display a wide range of beneficial & exploitable biological and medicinal effects[1]. such as anti cancer, antimicrobial, phytotoxic, HIV-1 protease inhibitors etc[2,3]. As part of our research programmed towards synthesis of new chemical leads with estrogen receptor modulating activities, we designed 4-aroyl-3,6-disubstituted 2-pyrone system as a suitable building block which could be modified with desirable substituents to develop target molecules as estrogen receptor ligands. The rationale to design these molecules was based taking into consideration the similarity of triaryl propenones such as cyclic trioxifene and acyclic E-TAP which are well known estrogen antagonists. The tetracyclic core of rings A, B, C & D of these two estrogen antagonist could mimic the central core of 3,6-diphenyl pyranone scaffold and the aroyl moiety with *tert*. amino alkoxy group at the 4-position of the 2-pyrone can act as the antagonist chain.



The compounds were synthesised through novel one step reaction between 1,4-diphenyl-but-2-yne-1,4-dione and diethylmalonate(1:1 equiv) using sodium hydride in DMF at room temperature to give the desired 4-aroyl-2-pyrones in very good yields.



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P-178

Studies on arene interactions: ^{1}H NMR and crystallographic studies of substituent effects on pyrazolo[3,4-*d*]pyrimidine core based flexible dissymmetrical polymethylene linker compounds

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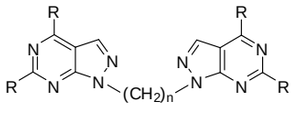
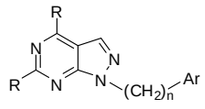
Attractive interactions between arene moieties are termed as arene interactions. They are ubiquitous in nature and plays a significant role in chemistry, biology and crystal engineering. However, the nature of arene interactions remains far from satisfactory. One of the strategies employed to study arene interactions include connecting two aromatic moieties with polymethylene linker so that arene interactions could be studied by ^{1}H NMR spectroscopy at molecular level.



1: R = SMe, SEt, OEt etc. and n = 2, 3,4



2

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

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P-179

Evaluation Of Flower Of *Barleria Prionitis* For Anti-Inflammatory And Anti-Nociceptive Activity

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Traditionally aerial parts of *Barleria prionitis* Linn. has been used in the inflammation, fever & toothache. The present study was undertaken to evaluate the anti-inflammatory and anti-nociceptive activity of 50% ethenolic extract from flower of *B. prionitis* (BPF) against different model in experimental animals. The BPF in doses of 50, 100 and 200 mg/kg caused a dose-dependent inhibition of swelling caused by carrageenin equivalent to 17.8–48.6% protection (P>0.05–P<0.001) and in cotton pellet granuloma, 15.32–36.4% protection (P<0.01-P<0.001) was observed from inflammation. There was a significant increase in analgesio meter force induced pain in mice equivalent to 26.3–48.23% protection (P<0.01-P<0.001) & 5.24 - 34.6 % (P<0.05–P<0.001) protection against Acetic acid induced writhing. Our results shows that flower of *B. prionitis* possess significant anti-inflammatory and anti-nociceptive activity.

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UV-Spectrophotometric Assay Method For Serratiopeptidase

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Serratiopeptidase is an anti-inflammatory enzyme widely used in the treatment regime of various diseases. It gives anti-inflammatory action by breaking down abnormal exudates and protein and by promoting the absorption of the decomposed product through the blood and lymphatic vessels. Present bioassay methods of Serratiopeptidase is very tedious so a new UV-spectrophotometric assay method was developed and compared with the existing Bioassay method. The bioassay of serratiopeptidase was carried out by 'Tyrosine bioassay method' using different concentrations in triplicate. The same solutions (in distill water) were scanned in UV at 276 nm as λ-max. The Absorbance (A) values of the bioassay directly correlate with the proteolytic activity of the enzyme. We compared the UV absorbance values with bioassay absorbance values and derived a common factor 0.82. If we multiply the UV readings with this factor, we get bioassay absorbance readings which we can directly put in the bioassay formula and get the proteolytic activity.

Thus the new UV-spectrophotometric method was found to be simple, reproducible and comparable with the tyrosine bioassay method.

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Development And Validation Of A Hptlc Method For The Simultaneous Estimation Of Simvastatin And Ezetimibe In Tablet Dosage Forms

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Objective - Development and validation of a hptlc method for the simultaneous estimation of simvastatin and ezetimibe in tablet dosage forms.

Introduction

Ezetimibe and simvastatin is an anti-hyper lipidemic medication which is used to lower cholesterol levels. Specifically, it appears to bind to a critical mediator of cholesterol absorption. It is also used in combination therapy with HMG-CoA reductase inhibitors.

Procedure

A simple, precise, accurate and rapid high performance thin layer chromatographic method has been developed and validated for the determination of simvastaitn and ezetimibe in a combined dosage forms. The method described utilizes precoated silica gel $60F_{254}$ on aluminum sheet as stationary phase and methanol: Glacial acetic acid as mobile phase (9.5:0.5)v/v which gives good separation of simvastatin (Rf-0.38) and ezetimibe (Rf -0.54).The developed method was validated as per ICH guidelines for accuracy, precision and repeatability. The detector response of simvastatin and Ezetimibe was found to be linear in the range 8-32 ng/mcL and 20-80 ng/mcL respectively. Precision of the instrument was checked by repeated scanning of the same spot of simvastatin and Ezetimibe (20ng/mcL and 50ng/mcL) on HPTLC plate (n=7).Repeatability of the method was checked by analyzing a standard solution of Simvastatin and Ezetimibe 10mcL on HPTLC plate (n=7) The average recovery for simvastatin and Ezetimibe is (99.84% and 99.71%) respectively, which indicated there is no interference of the other excipients present in the formulation. Low values of standard deviation and Co-efficient of variation are indicative of the high precision of the method.

Conclusion

The developed HPTLC technique is simple, precise, specific and accurate and the statistical analysis proved that method is reproducible and selective for the analysis of Ezetimibe and Simvastatin in bulk drug.

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Effect of 3-Thienylalanine-Ornithine-Proline on L-NAME Induced Hypertension in Rats

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Our previous study showed that 3-Thienyl-alanine-Ornithyl-Proline (TOP) exhibited longer duration of antihypertensive action than captopril in SHR model. Further, we demonstrated that TOP significantly increases the nitric oxide level in serum and different tissues isolated from SHRs. Therefore, in continuation of our previous study, presently, we investigated effect of TOP (20 mg/kg/day) and captopril (40 mg/kg/day) on blood pressure, ACE level, nitric oxide and lipid peroxidation in N^G-nitro-L-arginine methyl ester (L-NAME) induced rat model of hypertension. Chronic oral administration of L-NAME significantly increased systolic blood pressure from 104 ± 4.62 to 187 ± 3.74 mmHg, however L-NAME+TOP and L-NAME+captopril treated groups showed an increase of upto 132 ± 2.78 mmHg and 149 ± 3.24 mmHg respectively. In addition, significant decrease in the serum ACE level was observed in L-NAME+TOP treated group as compared to control. Furthermore, nitrite and malondeldehyde level which were decreased after L-NAME administration were significantly increased in L-NAME+TOP treated group. In conclusion, TOP although administered at two times lesser concentration than captopril showed equipotent effect on blood pressure, ACE level, lipid peroxidation and nitrite level in L-NAME induced hypertensive model. This can be attributed to the fact that thiophene ring in the test molecule being antioxidative in nature presumably accounting for the enhanced antioxidative action of TOP in this model.

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Aim: Surgery Improves Survival in Metastatic Breast Cancer

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The term, metastatic, describes a cancer that has spread to distant organs from the original tumor site. Metastatic breast cancer is the most advanced stage of breast cancer. Cancer cells have spread past the breast and axillary (underarm) lymph nodes to other areas of the body where they continue to grow and multiply. Breast cancer has the potential to spread to almost any region of the body. The most common region breast cancer spreads to is the bone, followed by the lung and liver.

Women with metastatic breast cancer live considerably longer if they receive surgery of the primary tumor rather than palliative treatment. Women who have distant metastatic disease upon diagnosis of breast cancer still benefit from removal of the primary tumor. In fact, these patients survive significantly longer than those who do not undergo surgery

Patients diagnosed with Stage IV or metastatic breast cancers have disease that has spread from the affected breast to one or more distant sites in the body. Approximately 3-10% of patients have distant metastatic disease upon initial diagnosis of their cancer.

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P-184

Polymer Bound Peroxomolybdenum Complexes: Synthesis, Stability and Effect On Alkaline Phosphatase Activity

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There has been a continuous upsurge in interest in metal containing polymeric materials due to their tremendous potential in diverse fields including catalysis, drug delivery systems and a host of other biomedical applications. Despite the enormous progress in the field of metal containing polymers, very little information is available dealing with synthesis or use of peroxometal compounds anchored to soluble polymers in catalysis, or their effect on inhibition and activation of enzyme function [1]. There has been a growing awareness on the importance of enzyme inhibition as a mode of action for inorganic drugs in recent years and is a thriving area of current research.

The present work deals with the first successful synthesis and characterisation of peroxomolybdate(pMo) complexes anchored to soluble polymers viz poly(acrylate) (PA), poly(methacrylate)(PMA) and polyacrylamide(PAm) of the type $[Mo_2O_2(O_2)_4$(carboxylate)]-PA (PAMo), $[MoO(O_2)_2$(carboxylate)]-PMA (PMAMo) and $[MoO(O_2)_2$(amide)]-PAm, PAmMo. The compounds were characterised by elemental analysis, spectral and physico-chemical methods including SEM and EDX analysis. These macrocomplexes are stable in solution of a wide range of pH values and are relatively resistant to degradatiion by the enzyme catalase compared to its natural substrate, H_2O_2. These compounds induce a strong inhibitory effect on alkaline phosphatase(ALP) activity with IC_{50} in the range of 28.2µg/ml to 34.5µg/ml. The enzyme kinetic studies shows that the mode of inhibition induced by macromolecular pMo compounds is non-competitive.

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P-185

Aromatization of Hantzsch 1,4-dihydropyridines and synthesis of 5-benzylated barbituric acids *via* a microwave-assisted three-components reaction in solvent-free conditions

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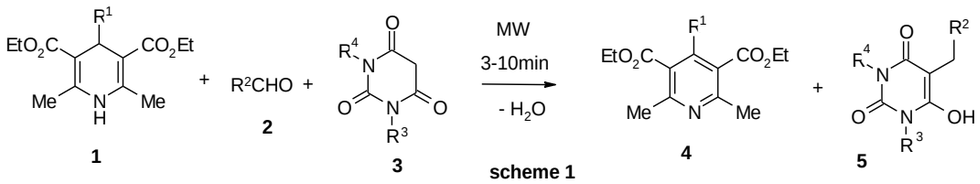
Hantzsch 1,4-dihydropyridines (1,4-DHP) are an important class of drugs for the treatment of cardiovascular disease such as hypertension and angina pectoris [1]. Some commercial representatives such as amamodipine, felodipine, nifedipine and nicardipine are among the best selling DHP drugs used in the treatment of cardiovascular diseases. In the human body these compounds are oxidized to pyridine derivatives, by the action of cytochrome P-450 in the liver [2]. The oxidation of 1,4-DHPs to the corresponding pyridine derivatives constitutes the principal metabolic route in biological systems, as well as a facile access to the corresponding pyridine derivatives, which show anti-hypoxic and anti-ischmic activities,[6] from easily available DHPs. In order to understand these biological process, as well as to develop a useful synthetic approach to poly substituted pyridines, the oxidative aromatization of 1,4-DHP derivatives has received considerable attention from synthetic chemists. A variety of reagents have been developed for the aromatization of DHPs. These include the use of stoichiometric or excess amount of inorganic oxidants or organic oxidants. However, all these methods have some limitations and drawbacks. Therefore development of more efficient method for the oxidation of 1,4-DHPs is still sought after.

5-Alkylated barbituric acids are an important class of compounds of medicinal importance. A number of clinically used hypnotic drugs of barbiturates class, for example veronal, seconal, phenobarbital, sodium

pentothal etc, are simply 5-alkylated derivatives of barbituric acid [3]. Bucolome is an antiinflamatary drug. Moreover, 5-Benzyl barbituric acids are an important class of HIV-1 and HIV-2 protease inhibitors.
The development of resource and eco-friendly process in terms of sustainable chemistry has become a focal point of chemical research in recent years. In the present world of green chemistry, chemical processes with high atom economy have received a growing interest from the scientific community.
In our continued interest [4] in the development of highly expedient methods for the synthesis of diverse heterocyclic compounds of biological importance, we report here a novel and green oxidative aromatization of 1,4-DHP and synthesis 5-benzylated barbituric acids *via* a micro-wave (MW) assisted one-pot three-component reaction in solvent-free conditions (Scheme 1).



1 **2** **3** **4** **5**

scheme 1

The details of the work will be presented.

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Synthesis And Studies Of Novel Porphyrin Thiazoles

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There has been continuous and increasing interest towards the synthesis of porphyrins due to its diverse medicinal and spectral properties [1]. It is imperative to prepare porphyrin macrocycle with diverse functional groups in order to explore their utility in biomimetic and materials chemistry. The change of substituent at *meso*- and the peripheral positions of the porphyrin ring have shown profound effect on its physical, chemical and biological properties [2]. Porphyrin attached nitrogen heterocycles are of immense significance due their contribution in hydrogen bonding, metal coordination, alkylation properties and generally showed enhanced biological activities [3]. Peripheral nitrogen heterocycles also provides easy access to diverse porphyrins with tunable biological and electronic properties. In our efforts to prepare novel porphyrin heterocycles we have synthesized a series of novel prophyrin thiazoles (Figure 1) and studied their spectral and biological properties. Details of this study will be presented.

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A Three Component Coupling Protocol for the Synthesis of Porphyrin Tetrahydroquinolines

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Multi component coupling reactions are of growing interest in synthetic organic chemistry, because of their wide applications in combinatorial chemistry. These reactions provide access to novel heterocyclic structures that are particularly useful as scaffolds in pharmaceutical development [1]. Tetrahydroquinolines moieties became interesting after the isolation of alkaloids martinelline and martinellic acid from the roots of *Amazonian plant Martinella iquitosensis* [2]. They are found in a number of pharmaceutically active compounds. Porphyrin molecules and its derivatives are known for their wide applications in medicinal chemistry such as photosensitizer in PDT, boron neutron capture therapy (BNCT), radiation therapy (RT) and in magnetic resonance imaging (MRI) [3]. In continuation of our interest in synthesis and study of porphyrin appended heterocycles, we have developed an efficient route, involving a three component coupling reaction of 5-(4'-aminophenyl)-10,15,20-triarylporphyrins, aldehydes and pyran for the synthesis of porphyrin appended tetrahydroquinolines. It is expected that *in situ* formed imine by condensation of aminoporphyrin and aldehyde acts as a diene in a hetero Diels-Alder reaction with the electron-rich dienophile [4]. Details of the synthesis and characterization will be discussed in the presentation.

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Anti-hyperglycemic, anti-hyperlipidemic and spermatogenic potential of Tridax procumbens Linn. in alloxan-induced diabetic rats

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Diabetes is a potentially life-threatening illness in which blood glucose levels are abnormally high. Abnormalities in lipid profile and fertility are the most common complications in diabetes mellitus, which is found in most of diabetics. *Tridax procumbens* Linn. (Family- Asteraceae; common name- Dhaman grass) is common herb found in India. The effects of oral administration of 50% methanolic extract of whole plant of *Tridax procumbens* Linn. (250 mg/kg body weight) were studied for anti-diabetic, anti-hyperlipidemic and spermatogenic effects in diabetic rats. In alloxan (ALX)-induced diabetic rats, it was observed that both the standard drug (Glibenclamide) and methanolic extract of *Tridax procumbens* Linn. exhibited significant lowering of blood glucose level on a 30 day model. Further, the methanolic extract also showed significant anti-hyperlipidemic and spermatogenic effects in ALX induced diabetic rats. The administration of extract has also accelerated the process of spermatogenesis by increasing the sperm parameters, relative sex organ weights and serum testosterone levels as compared with diabetic control rats. The hypolipidemic and spermatogenic effects mediated by *Tridax procumbens* may also be

anticipated to have biological significance and provide a scientific rationale for the use of *Tridax procumbens* as an anti-diabetic plant.

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Title: Mining the bioactive compounds from mine microbes

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Methicillin-resistant Staphylococcus aureus (MRSA) is the most problematic gram-positive bacterium in public health not only because it is highly prevalent but also because it has become resistant to almost all available antibiotics except vancomycin and teicoplanin. Recently, its susceptibility to vancomycin has decreased, and vancomycin-intermediate and vancomycin-resistant *S. aureus* have increasingly been found in several countries. Furthermore, a decrease in the susceptibility of MRSA to teicoplanin has also been reported in several hospitals around the world. Although the chemical compounds of terrestrial and marine microorganisms are being explored, however recently it is seen that the frequency of redundancy is very high in these resources, especially terrestrial soils. Within terrestrial soil there is urgent need to quest for unique ecological units having extreme conditions. Mine is one of such area, which has been least explored compared to many other terrestrial resource samples. Each mine is by itself a selective ecosystem for allowing certain microbes. To date there is hardly any report of any antibiotic isolated from microbe from mine origin.

Method:

In the present study we have isolated and purified 129 actinomycetes and 25 other eubacteria from soil samples iron and coal mines from India. These were grown in specially designed isolation medium by conventional shake flask fermentation methods.

Results:

Out of the 129 actinomycetes isolated, 27 showed antibacterial activity and 1 is a broad spectrum antifungal. The study further describes *in vitro* antibacterial and antifungal screening of these isolates specifically looking anti-MRSA and anti-VRE activity. The results of these studies are discussed in the paper. The potency of these isolates can be exemplified from result of one of the broad spectrum antibacterial sample which has shown an MIC of 1.95 µg/ml.

Conclusion:

From the studies done, we can conclude that actinomycetes reside in a variety of extreme geographical locations and it is evident that mines are one of the habitats that can be potential resource of actinomycetes. This indicates that mines can be explored in order to meet the current desperate drug market demands against resistant super-bugs.

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A simple method of screening for the identification of estrogen receptor subtype -α and -β selective ligands using recombinant ER-LBD proteins

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Being associated to a broad spectrum of diseases which includes breast cancer, prostate cancer, endometrial carcinoma, osteoporosis and leukemia, ERα and ERβ are considered to comprise a very important class of drug targets [1]. Several classical as well as newer methods have been used to identify novel ER selective ligands that include the use of receptor binding assay as the basic experiment followed by assessment of their functional activity by means of transactivational methods and also by *in vivo* efficacy [2,3]. But the limitation to get ER in enormous amount for such purpose is the retarding factor. Since bacterial expression system is considered to be advantageous over other methods in terms of simplicity and cost, in this study, overexpression of ligand binding domain (LBD) of ERs in bacterial system has been attempted and used to screen the antiestrogenic compounds. Since LBD has been described to be sufficient for specific ligand binding [4], the present study was undertaken to over-express LBD of human ERα and ERβ in *E. coli*. We were able to recover the adequate amount of protein (6-8 mg/l) in

soluble fraction without the requirement of detergent. Both the purified as well as crude protein preparations were found suitable for the purpose of assessing the binding affinity of various ER ligands. The activity of LBDs was characterized by immunoblotting and also by studying receptor binding parameters. The K*d* values of ^{3}H -estradiol binding was found to be 4.2 nmol/l for ERα-LBD and 2.2 nmol/l for ERβ-LBD as determined by Scatchard analysis which indicates the high affinity binding activity of ER-LBDs. Our LBD preparations displayed appreciable ligand specificity as observed in competitive binding assay. This method has been developed as a simple and low-cost *in vitro* screening system to identify ER specific ligands. It may help in the lead identification process which can further be evaluated for their functional efficacy and used as therapeutic agents.

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Electro-chemical and Microbial Study of Anti Aids Drug with Fe (III)

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The anti HIV drug Perfenazine has been qualitatively and quantitatively analysed by direct current polarographic (DCP), differential pulse polarographic(DPP) and amperometric technique.

Physicochemical, and microbial studies on Fe (III)-Perfenazine complex have been done in solid and aqueous phase. On the basis of elemental analysis, polarographic studies and amperometric titrations, the metal:drug ratio has been worked out to be 1: 1. The metal ligand interaction has been studied using polarographic method at 25±l°C and at ionic strength of μ = 1.0 (KCI). IR spectral studies have been used to ascertain metal:ligand binding site which speaks of the complex formation between the metal and the Perfenazine ligand through the primary –OH group. Microbial studies on the complex was done against various pathogenic bacteria viz. *Eschirichia coli, Salmonella typhi, Vibrio cholerae* and *Diplococcus pneumoniae.* The results of the microbial studies with the metal:drug complex revealed that the drug: metal complex is more potent against the pathogenic

bacteria as compared to the pure drug, Perfenazine. As such Fe (III)-Perfenazine complex may be recommended to the therapeutic experts for its possible use as more potent anti-AIDS drugs.

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Hemiketal and Furano Diterpene of *Caesalpinia bonduc*

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In medicinal chemistry natural products play a important role to provide different molecules to act as a lead molecule for various activities. Natural products are derived from the plants and *Caesalpinia bonduc* is one of them. Different part of *Caesalpinia bonduc* L. Roxb., (Fabaceae) are used to treat asthma, chronic fever, cough, headache and stomach upset.[1, 2] Different parts of the plant have shown a variety of pharmacological activities such as antimicrobial, adaptogenic, contractile activity in smooth muscles and skeletal muscles and antifilarial activity.[3, 4]

In the continuation of activities of *Caesalpinia bonduc* significant inhibition of breast cancer cell lines in ethanolic extract. Antiproliferative activity guided fractionation of ethanolic extract of *Caesalpinia bonduc*, resulted in the isolation of three cassane ditepenes hemiketals, caesalpinolide-C, caesalpinolide-D, caesalpinolide-E and one cassane furanoditerpenes. The isolated compounds were tested for their

antiproliferative activity against MCF-7 (Breast adenocarcinoma), DU145 (Prostate carcinoma), C33A (Cervical carcinoma) and Vero (African green monkey kidney fibroblast) cells.

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Synthesis, kinetics and biological activity of benzimidazoles analogues

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Compounds with the structure of -C=N- (azomethine group) are known as Schiff bases, which are usually synthesized from the condensation of primary amines and active carbonyl groups. Schiff bases are a important class of compounds in medicinal and pharmaceutical field. They shows biological activities including antibacterial , antifungal and antitumor activity.Similarly benzimidazole derivatives have been used for a long time for a variety of biological activities such as CNS depressant,anti cancerous,antibiotic,antihistaminic ,anticonvulsants and many others.

Based on mentioned properties for Schiff bases and benzimidazole analogues we reported herein the synthesis, spectroscopic characterization as well as their efficacy for radiopharmaceuticals and as antimicrobials. In this paper we have synthesized eight biologically important unsymmetrical schiff bases of amino benzimidazole with different alehydes.

Which are characterized by various spectroscopic methods (IR, FAB-MS, ^{1}H NMR). Evaluation for specific radiopharmaceuticals through radiolabeling with ^{99m}Tc shows more then 97% efficiency and complexes were stable for about 12-15 hours at 30^{0} C in the presence of serum. Biodistribution studies show very good tumor uptake of two compounds.Some amino acid analogue as well as Compounds containing hydroxyl-rich side chains shows enhanced antimicrobial activity against Bacillus subtilis, Pseudomonas fluorescence, Staphylococcus aureus, Aspergillus Niger, Candida albicans and Trichophyton rubrum.

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Transitional Metal oxide nanoparticles Synthesis, Characterization, and their sustain delivery in cancer agent

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Magnetic nanoparticles offer exciting new opportunities toward developing effective drug delivery systems, as it is feasible to produce, characterize, and specifically tailor their functional properties for drug delivery applications. An external localized magnetic field gradient may be applied to a chosen site to attract drug-loaded magnetic nanoparticles from blood circulation. Drug targeting to tumors, as in other pathological conditions as well, is desirable since anticancer agents demonstrate nonspecific toxicities that significantly limit their therapeutic potentials.

Formaline and different aromatic aldehyde based transitional metal oxide magnetic nanoparticles are synthesized and formulated that can be loaded easily with high doses of water-insoluble anticancer agents. Neither the formulation components nor the drug loading affected the magnetic properties of the core oxide nanoparticles. Sustained release of the incorporated drug is observed over 2 weeks under in vitro conditions. The nanoparticles further demonstrated sustained intracellular drug retention relative to drug in solution and a dose-dependent antiproliferative effect in breast and prostate cancer cell lines. This nanoparticle formulation can be used as a universal drug carrier system for systemic administration of water-insoluble drugs while simultaneously allowing magnetic targeting and/or imaging.

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World Facing - "SWINE FLUE"

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Now a day's world is facing **swine flue**. In true, it is not a disease butdisorder, but it may cause the disease. How swine flue occurs andwhich is the factors responsible for it are included. Diagnosis of **Swine flue** and which influenza viruses are involved for to cause the disease are described. How it can transmitt to other person and treatment of swine flue are also involved. How to prepare the oral suspension for tamiflue, and how can we use the solution.Which dose is required for different patient and precaution are involved in it. What is the effect of over dose, missed dose and drug interaction and storage condition are described

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Nod Factor-Binding Protein in Legume Roots

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A lectin present in roots of seedlings was isolated and purified by affinity chromatography. Sugar specificity assayed by hemagglutination-inhibition activity indicated that lectin belongs to glucose/mannose-specific group. The roots of the legume *Dolichos biflorus* contain a lectin (Db-LNP) that binds to the Nod factor signals produced by rhizobia that nodulate this plant. Db-LNP is differentially distributed along the surface of the root axis in a pattern that correlates with the zone of nodulation of the root. Db-LNP is present on the surface of young and emerging root hairs and redistributes to the tips of the root hairs in response to treatment of the roots with a rhizobial symbiont or with a carbohydrate ligand that initiate nodule formation. Maximum levels are found in 2-d-old roots, in the absence of NO3 and NH4 expression this root protein is increased. This indicates that Db-LNP is involved in the initiation of the *Rhizobium* legume symbiosis.

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Synthesis and Screening of Mannich Bases of Gabapentin as Antibacterial Agents

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The present investigation deals with the synthesis of Mannich bases of gabapentin which were synthesized via Mannich reaction with biologically potent sulphonamides. Their chemical structures were established on the basis of UV, IR, ^{1}HNMR and elemental analysis data. The purity has been ascertained by chromatographic resolution using methanol-chloroform as binary elutant. All the compounds have been tested for their antimicrobial activity against pathogenic bacteria. All the compounds were found to exhibit profound antibacterial activity. Gabapentin, a biologically potent drug showed no significant antibacterial activities but its Mannich bases were found to show potent antibacterial activity against the pathogenic bacteria.

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Plasminogen a future prospective for the Treatment of Neurological Disorders

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Neurological disorders are health conditions involving the nervous system. A neurological disorder is a disease or injury of the central nervous system that causes paralysis of any part of the body. Sometimes physical injury to the brain, spinal cord, or nerves can be the cause of neurological disorders. Sometimes

they can result from biochemical causes. Other times, the cause may be unknown and only the effects are seen. Neurological disorders can be a sign that there is an imbalance in your system. When you have an imbalance, you are also susceptible to various diseases which can settle in weak areas of your body. Complete treatment of neurological disorder in present days is not possible but we can reduce the affect of disorder our life. There are various treatments are available but these are insufficient to overcome the disease. Here we have focused on plasminogen for the treatment of neurological disorders. Plasmin is an important enzyme present in blood that degrades many blood plasma proteins, most notable, fibrin clots. The degradation of fibrin is termed fibrinolysis. In humans, the plasmin protein is encoded by the *PLG* gene. Plasminogen (PLG) is a circulating zymogen that is converted to the active enzyme plasmin by cleavage of the peptide bond between Arg-560 and Val-561, which is mediated by urokinase and tissue plasminogen activator. The main function of plasmin is to dissolve fibrin blood clots. Plasmin, like trypsin, belongs to the family of serine proteases. Recent reports have established that plasminogen is synthesized in neuroendocrine tissues, making this protein and the proteolytic activity of the product of its activation, plasmin, available at sites separated anatomically from circulating, hepatocyte-derived plasminogen.Various studies also shown that that plasminogen participates in neurite outgrowth and also suggests that laminin-1 degradation by plasmin contributes to the process of neuritogenesis. Here we outline key elements of our target and provide examples of how we integrate technologies in the search for neurodegenerative disease targets.

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The molecular biology of human immunodeficiency virus (HIV-1) type I infection

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Infection with human immunodeficiency virus type 1 (HIV-1) causes AIDS, a fatal disease that has been diagnosed in more than 132,000 people in the US alone. Many more are infected with HIV-1; predictions place the number of these people at 15 to 20 million worldwide by the year 2000. The virus is transmitted by sexual contact, exposure to infected blood or blood products, and from mother to child; more than 60 percent of all cases involve heterosexual transmission. Effective drug treatments will depend on learning more about HIV and the ways it infects its host. A review is presented of current knowledge related to the molecular biology of the infection. HIV is a lentivirus (a class of viruses that cause slowly-developing infections) of the retrovirus family (viruses that copy their RNA into DNA, which is then inserted into the host genome). Besides causing characteristic symptoms (nervous system involvement, weak immune responses), lentiviruses have complex viral genomes. The viral structure is depicted and described. Its life cycle, from infection of host CD4-positive T cells (immune system cells), the main viral target, and other immune system cells, is described. The steps covered include: attachment of the virus to host cells; internalization into the cell; transcription of viral RNA and integration of DNA into the host cell; the latent period, when the HIV-1 infection may lie dormant; late and early expression of the aberrant genes; and construction of new viral particles. The ways HIV-1 kills and damages cells are not understood; hypotheses are briefly listed. Development of an HIV-1 vaccine has been hindered by the structural variability in one of the proteins that form the viral envelope (coat); however, recent developments in research concerning SIV-1 (simian immunodeficiency virus, type 1) are more encouraging. An effective vaccine should induce an immune response from both the cellular (T cell) and humoral (B cell) components.

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Factor favouring the development of obesity due to failure of dietary fat intake

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Obesity is a major health problem in affluent societies. In part this is considered to result from both low physical activity and the high fat content of Western diets. Previous work has shown that the ingestion of carbohydrate elicits a complex metabolic response that acts to increase utilization of carbohydrate and

elevates basal energy expenditure. When diets are supplemented with fat there is no increased utilization of the fat as would be the case in carbohydrate supplementation. Thus, it appears that regulation of metabolism is significantly more dependent on carbohydrate consumption than on dietary fat. A review from these studies have only followed the metabolic rate for nine hours after meals; the experimental design described in this review allows for the possibility that an adjustment in metabolism from fat ingestion could occur later. The current study expands the period of study to 24 hours following a fat supplement. Seven healthy, non-smoking males aged 20 to 26 were included in the study. All had stable body weights and no family diabetic history. The subjects were placed in a respiration chamber where they were provided with the facilities of a one-room suite. They could communicate with investigators through a window and by intercom. All urine was collected and analyzed for nitrogen (urea). Subjects exercised on a treadmill for one hour each day and their general movements were monitored by radar. Temperature and humidity were maintained at constant levels and the air of the chamber was constantly evaluated for oxygen and carbon dioxide concentration. The measurements of oxygen, carbon dioxide and urinary nitrogen allowed the calculation of basal energy expenditure. During the first 24 hour period total energy expenditure measured 2,783 kcal per day. When 987 kcal of dietary fat was added to the diet there was no change in 24 hour energy expenditure. Thus the previously collected data on the inability of fat supplementation to shift energy expenditure appears valid when the length of observation is extended to include a 24 hour period of supplementation.

References: American Journal of Clinical Nutrition

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Design of imaging agent for Biomedical Application: Correlation Analysis of the Structures and Stability Constants of Gadolinium (III) Complexes

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Studies on quantitative structure—property relationships (QSPR) have suggested that properties are related to the corresponding structures. Thus if we can describe effectively a molecular structure, we can build a mathematical model to predict the properties for that compound and consequently it will be possible to define new compounds to be synthesized. In recent decades, enormous efforts have been made by many investigators to study various compounds in this field, but metal complexes have been involved only a little in these investigations.

The general requirements for MRI contrast agents are as follows: (1) high relaxivity; (2) specific in vivo distribution; (3) in vivo stability and lack of toxicity; (4) considerable water solubility; and (5) excretability. In the required doses of contrast agents, free lanthanides and transition ions may induce obvious toxic effects in human and animal bodies. Both metal ions and free ligands tend to be more toxic than metal chelates, thus MRI contrast agents must be kinetically and thermodynamically stable complexes.

Twenty different ligands based on polycarboxilic acid/phosphonic acid are taken for stability stabilities. In this paper, different types of descriptors have been examined. These include topological, geometric, electronic, and hybrid features. Topological descriptors yield information about the connectivity of compounds. Geometric descriptors provide information about the shape of the compound. Charge information is encoded by electronic descriptors, such as dipole moments, electron density, the energies of the highest occupied molecular orbital, and the lowest unfilled molecular orbital. Final equation gives good correlation with topological descriptors and stability constants.

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A Novel Ornidazole Bio-Microbags Using *Allium cepa* Biomaterial

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The current aim of the research work is to prepare ornidazole bio-micro bags using *Allium cepa* biomaterial and other co-processing agents. *Allium cepa* biomaterial was separated from the bulb by peeling of thin inner membrane of *Allium cepa*. The membrane was subjected for drying 50˚ c at for four

hrs. dried and powdered and screened through 120 mesh. Four different ornidazole bio-micro bags were prepared by using ornidazole as a model drug and bio material in various concentration and other processing agents by solvent evaporation method. The formulated bio-micro bags were subjected for particle size, particle shape determination and drug release kinetics. Our experimental result revealed that the all formulated bio-micro bags showed average particle size ranging from 5.6 µm to 7.14 µm and uniform shape. The formulation FM B3 was selected as a best formulation on the basis of drug release kinetic profile. Hence conclusion was drawn that the bio material serve as a wall material for formulating various drug loaded bio- micro bags.

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Breast Cancer Treatment Leaves Patients with Chronic Pain.

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Even three years after finishing treatment for breast cancer, almost 50 percent of women report long-term pain, a new Danish study finds. Cancer is a class of diseases in which a group of cells display uncontrolled growth, invasion, and sometimes metastasis.

Chronic pain is defined as pain that persists longer than the temporal course of natural healing, associated with a particular type of injury or disease process.The months following breast cancer treatment can bring a difficult combination of emotional and physical challenges, including a decreased range of motion, pain, fatigue, and depression.

The International Association for the Study of Pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is subjective in nature and is defined by the person experiencing it, and the medical community's understanding of chronic pain now includes the impact that the mind has in processing and interpreting pain signals.

Please note all these suggestions are made with a view to earn money for themselves and do not offer any replacement to chemotherapy. Cancer such a dangerous disease and here also the chemo therapies doe not work permanently and the recurrence of disease has been witnessed in all most all case. Yet we have no other option to rely on Chemotherapy, Radiation and Surgery treatments for Cancer.

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A Novel Bio-solid dispersant from fruit pulp of *Pyrus communis*

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The current aim of the research work is to isolate biomaterial from the *Pyrus communis* fruit and prepare bio-solid dispersion using isolated biomaterial. Peeled *Pyrus communis* fruit was collected and biomaterial was isolated by simplified economical process. The biomaterial was subjected for physiochemical properties like colour, solubility and chemical test. Four different bio-solid dispersions were prepared using Nimesulide as a model drug by precipitation method and biomaterial as dispersant. The biomaterial was dissolved in suitable amount of water ,nimesulide was dissolved in alcohol and measured quantity of Nimesulide solution was added drop wise with constant stirring.Then the mixture was kept aside for 10 mins bio-solid dispersions were collected by centrifugation,dried and subjected for various evaluation parameters like particle size, solubility and in-vitro dissolution studies in pH 1.2 buffers at 450 nm. The experimental results revealed that the formulated solid dispersions showed uniform particle size and solubility. 80% of drug release was observed in **Fs4** in **32** mints. Hence this formulation was selected as best formulation. Finally conclusion was made that biomaterial can serve as a bio-dispersant for poorly soluble drugs.

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A greener & rapid methodology for the synthesis of 1, 3-diallyl(benzyl)-6-methylpyrimidine-2,4-diones

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There has been a growing realization in the academia and industry regarding the grave environmental ramifications of hazardous chemicals & processes. Consequently, the realm of synthetic organic chemistry has been witnessing a remarkable conceptual upheaval in the form of incorporating green chemical processes in synthetic design. [1]. The edifice of green chemistry is built on the premise of chemical processes. Especially, the use of microwave (MW) synthesis has come to the fore in view of the unique benefits like energy efficiency, enhanced reaction rates & increased yields. [2].

Pyrimidines and their derivatives are arousing a great interest as potential therapeutics, pharmaceuticals & agrochemicals [3,4,5]. This emerged a quest & stimulated us to devise a novel synthesis of 1,3-diallyl(benzyl)-6-methylpyrimidine-2,4-diones using methylacetoacetate (MAA) with disubstituted ureas such as dibenzylurea (DBU) and diallylurea (DAU) as raw material. The target pyrimidinediones were synthesized by MW irradiation of mixture of MAA with DBU or DAU with catalyst such as the nanoclays, (Montmorillonite K-10 & Mont. KSF) and other environmental friendly catalysts such as zeolites and silica gel and isolating the products by column chromatography. Structural determination and their confirmations were done by Elemental analysis, IR, 1H-NMR and Mass spectroscopy technologies.

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Design And Synthesis Of 2, 3-Dideoxy Hex-2-Enopyranosid-4-Uloses As Promising Anti-Tubercular Molecules

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The emergence of MDR-TB and of late XDR-TB along with the problem of co-infection with HIV has made the threat from TB very grave. To effectively combat the scourge of TB in its present manifestation there is an urgent need for the development of new, potent anti-TB drugs having unique mechanisms of action from currently used anti-TB drugs. In our ongoing programme on the discovery of new anti-tubercular agents we have been focusing our efforts towards the syntheses of monosaccharide derived acyclic and cyclic modified deoxy sugar as anti-tubercular agents, which in turn has led to the discovery of a number of promising leads.[1] Recently we reported the synthesis of novel, unsaturated C-3-alkyl and -alkylaryl 2,3-dideoxy hex-2-enopyranosides as promising anti-tubercular compounds.[2] In continuation of our efforts we have now synthesized 2,3-dideoxy hex-2-enopyranosid-4-uloses as a new class of anti-tubercular molecules. These easily accessible, small molecules were found to be exhibiting many fold better activity and lesser toxicity [3] than our previously reported, sugar derived anti-tubercular agents. The detailed findings will be presented in this poster.

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Synthesis, Characterization, Antimicrobial Activity, Sod Mimic Activity And Dna–Binding Behavior Of The Copper(Ii)–Pefloxacin Complexes

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A square pyramidal copper(II) complexes with second-generation fluoroquinolone agent pefloxacin and phenanthroline derivatives, were prepared and characterized. The synthesized compounds have been screened in-vitro against two gram +ve and three gram -ve microorganisms. The Minimum Inhibitory Concentration (MIC) of the complexes ranging from 0.1 to 5.9 µM. All complexes were investigated for superoxide dismutase (SOD) like activity by using nonenzymatic NBT/NADH/PMS system. Superoxide is involved in a plethora of pathological and physiological processes via oxidative stress and/or signal transduction pathways. Superoxide dismutase (SOD) mimics have, thus, been actively sought for clinical and mechanistic purposes. All complexes show good antioxidant activity. The concentrations of complexes required to inhibit the reduction rate of NBT by 50% (IC_{50}) ranging from 0.425 to 1.305. The complexes are an avid DNA binders having binding constant (K_b) with power of 4. Viscosity measurement data confirmed that complexes bind through classical intercalative mode of binding. The cleavage of pUC19 plasmid DNA was carried out using gel electrophoresis technique.

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Third Generation Fluoroquinolone Antibacterial Drug Based Square Pyramidal Complexes Of Metal(Ii): Structure, Antibacterial Activity , Superoxide Dismutase Activity And Dna-Binding Interaction Approach

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The complexes of copper(II) of the type [Cu(SPF)(L)Cl] [where SPFH = sparfloxacin and L=2,2'-dipyridyl amine/ pyridine-2-carboxalehyde/ thiophene-2-carboxaldehyde] were synthesized and found to have pyramidal geometry with square base. The superoxide dismutase (SOD) like activity of the complex has been measured by using NBT/NADH/PMS system, and the IC_{50} value (Concentration of complex which cease the formation of formazan by 50%) ranging from 0.9 to 13.9 µM. The interactions of complexes with DNA were studied by absorption titration, viscosity measurement and gel electrophoresis under physiological conditions.

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Synthetic, Spectroscopic, Thermal And In-Vitro Antibacterial Significance Of Drug Based-Mn(Iii) Mixed Ligand Complexes

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The antibiotic agent ciprofloxacin (HL) is well known for its drug design and coordinating ability towards metal ions. Novel Mn(III) mixed ligand complexes of ciprofloxacin with various bispyrazolone based dinegative bidentate ligands (H_2A^n) were prepared. The structure of the synthesized complexes was characterized using elemental analyses, infrared spectra, ^1H & ^{13}C-NMR spectra, electronic spectra, magnetic measurements, FAB-mass spectrum and thermo gravimetric analyses. The kinetic parameters such as order of reaction (*n*) and the energy of activation (*Ea*) are reported using the Freeman−Carroll method. The pre-exponential factor (*A*), the activation entropy ($\Delta S^{\#}$), the activation enthalpy ($\Delta H^{\#}$) and the free energy of activation ($\Delta G^{\#}$) were calculated. Complexes were also screened for their *in vitro* antibacterial activity against a range of two Gram-negative (*Escherichia coli*, *Serratia marcescens*) and two Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*) microorganisms.

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Synthesis Of Pyrazolothiazole Derivatives And Their Antimicrobial Activity

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Furfuryl amine (1) undergoes facile condensation with aromatic aldehydes to afford the corresponding N-benzylidene – 1 – (furan-2-yl) methanamine (2a-h) in good yield. Cyclocondensation of compounds (2a-h) with thioglycolic acid yields 3 – (furan-2ylmethyl) – 2 – phenyl thiazolidin – 4 – one (3a-h). This (3a-h) compounds are furthers reacted with benzaldehyde in presence of C_2H_5ONa, they gives (Z) – 5 – benzylidene – 3 – (furan – 2 - ylmethyl) - 2 – phenylthiazolidin – 4 – one (4a-h). The structures of these compounds were established on basis of analytical and spectral data. The newly synthesized compounds were evaluated for their antibacterial and antifungal activities.

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Enantioselective Synthesis of α-Hydroxy-β-Amino Acid Analogs

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β-Amino acids are present in several peptides and in different natural products either in free form or in the form of different derivatives [1]. Incorporation of these unnatural amino acids in peptide analogs offer several pharmacological effects by enhanced enzymatic stability and improved pharmacodynamics and bioavailability. α-Hydroxy-β-amino acids are the most important members of the β -amino acid family. They are the essential moiety of many well-known natural products endowed with significant biological activity. The best known example is the potent neoplastic agent taxol.

The synthesis of α-Hydroxy-β-amino acids have been reported either by formation of chiral oxiranes using chiral reagents or direct amino hydroxylation of olefins [2]. Recently Shibasaki et al reported chiral epoxidation of cinnamates using lanthanides and Binols in high yields with high enantiomeric excess [3]. These oxiranes can be further converted to α-Hydroxy-β-amino acids via treatment with sodium azide and its subsequent reduction. Using this strategy we have synthesized a series of the α-Hydroxy-β-amino acid amides. This class of the compounds may be potent inhibitor of DPP-IV. Therefore some of the compounds will be tested for their DPP-IV inhibition potential. The details of the studies will be presented.

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Synthesis and biological activity of amino acid conjugates of 4-Aminoquinolines as antimalarial agent

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Malaria is one of the world's most widespread protozoal diseases. It is endemic in tropical regions including India. In India especially Northeastern regions are one of the hot spots for malaria transmission. Focal outbreaks of malaria are of common occurrence especially in forest-fringed villages of Assam, bordering Arunachal Pradesh [1] .Orissa alone contributes to more than 40% of falciparum deaths in India, south Orissa is a known hyper-endemic area of the state [2] . Malaria is caused by four different types of parasites, *Plasmodium falciparum, P. malariae, P. vivax and P. ovale*. Among these, *P. falciparum* is the most fatal affecting all ages with multiple-systemic complications. The developments of Chloroquine resistant strains are further complicating the situation. In the quest of superior CQ analogs which could be active against resistant strains, a number of new molecules were synthesized and tested. These studies suggested that 7-chloro-4-aminoquinoline nucleus is most suitable for antimalarial activity, particularly, inhibition of hematin formation and accumulation of the drug at the target site [3, 4] . But modification in side chain viz. carbon chain length and basicity of nitrogen in chain of CQ has significant impact on activity [5].

Considering these two facts we have designed molecules where amino acids are condensed in side chain. Amino acids impart a chiral center to the molecule and provide opportunity to study a variety of lipophilic moieties in the side chain. Coupling of amino acid with various diamines incorporate additional nitrogen with variety of modifications at terminal position. These modifications have been done according to bioisosteric concepts. Details of synthetic procedure and biological activities of these compounds will be discussed in detail.

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Synthesis of Glucagon Like Peptide-1(GLP-1) analogs as anti-diabetic agents

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Glucagon like peptide-1 (GLP-1) is a gut-derived incretin hormone released from L cells in small intestine in response to oral meal ingestion. Due to its multifaceted action it has potential to improve the different conditions defining the diverse physiopathology seen in type 2 diabetes. In animal studies, GLP-1 stimulates β-cell proliferation and neogenesis and inhibits β-cell apoptosis. In humans, GLP-1 stimulates insulin secretion and inhibits glucagon and gastrointestinal secretions and motility. It enhances satiety and reduces food intake. The incretin effect is severely reduced in type 2 diabetic patients. Short-term intravenous or subcutaneous infusions of native GLP-1 significantly lower the blood glucose in patients with type 2 diabetes. Unfortunately, the pharmacokinetic properties of GLP-1 limit the feasibility of this approach, as GLP-1 is rapidly degraded in vivo by aminopeptidase enzyme, DPP-IV leading to its very short half-life. GLP-1(7–36)-NH_2 is rapidly degraded to GLP-1(9–36)-NH_2 by DPP-IV, which removes the N-terminal dipeptide His^7-Ala^8. Enhancing incretin action for therapeutic use includes GLP-1 receptor agonists resistant to degradation (incretin mimetics) and dipeptidyl peptidase DPP-IV inhibitors. To make GLP-1 resistant to DPP-IV requires N-terminal modification by substituting amino acids with others so that it is not recognized by DPP-IV, which will prolong the life of GLP-1 and activate GLP-1R. [1-3]

Therfore in order to synthesize DPP-IV resistant GLP-1 derivatives we have replaced α-amino acids with β L-amino acids and β D-amino acids at 8 and 12 position of GLP-1. Replacement of α-amino acids with β

amino acids can provide improved resistance to proteolytic cleavage. This substitution can lead to DPP-IV resistant GLP-1anologs. Synthesis and purification of GLP-1 analogs will be presented.

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Allium Sativum L.: A Potent Clinically Used Antioxidant

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Allium Sativum, Garlic is among the oldest of all cultivated plants and has played an important dietary and medicinal role throughout the history of mankind. It has been used both as food and medicine by ancient scholars. As one of the earliest cultivated plants, Garlic is mentioned in the Bible, egyptian Codex Ebers and indian vedas and puranas. Being a nature's boon to mankind, it is a multipurpose and versatile plant with many medicinal effects like antimicrobial, antitumor activity, antithrombotic, antiarthritic, hypolipidemic, hypoglycemic, antidepressant, neuroprotective, immune booster, hair re-growth inducer, heart and artery protector etc.

Reactive Oxygen Species (ROS) cause damage to DNA, lipids and proteins leading to disease and aging and may induce cancer-causing mutations, disrupt enzymes, injure membranes and reduce immunity. ROS, which are byproducts of normal metabolism, are normally neutralised by cellular antioxidant enzymes and small molecules like glutathione and by vitamins, minerals and other phytochemicals obtained in the diet. Increased levels of ROS cause oxidative stress, which plays an important role in arthritis, atherosclerosis, heart disease, AIDS, cancer, ageing and in apoptosis of neurons, that leads to Alzheimer's disease and other neurodegenerative diseases. Aged garlic extract (AGE), that helps maintain a healthy immune system owing to its rich antioxidant property, has been shown to offer protection against the cardiotoxic effects of doxorubicin, an antineoplastic agent used in cancer therapy. Some components of garlic have tremendous antioxidant properties, including the ability to scavenge free radicals, increase the activity of several antioxidant enzymes in the body like superoxide dismutase, catalase, glutathione peroxidase etc., inhibit lipid peroxidation and block inflammatory prostaglandins. Aqeuous extract from raw garlic or garlic powder, which contains compounds like allicin, S-allylcysteine, N-acetyl-S-allylcysteine, S-allylmercaptocysteine, alliin, allixin, S-ethylcysteine, N-acetylcysteine, diallyl sulfide and diallyl disulfide, is found to be effective in reducing Cu(+)-initiated oxidation of low density lipoproteins (LDL).

As garlic consumption causes increase in activity of some antioxidant enzymes, reduction in peroxidation processes and oxidation reactions, it may prove very beneficial to diseased and elderly subjects.

P-215

Evaluation of Superoxide anion radical Scavenging activities of *Solanum species* of North-East India

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Three Solanum species berries, used as medicinal vegetables in N.E.India viz. *Solanum indicum*, *Solanum nigrum* and another unidentified *Solanum* species were investigated for their ability to scavenge superoxide anion radical ($O^{\bullet -}$) by Xanthine/Xanthine oxidase assay using Nitro Blue Tetrazolium(NBT). Hexane, ethyl acetate and methanol extracts of all the three species inhibited superoxide anion radical induced reduction of nitro blue tetrazolium in a moderate level. The methanol extracts of all the three species showed highest inhibition of NBT reduction. *Solanum nigrum* and unidentified *Solanum* species have comparable scavenging activity of superoxide anion radical. As these plant species are used as

medicinal vegetables to cure some hepatic disorders, so the reactive oxygen species (ROS) scavenging ability of them may have some synergistic action.

P-216

Investigation of Antioxidant Activities of Some Medicinal Plants of North East India having Antibacterial, Anticancer and Antihepatotoxic Activities

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The antioxidant activities of four ethno medicinal plants of North East India viz., *Solanum spirale* Roxb. (Solanaceae), *Tacca integrifolia* (Taccaceae), *Commelina bengalensis* (Commelinaceae) and *Rhynchostylis retusa* (Orchidaceae) having different medicinal properties such as antibacterial, anticancer and antihepatotoxic activities have been investigated by DPPH radical scavenging method. All of these plants have shown significant DPPH scavenging activity. On calculation of the percentage inhibition at 30 minutes, it was observed that among hexane, ethyl acetate and ethanol extracts, the ethanol extracts of all have shown the maximum radical scavenging activity. The ethanol extracts were also found to be rich in polyphenolic contents, which suggests a possible direct correlation between the radicals scavenging activity and polyphenolic contents. Further studies are going on to evaluate the antibacterial, anticancer and antihepatotoxic activities.

P-217

Chemoselective Esterification of Some Biologically Important Polyphenolic Acids with Star type Alcohols using Mitsunobu Reaction

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As part of a study on dendritic polyphenolic esters and amides as antioxidants, Mitsunobu reaction has been exploited for chemoselective esterification of some biologically important phenolic acids with some star type alcohols as core. Moderate to good yields have been achieved. Further studies are going on to investigate any possible role of dendritic architecture on antioxidant activities. Mitsunobu reaction provides an excellent route for synthesis of polyphenolic esters with alcohols, which avoids harsh reaction condition and tedious steps of protection and deprotection of several phenolic groups.

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P-218

Cloning and Expression of *Plasmodium yoelii* Phosphoribosylpyrophosphate synthase

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Malaria is thought to be a world-wide problem. Lack of an effective vaccination and the spread of drug resistance necessitate the identification of new drug targets. Parasite specific pathways can serve as suitable chemotherapeutic targets. Differences in the structural and kinetic characteristics of parasitic

enzyme as compared to host are being successfully exploited for designing of new antimalarial compounds. Phosphoribosylpyrophosphate (PRPP) is an important compound of intermediary metabolism which is required for the *de novo* biosynthesis of purine and pyrimidine nucleotides, as well as for the salvage of preformed purine, pyrimidine, and pyridine bases by the malarial parasites. The synthesis of PRPP is catalyzed by PRPP synthase (EC 2.7.6.1), which catalyzes the transfer of the β, γ-diphosphoryl moiety of ATP to the C-1 hydroxyl of Rib-5-P.We have selected PRPP synthase as putative drug target for synthesis of new antimalarial compounds, hence PRPP synthase gene was PCR amplified using gene specific primers and *Plasmodium yoelii* cDNA. The cloning of the enzyme has been carried out in suitable vectors for expression of protein.

P-219

Stem Cell Therapy: A Promising Perspective In Treatment Of ALS (Amayotrophic Lateral Sclerosis)

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ALS is a progressive fatal neurodegenerative disease that affects nerve cells in the brain, leading to the degeneration of cells and death of the motor neurons in the spinal cord that control muscle movement.It affects about 30,000 Americans with about 5,600 new diagnoses per year. The causes of ALS are not well known but it occurs due to following circumstances: mutations of copper/zinc superoxide dismutase (SOD1), glutamate excitotoxicity, neurofilament dysfunction, impairment of neurotrophic factors, mitochondrial dysfunction, enhanced motor neuron apoptosis and microglial proliferation or inflammation. Stem cells are cells which can develop into any of the tissues that form the body and are considered to be pluripotent. For example, multipotent stem cells in the brain give rise to different neuronal cell types and glia this finding leads to focus on its use in treatment of ALS disease. Recent study by Clement and colleagues show that in chimeric, genetically engineered mouse models, motor neurons carry mutated *SOD1* genes and glial cells carry healthy genes. Survival is extended in these chimeric mice, as compared with nonchimeric mice in which all motor neurons and all glial cells carry mutated *SOD1* genes. This finding suggests that if healthy stem cells could get to the spinal cords of patients with ALS, their survival might also be extended. This leads to conclusion that stem cell research carries promise for patients with ALS and may result in the development of new treatments to slow the progression of the disease.

P-220

An efficient synthesis of 5-((4-((2-chloroquinolin-3-yl) methoxy) phenyl) methylene) thiazolidine-2, 4-diones carried using L-proline in PEG-400

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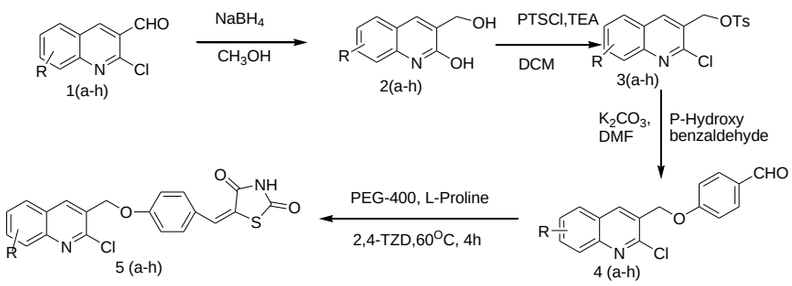
2, 4-Thiazolidinediones are a class of oral insulin-sensitizing agents that improve glucose utilization without stimulating release of insulin. They significantly reduce glucose, lipid and insulin levels in rodent models of type II diabetes mellitus and obesity. Quinoline also shows the antibacterial and hypoglycemic activities.

Keeping the above significance in mind here, we have developed the convenient synthetic route for knoevenagel condensation of 4-((2-chloroquinolin-3-yl) methoxy) benzaldehydes (4a)with 2,4-thiazolidinedione using the organocatalyst, L-proline in greener reaction medium PEG-400 at 60^{o}C for 4h to obtain 5-((4-((2-chloroquinolin-3-yl) methoxy) phenyl) methylene) thiazolidine-2,4-diones (5a) with better yields.The details of the synthetic route will be presented.



Scheme I

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P-221

Cyclocondensation catalyzed by bakers yeast leading to 1, 4 benzothiazines

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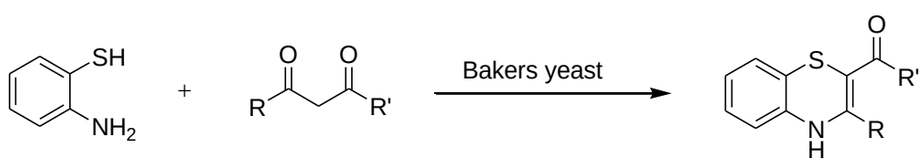
1,4 Benzothiazine derivatives are interesting compounds because they possess wide biological and pharmacological activities. These compounds are used as anti-inflammatory, antibacterial, anticancer, ataractic and antirheumatic agents.

Biocatalysis represents an effective and preferable alternative for the traditional chemical catalysis to run the synthesis of fine chemicals and optically active compounds. Bioconversions with living cells (Whole-cell), with ability to regenerate their own respective cofactors are more advantageous. The use of bakers' yeast (whole-cell biocatalyst) to perform functional group transformations of organic compounds has become a well established and valuable methodology in organic syntheses.

By considering the importance of 1, 4 benzothiazines and need to develop eco-friendly routes, we have tried to develop a new biocatalytical route for the synthesis of 1, 4 benzothiazines using bakers yeast as a catalyst. The details of the work will be presented.



P-222

Water mediated synthesis of pyrazolo[3,4-*b*]quinolines

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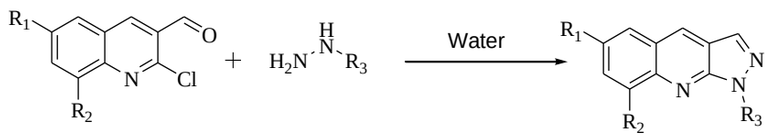
Pyrazolo[3,4-*b*]quinoline and its derivatives have been gaining significance in organic and medicinal chemistry. They have been displaying wide range of biological and pharmacological properties, such as *anti*-cancer, *anti*-viral, *anti*-microbial, parasiticidic, and anti-malarials. The use of pyrazolo[3,4-*b*]quinoline derivatives as optical brighteners has been long known.

Organic reactions in water/aqueous medium are of current interest in organic syntheses. The use of water as the reaction medium offers several advantages like, non-toxicity, ready accessibility in abundant quantity and unique reactivity and selectivity.

Keeping the above finding in mind here, we have synthesized pyrazolo[3,4-*b*]quinolines by the condensation of 2-chloro-3-formyl quinolines and hydrazine hydrate or phenyl hydrazine using water as reaction medium. It is found that, this route is relatively economic, eco-friendly and high yielding.



1a **2** **3a-j**

R_1= H, OCH_3, CH_3, OCH_2CH_3

R_2= H, $-CH_2CH_3$

R_3= H, Ph

P-223

Carboxy Functionalized Ionic Liquid As A Catalyst For The Rapid And Green Synthesis Of 3, 4-Dihydropyrimidine-2(1h)-Ones

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The condensation reaction involving an aldehyde, diketone and urea or thiourea was efficiently promoted by the carboxy functionalized ionic liquid ([cmmim][BF_4]) in ionic liquid [bmim][BF_4] under milder conditions to afford the corresponding 3,4-dihydropyrimidine-2(1H)-ones (DHPMs) in excellent yields. The reaction was also carried out under microwave and ultrasonic irradiation with the same reaction media. The advantages of this method include operational simplicity and environmental benignancy together with enhanced atom utilization. Moreover, the reaction media can be recovered conveniently and reused effectively for at least six times. The reaction times and yields are compared with [bmim][BF_4] sole as the solvent.

P-224

Docking Simulation And Antifungal Evaluation: Imidazoles As Potential Cytochrome P450 14a-Sterol Demethylase Cpy51 Inhibitors

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Candida albicans, the most prevalent opportunistic fungal pathogen in humans has been implicated in a general increase in the number of infections i.e. Candidiasis [1] ranging from superficial mucosal infection to life-threatening systemic diseases in immuno compromised patients (with AIDS, Cancer, or Organ transplants). These increasingly frequent and invasive fungal infections are associated with unacceptably high mortality: up to 40% for bloodstream infections caused by *Candida albicans* and more than 50% in invasive aspergillosis. Several factors, including difficulties in diagnosing deep mycosis, impaired immunity of the patients, and high treatment failure rates, presumably contribute to extremely poor prognosis for invasive fungal infections.

Azoles possessing N-C-N grouping display anti-inflammatory, hypotensive, anti-convulsant, amoebicidal activity. The search for better antibacterial and antifungal agents with increased specificity towards bacterial as well as fungal enzymes remains a primary target in medicinal chemistry research. The molecular mechanism by which Azoles exert effects on the fungal parasite *Candida sp* involves targeting lanosterol 14 α-sterol demethylase and block ergosterol synthesis by interfering with the demethylation

of its precursor. Their broad therapeutic window, wide spectrum of activity and low toxicity confers interest in furthering antimycobacterial and antifungal activity.
Synthesis of hybrid molecules is of interest as a way of synergistically increasing the drug discovery portfolios. A docking study of enzyme-inhibitor complex provides a template that can be utilized to develop more efficient antifungal hybrid analogues. The recent renewed interest in various quinoline-azole, pyrimidine-azole analogues stimulated our efforts to demonstrate successful application of synthetic and docking techniques to inhibit the cytochrome p450 14α-sterol demethylase CPY51 enzyme and identify new anti-fungal hybrid-azole pharmacophores.
To understand the response of *C. albicans* to perturbation in the ergosterol pathway, genome wide transcript profiles following exposure to a number of antifungal agents targeting ergosterol biosynthesis i.e. Clotrimazole, Fluconazole, miconazole and also Griesofulvin have been studied.
We have synthesiszed a series of imidazoles i.e. 2 (2 – amino – 5H imidazoly – 4 – yl) – phenols and evaluated them for their antifungal and antibacterial activities *in vitro*. Computational evaluations of imidazoles- enzyme cytochrome P450 sterol 14α – demethylase (14DM) interactions comprised docking simulations in terms of lead-protein binding energies. Such a combined experimental and computational study assists in designing exquisite moieties with varied architecture of heterocycles and designing appropriate templates which are potential sites for therapeutic recognition, providing a rich palette for discovery. Our proprietary heterocyclic scaffold libraries potentially provide biologically validated anti-fungal agents having diverse therapeutic significance with higher specificity and affinity.

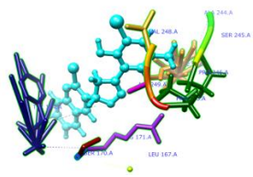

Figure 1. Active site residues of cytochrome P450 (14DM) CPY51 with Imidazole derivative. Hydrogens are suppressed for clarity.

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P-225

A novel smart bio-binder from Spinacia olerecea leaves.

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The current aim of our research work is to isolate bio material from leaves of spinacia olerecea .and formulate tablet by using isolate biomaterial as a binder.the biomaterial was isolated from the spinacia olerecea leaves by simplified economic process. the isolated bio material was subjected for physical characterstic study like color,solubility,color changing point.ornidazole tablet were formulate in 3 different batches with varying bio binder concentration ranging from 1%,1.5%,2%(fp1,fp2,fp3) solution and formulated tablet were subjected for various evaluation parameters like thickness,weight variation,friability,disintegration,dissolution study.experimental results shows that isolated bio material is soluble in water and all formulated tablet using bio material as a binder showed good hardness &uniformity in thickness,with release 91-95%of drug was released with in 60 minutes. on comparison with t80 values of release data fp1 was selected as best formulation. Conclusion was drawn that the biomaterial can serve as a potent biobinder for formulating drug loaded tablet.

P-226

One Pot Synthesis of Isoxazole

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We have discovered that reaction of aldoximes with acetylenes directly leads to the formation of an isoxazoles in one step. Conventional method requires a chlorination of aldoximes first and then cyclization of the resultant chloroaldoximes with acetylenes to give isoxazoles. Isoxazole have emerged as a useful pharmacaphore in several therapeutic targets. Scope and details of this new and facile methodology will be presented.

P-227

Role of Bisphosphonates in Multiple Myloma

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Multiple myeloma (MM) is the second most common hematologic malignancy and the most common malignancy to involve bone. More than 85% of patients with MM have bone involvement, which can be devastating. Bisphosphonate therapy is the mainstay of treatment for MM bone disease; it has decreased the frequency of skeletal events in MM and delayed their development. Further, the toxicity of these drugs is low and generally manageable. Whether bisphosphonates have any antitumor effects in MM patients (in contrast to what has been reported in preclinical models) is unclear and requires further study. Although bisphosphonates have been extremely effective for treating MM bone disease, they do not completely inhibit the development of skeletal events, but only decrease them significantly. Other antiresorptive agents now being developed may further enhance the quality of life for MM patients when used in combination with bisphosphonates.

P-228

Nanocarriers in Ocular Drug Delivery system

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Controlled drug delivery to eye is one of the most challenging fields of pharmaceutical research. Low drugcontact time and poor ocular bioavailability due to drainage of solution, tear turnover and its dilution or lacrimation are the problems associated with conventional systems. In addition, anatomical barriers and physiological conditions of eye are also important parameters which control designing of drug delivery systems. Nanosized carriers like micro/nanosuspensions, liposome, niosome, dendrimer, nanoparticles, ocular inserts, implants, hydrogels and prodrug approaches have been developed for this purpose. These novel systems offer manifold advantages over conventional systems as they increase the efficiency of drug delivery by improving the release profile and also reduce drug toxicity. Conventional delivery systems get diluted with tear, washed away through the lacrimal gland and usually require administering at regular time intervals whereas nanocarriers release drug at constant rate for a prolonged period of time and thus enhance its absorption and site specific delivery. This review presents an overview of the various aspects of the ocular drug delivery, with special emphasis on nanocarrier based strategies, including structure of eye, its barriers, delivery routes and the challenges/ limitations associated with development of novel nanocarriers. The recent progresses in therapy of ocular disease like gene therapy have also been included so that future options should also be considered from the delivery point of view. Recent progress in the delivery of proteins and peptides via ocular route has also been incorporated for reader benefit.

P-229

SOD Mimic and DNAInteraction Studies Of Drug Based Copper (Ii) Mixed- Ligand Complexes

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There is a worldwide agreement over the present need to develop novel agents to treat bacterial infections that have become increasingly unresponsive to standard antibacterial therapy. Emergence of bacteria resistance to a number of antimicrobial agents is becoming a major health problem. This has led to studies on the novel neutral mononuclear copper complexes with the quinolone antibacterial drugs ciprofloxacin in the presence of the nitrogen donor heterocyclic ligand of bipyridine. The antibacterial activities of the newly synthesized compounds were evaluated and correlated with their physicochemical properties. Results revealed that some of the tested compounds exhibited better inhibitory activities than the reference antibiotic antibacterial quinolone drug against gram $^{+ve}$ and gram $^{-ve}$. The coordination compounds can act as catalysts for the dismutation of superoxide radicals (0_2^-). The detection of rate constant of reaction of superoxide ion with nitro blue tetrazolium (NBT) which is inhibited by superoxide dismutase (SOD). CT-DNA binding ability of complex to DNA is examined by viscosity and absorption titration. Absorption studies revealed that each of these complexes is an avid binder of calf thymus DNA. The viscometry data suggested a partial intercalative mode of binding to DNA.

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Mixed-Ligand Copper(Ii) Complexes With Derivatives Of Terpyridines And Ciprofloxacin: Synthesis, Characterization, Antibacterial, Demonstration Of SOD-Like Activity And DNA Interaction Studies

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Transition metal complexes that bind to DNA have been the focus of extensive research aimed at increasing the understanding of genetic information processing, for this purpose we have synthesized some drug based mixed-ligand complexes having formula [Cu(Cip)(L)Cl] (where L = terpyridine derivatives and CipH = ciprofloxacin) and characterized by elemental analysis, magnetic moments, ^{1}H-NMR,^{13}C-NMR, FAB-mass and IR spectra. The antibacterial activities of the compounds were screened for their activity against gram^{+ve} bacteria: *Staphylococcus aureus, Bacillus subtili*s and gram^{-ve} bacteria: *Pseudomonas aeruginosa, S .merscences, and Escherichia coli* by using the double dilution broth method. Antibacterial activity showed that complexes are more potent against gram^{+ve} bacteria than gram^{-ve}. Binding behavior of mononuclear complexes with sperm-herring DNA has been investigated by absorption spectra and viscosity measurements. The catalytic activity of the copper(II) complexes towards the superoxide anion ($O_2^{\bullet -}$) dismutation were assayed by their ability to inhibit the reduction of nitroblue tetrazolium (NBT). IC_{50} value observed in between 0.78 μM to 0.90 μM.

P-231

Macrofilaricidal efficacy of gum of *Moringa oleifera* Lam against *Brugia malayi in vitro* and *in vivo*.

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Lymphatic filariasis caused by filarial nematodes *Wuchereria bancrofti*, *Brugia malayi* and *B. timori*, continues to be a major health problem in tropical and subtropical countries. There is an urgent need for a macrofilaricidal agent capable of eliminating adult filarial parasites or permanently sterilize the female worms. In the present study, we investigated the antifilarial activity of methanol extract of resin of *Moringa oleifera* Lam both *in vitro* and *in vivo*. The extract of the resin showed both microfilaricidal and macrofilaricidal activity *in vitro*. In rodent models it killed 44-69% of adult worms and sterilized 70% of female worms. It also suppressed microfilaraemia. The methanol insoluble extract of the resin was not effective. The findings indicate the potential of this plant as a source for a new macrofilaricidal agent. This

is the first ever report of antifilarial efficacy in this plant. Localization of the macrofilaricidal efficacy in the fractions of the extract is currently in progress.

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Recent Trends In Development Of Targeted Drug Delivery By Using Nanotechnology

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Nanotechnology is a field of applied science and technology covering a broad range of topics. A nanoparticle (or nanopowder) is a microscopic particle with at least one dimension less than 100nm. Nanospheres, nanorodes and nanocups are just a few of the shapes that have been grown. These nanoparticles are classified in different subclass. All have different mechanism of action, properties, and side effects. Nanoparticles in particular have exhibited tremendous potential for detecting fragments of viruses, pre-cancerous cells, disease markers, and indicators of radiation damage. Gold coatings have made it possible to use toxic cobalt nanoparticles for biomedical applications. The use of magnetic nanoparticles in targeted drug delivery systems is under investigation by several research groups. The new technique for cholesterol removal and to treat osteoporosis is the use of Nanocapsules and nanostructure silicon. Nanotechnology is a very broad term, there are many disparate but sometimes overlapping subfields that could fall under its umbrella. Various types of liposome nanoparticles are currently used clinically as delivery systems for anticancer drug Characterization

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Recent Trends In Development Of Targeted Drug Delivery By Using Nanotechnology

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Nanotechnology is a field of applied science and technology covering a broad range of topics. A nanoparticle (or nanopowder) is a microscopic particle with at least one dimension less than 100nm. Nanospheres, nanorodes and nanocups are just a few of the shapes that have been grown. These nanoparticles are classified in different subclass. All have different mechanism of action, properties, and side effects. Nanoparticles in particular have exhibited tremendous potential for detecting fragments of viruses, pre-cancerous cells, disease markers, and indicators of radiation damage. Gold coatings have made it possible to use toxic cobalt nanoparticles for biomedical applications. The use of magnetic nanoparticles in targeted drug delivery systems is under investigation by several research groups. The new technique for cholesterol removal and to treat osteoporosis is the use of Nanocapsules and nanostructure silicon. Nanotechnology is a very broad term, there are many disparate but sometimes overlapping subfields that could fall under its umbrella. Various types of liposome nanoparticles are currently used clinically as delivery systems for anticancer drug Characterization

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Herbal Excipients In Pharmaceutical Dosage Form

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The use of natural excipients to deliver the bioactive agents has been hampered by the synthetic materials. However advantages offered by these natural excipients are their being non-toxic, less expensive and freely available. The performance of the excipients partly determines the quality of the medicines. The traditional concept of the excipients as any component other than the active substance has undergone a substantial evolution from an inert and cheap vehicle to an essential constituent of the formulation. Excipients are any component other than the active substance intentionally added to

formulation of a dosage form. This article gives an overview of herbal excipients which are used in conventional dosage forms as well as novel drug delivery systems.
Excipients are primarily used as diluents, binders, disintegrants, adhesives, glidants and sweeteners in conventional dosage forms like tablets and capsules. As the establishment of toxicity and approval from regulatory authorities poses a problem with synthetic excipients, of late more interest is being shown by researchers in herbal excipients. The drawback posed by heavy metal contamination often associated with herbal excipients is suppressed by their lack of toxicity, easy availability, and economic considerations in pharmaceutical industry as compared to their synthetic counterparts. Present day consumers look for natural ingredients in food, drugs, and cosmetics as they believe that anything natural will be more safe and devoid of side effects.
The traditional view that excipients are inert and do not exert any therapeutic or biological action or modify the biological action of the drug substance has changed and it is now recognized that excipients can potentially influence the rate and/or extent of absorption of a drug. As herbal excipients are non toxic and compatible, they have a major role to play in pharmaceutical formulation. Hence, this paper is an attempt to review herbal excipients used in NDDS.

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Development and validation of a HPLC method for the preformulation studies of candidate drug 99-411.

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Artemisinin derivatives and simplified trioxane analogs constitute a promising class of antimalarial chemotherapeutic agents. Antimalarial compound CDRI 99-411 (I) is a trioxane derivative for the treatment of cerebral malaria in mammals. It is patented, licensed for further development and IND application has been filed.
In this method HPLC separation was achieved on a CN Lichrospher® column (250mm, 4.6mm I. D., 5μm particle size). Column effluents were monitored at 240 and 225 nm. The mobile phase was 0.05% acetic acid in triple distilled water and acetonitrile (1:1) with a flow rate of 1 ml/min. This method used for the analysis of the samples of stability studies, partition coefficient, and dissolution studies. For temperature stability studies samples were kept at 37, 50 and 60^0 C. The rate constant (K), half life ($t_{1/2}$), shelf life (t_{10}) were calculated by LINREG program. The partition coefficient of (I) was determined between octanol and water and octanol and phosphate buffer pH 7.4.
By the present HPLC method retention times of (I), and starting materials were found to be 10.09 minutes, 3.95 minutes, 4.8 minutes respectively. Based on the signal to noise ratio of 3, the detection limit was 0.1 μg/ml. However the limit of quantitation was 0.48 μg/ml, as more than 5 % variation was found in inter and intra assay variation studies below this concentration. The calibration curves were linear in the range of 0.48 μg/ml to 11.5 μg/ml (r=0.99992). The partition coefficient results are C Log Oct/Aq = 3.31, C Log Oct/Buffer = 4.055.

P-236

Preparation of Inclusion complex of Lovastatin-β cyclodextrin to improve the *in vitro* Bioavailability

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In the present study inclusion complex between lovastatin and β cyclodextrin was prepared to improve aqueous solubility and bioavailability of drug. Inclusion complex was prepared by kneading method. Inclusion complex was studied by phase solubility study. Phase solubility study showed a linear relationship between solubility of lovastatin and concentration of β cyclodextrin, which is classified as Higuchi Type AL diagram indicating a inclusion complex in 1:1 ratio. The physicochemical characterization was carried out by X-ray diffraction study, DSC and dissolution study. The studies showed that lovastatin

got entrapped in to β cyclodextrin cavity in amorphous form. Dissolution study showed increase in solubility and dissolution rate of core tablet prepared by inclusion complex as compare to core tablet prepared by pure drug, which is useful for increasing bioavailability.

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Antianemic and Anticancer effects of Wheat grass juice"

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Wheat grass juice containing chlorophyll and several minerals used in anemia. The structure of chlorophyll molecule is similar to hemoglobin. The center molecule of chlorophyll is Mg while the Fe in hemoglobin due to this reason wheat gram juice help in formation of blood cells. The wheat grass juice was prepared fresh each day and consumed within an hour of extraction which is more effective. The initial dose was 20ml/day but after extraction of juice we can prepared the different dosage form i.e. Tablet, Capsule etc. Wheat grass juice containing chlorophyll and β-carotene has an anticancer activity. Chlorophyll which is similar to hemoglobin carries O_2 in the blood saying that wheat grass rise the body O_2 level. The anticancer activity of wheat grass juice understood by emphasizing the role of hypoxia in cancer.

P-238

Anti dermatophytic activity of roots of *Butea monosperma* "flame of the forest"

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Skin ailments are a common problem in all climatic zones. Marked resistance to existing chemotherapeutic agent poses challenge for management of dermal infection. Different parts of *Butea monosperma* (Fabaceae) are used to treat skin coundition in folklore and alternative medicine. Hence this study was aim to evaluated activity of roots of *Butea monosperma* against dermal microbes. Different extracts (Pet. Ether, chloroform, acetone and water) of the roots prepared by soxhlation were tested against lab mantained and clinical isolates of dermatophytes and determination of MIC was done. Aqueous and chloroform extracts possessed marked antidermatophytic activity and MIC of aqueous extract was least (0.13mg/ml).

P-239

Cyclisation of 2- substituted-aminocinnamanilides – One pot synthesis of 1-substituted-2-styryl-4-Arylidene-2-imidazolin- 5- ones and their biological evaluation.

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Biological activities of substituted 5-imidazolone derivatives have been a major subject of research. These imidazolone derivatives have been found to possess a broad spectrum of biological activities i.e. anti-inflammatory, anti-eubacterial, anti-microbial etc. Recently, a few imidazolone derivatives have attracted the attention in polymer chemistry [1]. Acetic acid mediated cyclisation of 2-substituted aminocinnamanilide (**1)** to the corresponding 2-methyl-2-imidazoline-5-one was reported to be unsuccessful. In order to trap and convert it into more stable compound, the present work was initiated. We reinvestigated this reaction and have found that was indeed formed but it decomposes on heating. With a view to converting the thermally unstable compound, generated in *situ*, into a more stable system, (**1)** is cyclised in the presence of aromatic aldehydes and have found that the products are 1-substituted-2-styryl-4-arylidene 5-imidazolones [2]. The conversion of (**1)** by the reported method requires longer time and involves additional steps. The present one pot synthesis overcomes these difficulties. This method is also applicable even to the synthesis of 5-imidazolones bearing free phenolic gp which is very

difficult to prepare by reported method.. The starting materials are easily available and the reaction is quite fast. A series of novel 5- imidalones derivatives have been synthesized and biological evaluation of their compounds are in progress. The details of the work will be presented in the poster.

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Docking Simulations Of Dihydro Pyrimidine Acid Derivatives As Potent Cox-1 And Cox-2 Inhibitors And Their Anti-Inflammatory Evaluation

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Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the enzymatic mechanism of cyclooxygenase (COX) enzyme responsible for transformation of arachidonic acid to Prostaglandin H_2. Prostaglandins are recognised for inflammation, fever and pain as reported by Dannhardt et al [1]. In recent years two forms of cyclooxygenase enzymes were recognised as COX-1 and COX-2. Kurumbail et al [2] demonstrated that the COX-1 is constitutive and regulates the platelate aggregation and homeostasis of gastrointestinal tract whereas COX-2, the inducible form is associated with acute and chronic inflammation. The inhibitory activity of generally prescribed all NSAID is targeted on both COX-1 and COX-2 enzymes. The major drawback of these drugs is about their selective inhibitory potency. Although some NSAID are non selective and inhibit both isoforms which lead to life threatening gastrointestinal ulcers but some like celecoxib and rofecoxib are COX- 2 selective drugs. SC558 is another important such inhibitor. The demand of diverse scaffolds for screening in search of potent drug is the need of day. Pyrimidine nucleus is the essential building block of DNA; RNA represents the genetic information of an organism. In medicinal chemistry more emphasis has been laid on synthesis of Dihydropyrimidines (DHPMs) condensed with other heterocycles and investigation of their biological activity. Pyrimidines are also found to be calcium channel blocker, antihypertensive, antiviral, antibacterial and anticarcinogenic, alpha antagonists. Naturally occurring marine alkaloids, batzalladines found to inhibit the binding of HIV gp-120-CD4 cell and providing an opportunity to develop as anticancer agents. Bahekar et al [3] confirmed the Pyrimidine derivatives to be anti-inflammatory and analgesic. Acid derivatives of Pyrimidines are characterised by potent anti-inflammatory agent with high degree of selectivity as reported by Tozkoparan et al [4]. We have synthesized 1, 2, 3, 4 tetrahydro-2-oxo (thieno)-4 subsituted phenyl-6-styryl pyrimidine-5 -carboxylic acids with traditional chemical approach. Computational protocol applied to investigate the protein-ligand interactions in terms of their binding energies. The best candidates to be pharmacologically efficient as COX-1 and COX-2 inhibitors were biologically evaluate as anti-inflammatory agents.

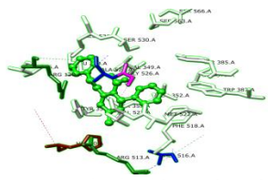

Fig 1: Ligand (green) docked in active site of 6 COX protein

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P-241

Study of acetone and ethyl acetate extracts of acorus by using different diseases (chemical and biological) models.

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Now day's different diseases are observed in one patient because of collapse in immunodeficiency by one of the diseases. This leads to problems in drug treatment for patients/diseases. Because of new drugs discovery is critical for today and in future life. Present study contents combination of various diseases models (chemical and biological assays).Chemical assays are used for estimation of antioxidant activity and polyphenolics where as polymerase enzyme inhibition, antimicrobial and cancer cell (HT-29) proliferation was study by using biological assays. Present work report indicates that antioxidant activity is higher in acetone extract as compare to ethyl acetate extract, total polyphenolics contents and phytochemicals are maximum in acetone extract. Suppression in microbial growth and cancer cell proliferation is observed in both extract with moderate variation. Polymerase inhibition actions are higher in act extract at ppm conc. of extracts. Present study result reports on Acorus are having different activities are concludes Acorus is beneficial for the future multi diseases therapeutic research study.

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Sub-chronic oral toxicity of vanadyl sulphate in male Wistar rats

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Vanadium is a trace element in mammalian nutrition and is distributed widely in the animal and plant kingdom. Vanadium compounds exert a variety of biological responses; Vanadyl ion and its complexes are effective not only in treating or relieving of diabetes mellitus but also in preventing the onset of this disease. But excess dietary Vanadium has been reported to cause toxicity in mammals; however there is scanty information available on its reproductive effects. The present study was designed to evaluate the adverse effects of vanadyl sulphate ($VOSO_4$. $5H_2O$) exposure on reproductive organs and fertility of Wistar male rats. Rats were orally exposed to vanadyl sulphate at 100 mg/kg b. wt/day for 60 days. The weight of reproductive organs, cauda epididymal sperm density and motility, histopathological assessment of testis, and biochemical parameters were measured. The relative weight of testes, epididymides and accessory sex glands were decreased significantly. Hormonal assay showed decrease in serum testosterone levels. The mating tests with untreated cyclic females revealed a decrease in pregnancy rate and mean numbers of the pups delivered at full term. Vanadyl sulphate caused a significant degenerative changes and impairment of spermatogenesis in seminiferous tubules. The diameter of seminiferous tubules and Leydig cells nuclei were reduced. Epididymal sperm motility and density were also significantly reduced. Vanadyl sulphate treatment showed significant elevation in the lipid peroxidation (TBARs level) and decline in the antioxidants levels. Based on the result of the present study, it may be concluded that vanadyl sulphate causes adverse effect on spermatogenesis and fertility of male rats.

P-243

Novel Substituted 4, 5-Dihydro-1H-pyrazole derivatives as potent peripherally acting CB1 Receptor Antagonists: Synthesis and Biological Evaluation

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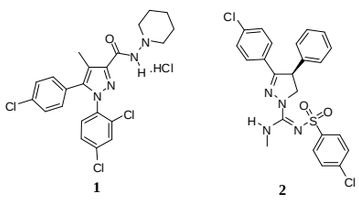
In the present study we are reporting the synthesis and biological testing of various 1, 5-diphenyl-4,5-dihydro-1H-pyrazole-3-yl methyl amide derivatives, which encompasses compounds with modest CB1 antagonistic activity to potent CB1 antagonistic activity.



1 2

Figure 1. Potent CB1 antagonists

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pH metric and Thermodynamic studies of rare earth metal ion (III) complexes derived from schiff bases in dioxane-water medium and their microbial studies

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The Schiff base have many applications in various fields like food, industry, dyes, catalyst, analytical, biological, antimicrobial, antifungal, and antibacterial study. The ligand containing N, O, S donor atom coordinate with lanthanum (III) ion forming stable complex. The interaction of La (III), Pr (III), Nd (III), Sm (III), Gd (III), Dy (III), Ho (III), and Er (III) metal ion with tridentate bilprotic ligands, namely 2- (α – benzoylmethylbenzylideneimino) phenol (H_2PDB), 2- (α -2-oxopropylbenzylideneimino)phenol (H_2PBA), 2-(α -2-oxopentylideneimino)phenol (H_2PAA),o-(N- α pyrrolideneimieno) ethane sulphonic acid (H_2PCT),o-(N- α -pyrrolideneimino) isopropyl ethanoic acid (H_2PCV) and o-(2- Pyrrolideneimino) propanoic acid (H_2PCA) have been carried out by employing bjerrum – Calvin pH titration technique at 25^0, 35^0 and 45^0C (μ = 0.01M, 0.05M, 0.1M $NaClO_4$) in 20% (v/v) dioxane water medium. The values of stability constant follow the Stag and Powell rule. The dissociation constant, Θ^0, pK^H m values of ligand have also been evaluated. The values of thermodynamic parameters (ΔG^0, ΔH^0 & ΔS^0) favor the complex formation.

P-245

A novel bio -penetrant from Solanum Lycopersicum for transdermal formulation

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The current aim of our research work is to formulate and evaluate topical bio-emulgel using a biomaterial from *Solanum Lycopersicum* pulp (belongs to *Solanaceae* family*).* The biomaterial was separated from the fruit pulp of *Solanum Lycopersicum by* simplified process.Three different bio-emulgel were prepared using *Diclofenac di-ethylamine, tween 80, liquid paraffin, sodium CMC, and biomaterial & purified water.* The formulated bio-emulgel was subjected for various evaluation parameters like spreadibility, grittiness & in-vitro diffusion release study.

Our experimental results revile that all formulation exhibited good spreadibility & free from grittiness.FEG3 emulgel shows 80% of drug release within 50 mins. Hence it is selected as a best formulation. Conclusion was drawn that the biomaterial can serve as a good bio-penetrant & the same can be use for formulation of various drug loaded bio-emulgels.

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Prepration And evalution of Diclofenac Neosomes using peanut butter

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The current aim of our research work is to prepare diclofenac neosomes for transdermal delivery by using peanut butter as a natural lipid. Diclofenac Neosomes was prepared using diclofenac, peanut butter,

water by lipid hydration method. The preprations (Neosomes) were subjected for various evaluating parameters like vesicles size & shape, entrapment efficacy and in-vitro release studies. Similar procedure was adopted for other two formulations by varying the lipid content. The prepared Neosomes were mixed in 5%HPMC & observed for spreadibility and texture. Our experimental results reveal that uniform vesicular size & shape and the drug release showed.

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Synthesis and Formation of Self-Assembled Nanocapsules of Resorcin [4] arenes and Pyrogallol[4]arenes and their Interaction with Anions

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The calix[4]arenes are of particular interest among the various macrocyclic compounds capable of functioning as hosts for molecular recognition, sensing and catalysts for various types of reactions. An efficient and fast synthesis of various resorcin[4]arenes and pyrogallol[4]arenes have been achieved by the cyclotetramerisation of resorcinol and pyrogallol respectively with aliphatic and aromatic aldehydes in the presence of Amberlyst^{TM}-15 under microwave irradiation. Aliphatic aldehydes form *rccc* stereoisomer with crown conformation on reaction with corresponding phenol, whereas mixture of stereoisomers are obtained from the reaction of 4-susbtituted benzaldehydes with resorcinol and pyrogallol in different reaction conditions.

Resorcin [4] arenes form hydrogen-bonded hexameric capsules consisting of six resorcin [4] arenes and eight water molecules both in the solid state and in solution. These nanocaspules encapsulate various neutral and charged molecules in their cavity. A broad peak at 3.038 ppm in ^{1}H NMR of resorcin [4] arenes have been assigned to encapsulated water molecules. The appearance of six signals in aromatic region in ^{13}C NMR of resorcin [4] arenes and pyrogallol [4] arenes instead of expected four signals have been used for characterization of hexameric nature of these macrocycles.

The interaction of tetrabutylammonium-4-nitrophenolate with resorcin [4] arenes exclusively in crown conformation have been used as colorimetric sensors for rapid detection of fluoride anion. The Interaction of other anions with resorcin [4] arenes have been studied by UV-Visible and ^{1}H NMR spectroscopic techniques.

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P-248

Pharmacognostical Standard For Polyphyto Mixture For Wound Healing

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The current objective of our research work is to formulate a poly herbal mixture of different crude drugs and to determine its pharmacognostical standards.

Poly herbal mixture was prepared in a definite ratio ranging from 2-10% in a geometrical distribution method. Poly herbal mixture was evaluated for various pharmacognostic standardization parameters like acid value, extractive value, phytochemical screening and pharmaceutical parameters like determination of particle size.

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Design, synthesis and pharmacological evaluation of pyrazoles and isoxazoles containing aryl sulfonate moiety as COX-2 selective inhibitors

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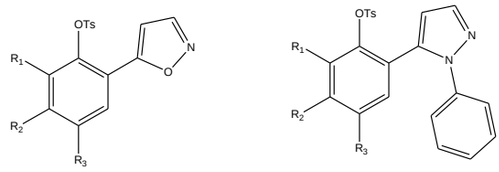
Pyrazole and isoxazole derivatives are very useful biologically active compounds and their dominant role in the history of heterocyclic chemistry has been previously reported. A wide variety of biologically active compounds are known to possess pyrazole and isoxazole nucleus in their chemical structure. On the other hand, the aryl sulfonate group is a common functionality present in many molecules and has found broad application in medicinal, drug and agricultural chemistry. Recently, E. B. Moawad et. al. described the synthesis of pyrazole and other molecules containing aryl sulfonate moiety. Pyrazole and isoxazole derivatives have exhibited a wide range of interesting biological activities like anti-inflammatory, anti-viral, anti-tumor, anti-depressant, antipsychotic, anti-inflammatory, herbicidal, fungicidal and pesticidal, analgesic and anticancer.

In present work selective synthesis of pyrazole and isoxazole derivatives containing aryl sulphonate moiety mediated by pyridine is described. Condensation of aromatic hydroxy acetophenones with N, N-dimethylformamide dimethylacetal in the presence of toluene has been studied. Reaction of enaminoketones with phenyl hydrazine and hydroxylamine hydrochloride gave the corresponding pyrazolyl and isoxazolyl phenols in good to excellent yield. The pharmacological evaluation of synthesized molecules is in progress as COX-1, COX-2 selective inhibitors.



4a-d **4e-h**

P-250

One pot synthesis of α-aryl propionic acids from arylalkenes under microwave: A facile route towards non steroidal anti-inflammatory compounds and their analogues

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The α-aryl propionic acids are an important class of compounds which are known for various biologically activities. In particular, such compounds constitute the core skeleton of commercial non steroidal anti-inflammatory drugs (NSAID) like Ibuprofen and Naproxen etc. A majority of the conventional approaches for such scaffolds have utilized elaborate steps and expensive air moisture/sensitive transition metal catalysts. In this context, a one pot approach for the direct conversion of easily available arylalkenes into α-aryl propionic acids has been developed under microwave irradiation in aqueous conditions. The developed protocol provides a green alternative to the hitherto indispensable multistep approaches besides eliminating the use of rare metal catalysts.

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Simultaneous estimation of Furosemide along with Phenol red and Naproxen along with Phenol red using RP-HPLC

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The objective of this study was to develop simple and rapid RP-HPLC methods for simultaneous quantification of high permeability marker (Furosemide) along with non-absorbable marker (Phenol red); and low permeability marker (Naproxen) along with non-absorbable marker (Phenol red). Versatility, suitability and robustness of method were checked and evaluated with several C18 columns and found that chromatographic resolution, selectivity and sensitivity were good with LiChroCART, RP-18 column.

Mobile phase comprising of acetonitrile: 0.04 M potassium dihydrogen phosphate, pH 5.2 (25:75 v/v) delivered at a flow rate of 1.0 ml/min with a total run time 8 min was used for Furosemide and Phenol red; while for Naproxen and Phenol red, the mobile phase used was acetonitrile: 0.04 M potassium dihydrogen phosphate, pH 5.2 (25:75 v/v) at a flow rate of 1.0 ml/min with total run time of 14 min. The calibration curves were acquired by plotting the peak area of analyte(s) against the nominal concentrations of calibration standards. The results were fitted to linear regression analysis using $1/X^2$ as weighing factor. The linearity range for Furosemide and Naproxen was across the range of 0.78-200 µm for each and for Phenol red 7.8-500 µm. The average regression (n=3) was found to be ≥ 0.996. The % accuracy observed for the mean of back calculated concentrations for three calibration curves were within 90 to 110 % ; while the % precision values ranged from 0.81 to 5.93 for all the analytes. We can conclude that the present methods can be useful for in-situ, PAMPA and Caco-2 permeability studies.

P-252

Microwave assisted one pot approaches for synthesis of some bioactive phenyethanoids and phenylpropanoids*

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Phenylethanoids (C_6-C_2 units) and phenylpropanoids (C_6-C_3 units) are important plant secondary metabolites derived from shikimic acid, a central molecule in plant metabolism, and occur in phenyl propanoid biosynthetic pathway. The phenylethanoids comprise diverse bioactive compounds like styrenes and stilbenes while the phenylpropanoid family is represented by diverse scaffolds like stilbenes, acetophenones, propiophenones, chalcones. A majority of conventional protocols for above compounds continue to be afflicted with limitations like employment of expensive, moisture sensitive catalysts, long reaction times besides the usage of harsh reagents which not only precludes their use with substrates possessing sensitive functional groups but also leads to deleterious environmental impact. In view of above, one pot approaches have been developed for the expedite synthesis of above compounds using green tools like microwave and ionic liquids etc.

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Studies on Sythesis of highly *O*-functionalized enantiomerically pure tetrahydrofuran alkynes

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The synthesis of enantiomerically pure 2,3,4-trisubstituted THF acetylenes from their corresponding domains by using various methodes. By using dimethyl 1-diazo-2-oxopropylphosphonate, the Bestmann–Ohira reagent, the transformation can be achieved in one pot is described. The synthetic route is depicted in the figure below.

References:

1. Sagar, R.; Reddy, L. V. R.; Saquib, M.; Kumar, B,; Shaw, A. K.; *Tetrahedron: Asymmetry* **2006**, *17,* 3294-3299.
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Anti-Ulcer Activity of *Smithia conferta* in Various Animals

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The present study was carried out to investigate anti-ulcer activity of petroleum ether, alcohol and aqueous extracts of leaves of *Smithia conferta*. All the three extracts were studied to phytochemical investigation as well as their toxic effects also carried out which revealed the presence of steroids in petroleum ether, isoflavonoids, alkaloids and carbohydrates in alcohol extract while aqueous extract contains aminoacids, carbohydrates and flavonoids. Aqueous and alcoholic extracts found to be non-toxic up to a dose of 5000 mg/kg while petroleum ether extract was safe only up to a dose of 2000 mg/kg after single dose administration of the extracts. Thus, these was significant reduction in the ulcer index with aqueous and alcoholic extracts and with petroleum ether it was less significant, there was a considerable reduction in the free acidity as well as the total acidity in pylorus ligated rats. There was a significant reduction in ulcer index wit all the three extracts in the case of stress induced ulcers and percentage protection of aqueous extract was nearly equivalent with that of standard.

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