Challenges in Drug Discovery and Development (CDDD-2011)
CSIR-CDRI, Lucknow, 9-10 December 2011,
SCIENTIFIC PROGRAM

Friday, December 9 , 2011

9.00 – 10.30 AM	**Registration**	
10.30AM-11.30AM	**Inaugural Session (Biochemistry auditorium)**	
	Address by president	**Prof. Anamik Shah, President, ISCB**
	Address by General Secretary	**Dr. P.M.S. Chauhan, General Secretary, ISCB.**
	Address by guests	**Prof. A.K. Singh, VC, Allahabad University** **Prof. G. C. Saxena, President ICC, former VC ,Avadh and Agra University**
	Vote of Thanks:	**Dr. P.M.S. Chauhan, Secretary, ISCB**
High tea	**11.30-1200**	

Session – I

Chairpersons: Dr.Greesh Saxena & Dr.K.C.Gupta

IL-2 **12.00PM-12.30 PM**	**Ashok K. Prasad,** *Department of Chemistry, University of Delhi,* *Glucose to LNA and Sugar-PEG Co-Polymer for Drug Delivery Applications*
IL-3 **12.30 PM-1.0 0 PM**	**Diwan S. Rawat,** *Department of Chemistry, University of Delhi,* **Cyclohexane Diamine Based Compounds: Synthesis and Biological Activity Evaluation**
Lunch	**1.00PM-200PM**
IL-4 **2.00PM-2.30**	**Vishnu K Tandon,** *University of Lucknow,Lucknow* **Impact of water as solvent in Organic synthesis**

IL-5 **2.30 PM-3.00**	Keshav Deo***, Vice President,CRD,Wockhardt Research Centre, Aurangabad*** **Enzymes as an attractive tool for Chemical transformation**

Tea: 3.00-3.30 PM

Session – II Chairpersons: Prof. Surya Kant & Dr.J.K.Saxena

O1 **3.30PM-3.45 PM**	**R. C. Maurya*** **and D. Sutradhar**, *R. D. University, Jabalpur*, **Vanadium-Based Sulfonamide derivatives of Medicinal Relevance: Studies on Some Oxovanadium(IV) Complexes in O, N-Donor Coordination Matrix of Sulfa Drug Schiff Bases Derived from 2-Pyrazolin-5-one Derivativ**
O2 **3.45 PM -4.00PM**	D. N. Singh***, Dr. Ram Manohar Lohia Avadh University Faizabad*** Activity optimisations of biologically active plant constituent
O3 **4.00PM -4.15 PM**	**Pratik Ambasana,** *Saurashtra University, Rajkot* **Synthesis and Biological evaluation of 1-[2,4-dimethyl-5-(5-aryl-1,3,4-oxadiazol-2-yl)-1H-pyrrol-3-yl]ethanones as potent Antitubercular and Antibacterial Agents**
O4 **4.15 PM -4.30PM**	**Shoeb R. Khan**, *Institute of Chemical Technology, Mumbai* **Hydroaminomethylation of olefins using Rhodium polyether diphosphinite complex anchored in polyethylene glycol as an efficient homogeneous recyclable catalyst**

Poster Session4.30 PM – 6.30PM

Conveners :**Dr. Raja Roy** , **Dr. Desh Deepak and Dr.Arun Sethi**

6.30 PM – 8.30 PM Cultural Programme
8.30 PM Dinner

Saturday, December 10, 2011

SESSION – III:

Chairpersons: Prof. Anamik Shah & Dr.A.K.Dwivedi

IL-6 **9.30 AM –10.00 AM**	**S K Puri,** *Division of Parasitology, CSIR-CDRI, Lucknow* **Challenges and Opportunities in drug discovery for malaria**
IL-7 **10.00AM-10.30AM**	Krishna Nand Singh, ***Dept. of Chemistry, BHU, Varanasi*** **Microwave Assisted Green Protocols in Organic Synthesis**
IL-8 **10.30AM -11.00AM**	**Surat Kumar,** *Dept of Chemistry, Faculty of Engineering, Dayalbagh* **Efficient Drug Design by Structural Biology Protocols**
IL-9 **11.00-11.30 AM**	**Dalip Kumar ,***Department of Chemistry, BITS* Design and Synthesis of Novel 1,2,4-Oxadiazoles as Tubulin Inhibitors

Tea: 11.30 AM-11.50 PM

Session-IV
Chairpersons: Dr. Pratibha Mehata Luthra & **Dr.S.B.Katti**

IL -10 **11.50AM-12.20PM**	**Neeloo Singh,** *CSIR-Central Drug Research Institute, Lucknow, India* **Driven to Death: Monastrol induced geranylgeranyltransferase inhibition in *Leishmania***
IL-11 **12.20PM -12.50PM**	**Rakeshwar Bandichhor,***Dr. Reddy's Laboratories, A.P* **Synthetic Case Studies: An Industrial Perspective**
IL-12 **12.50PM-1.20PM**	**Anil Kumar,** *Department of Chemistry, BITS, Pilani* **Synthesis of novel heterocyclic compounds employing multicomponent reactions and evaluation of their Src kinase inhibitory activity**

Lunch 1.20 PM - 2.00 PM

SESSION – V
Chairpersons: Dr. Vishnu K Tandon & **Dr.Krishna Nand Singh**

IL-13 **2.00 PM -2.30 PM**	**Jayant Khandare**, *Piramal Life Sciences Ltd. Mumbai, India* **Macromers as Targeted Nano Delivery Materials: Opportunities and Challenges**
IL -14 **2.30 PM- 3.00 PM**	**Anamik Shah,** *Saurastra University ,Rajkot* **Antitubercular molecules with "Hydrazide linkers" with/without spacer attached to small heterocycles"**
IL-15 **3.00 PM-3.30 PM**	**K.Avasthi,** *MPC Div.,Central Drug Research Institute,Lucknow-226001* **Pyrazolo[3,4-*d*]pyrimidine core based models for studying π–π interactions in flexible propylene and butylidene linker compounds at molecular and supramolecular level**
IL-16 **3.30 PM-4.00 PM**	**Pratibha Mehata Luthra,** Dr. B.R. Ambedkar Center for Biomedical Research University of Delhi, Delhi **Intricacy in selective targeting of CNS disorders: Rational approach to Design Antiparkinsonian agents.**

4.00 PM – 5.00 PM : Award session and Valedictory Session

High Tea: 5.00PM-5.30PM

5.30 PM – 6.00 PM : ISCB GENERAL BODY MEETING

Pl-1

A Journey From Beginning to the Present Day

S.P Singh

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This Lecture will describe the importance and centrality of chemistry in science. Chemistry as practiced in the early days will be illustrated in many processes. This will be followed by the growth of modern chemistry and landmark contributions made by eminent chemists. Interdisciplinary areas such as molecular biology, nanotechnology and spectroscopy will receive special attention. Significance of enantioselective synthesis in drug chemistry will be highlighted. In conclusion, the work of great Indian chemists will be mentioned.

IL-1

Chemical biology of Phosphatidylinositols and new drug discovery

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Since the discovery of phosphatidylinositol (PI) mediated signal transduction and glycosyl phosphatidylinositol (GPI) mediated membrane anchoring of specialized cell-surface proteins, the biology of PI/GPIs has remained in focus [1-2]. A number of key cellular events (trans-membrane signaling, cell proliferation, vesicular traffic, chemotaxis, glucose homeostasis and the membrane organization) are mediated by PI/GPIs with the involvement of specific biosynthetic and regulatory kinases and phosphatases. The pharmacological and clinical validation of phosphatidylinositol 3-kinase (PI3K) and downstream targets AKT and mTOR has provided new targets for discovery of specific kinase inhibitors for cancer and autoimmune diseases. The GPI-anchors and their protein-free counterparts are produced in abundance by protozoan parasites as essential virulence factors helping them to infect, proliferate and subvert the host immunity. The structural complexity and biological function of PI/GPIs present

substantial challenges, and despite the efforts of several groups, their synthesis remains a difficult undertaking; complicated further by the structural and functional differences among the species and significant micro-heterogeneity in their lipid and glycan domains. In our efforts on chemical biology of PI/GPI molecules [3-13] and drug discovery [14-18], we designed new and efficient approaches for the synthesis of the full-length GPI molecules and their structural and functional mimics to address specific questions pertaining to the biosynthetic inhibition and plasma-membrane micro-domain (lipid-raft) organization. Our current focus is on the medicinal chemistry of PI3K/AKT/mTOR axis for cancer and autoimmune diseases, and stem cell renewal and differentiation. Some of our contributions in this area will be discussed.

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IL-2

Glucose to LNA and Sugar-PEG Co-Polymer for Drug Delivery Applications

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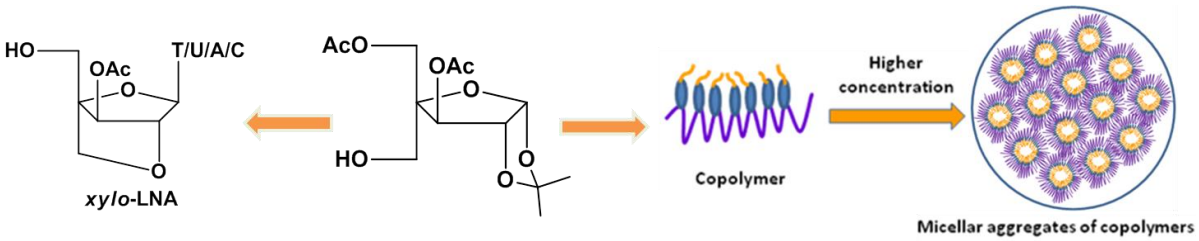
The discovery of sugar modified nucleoside derivatives as potential antiviral agents and the emergence of antisense and antigene oligonucleotides as potential and selective inhibitors of gene expression have led to the considerable rise in the synthesis of modified nucleoside derivatives and nucleic acids involving them. Further, there has always been need to have biocompatible drug carriers capable of delivering water insoluble drugs with high transport and controlled release capacity.

We have developed an efficient biocatalytic methodology for the transformation of a trihydroxy sugar derivative derived from glucose into *xylo*-LNA, a monomer of antisense oligonucleotide and sugar-PEG co-polymer having application as drug carrier and its controlled release. Detailed results will be presented in the meeting.



Acknowledgements: We thank the University of Delhi (DU-DST Purse Grant) and the International Division, Department of Biotechnology (DBT, New Delhi) for financial assistance.

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IL-3

Cyclohexane Diamine Based Compounds: Synthesis and Biological Activity Evaluation

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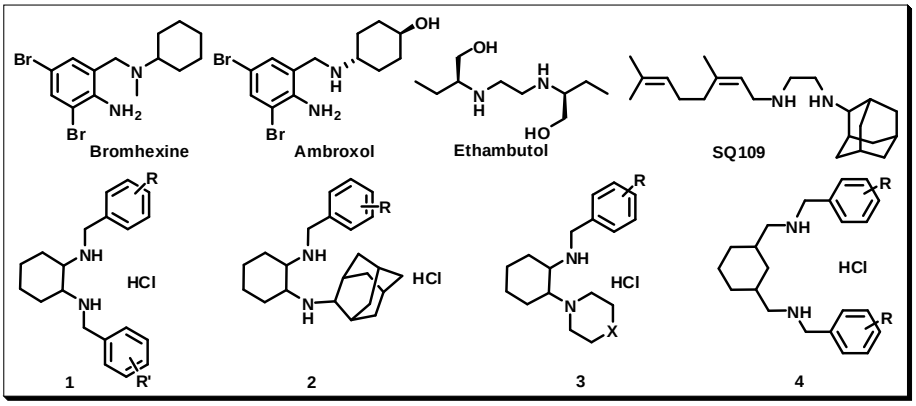
Infectious diseases are the second leading cause of death worldwide and over one-third of the world population is likely to get infected by bacterial infections such as tuberculosis, typhoid fever, typhus, plague, diphtheria, cholera, pneumonia and dysentery.[1,2] Unfortunately the emergence of antibiotic resistance due to Gram-positive bacterial pathogens such as methicillin-resistance *Staphylococcus aureus* (MRSA), vancomycin-resistance *enterococci* (VRE), penicillin resistance *Streptococcus pneumonia* and *Mycobacterium tuberculosis* has put tremendous pressure on public health and there is an urgent need to develop new chemical entities for the eradication of infectious diseases.[3] The empirical screening of synthetic chemical libraries or natural products and structural changes to the existing molecule has given a number of leads which show potent antimicrobial activity. Diamine based compounds have been subject of intense study due their potential role in the medicinal chemistry and other related areas.6 Some of the diamine based compounds such as ethambutol has been used as a drug for the treatment of tuberculosis, and many more compounds are at the various stages of clinical development, and SQ 109 is the latest entry in this series.[4,5] As a part of our ongoing efforts towards the synthesis of novel antimicrobial agents,[6-10] we became interested to modify the bromhexine, a mucolytic agent used as syrup. A number of symmetrical and unsymmetrical

cyclohexane-diamine hydrochloride salts (**1-4**) were synthesized and evaluated for their anti-microbial activity against Gram-positive and Gram-negative bacterial strains and activity against *M. tuberculosis* $H_{37}Rv$ strain. Many of these compounds have shown excellent *in vitro* antibacterial and anti-tubercular activity with no toxicity against the red blood cells at very high concentration. The synthesis and antimicrobial activity of these compounds will be presented.



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IL-4

Impact of water as solvent in Organic synthesis

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The influence of solvent in nucleophilic substitution reactions in Organic synthesis "On-H_2O"[1] and "In-H_2O" has been demonstrated. Comparative effects for synthesis of biologically active 1,4-quinone derivatives "On-H_2O"and "In-H_2O" have been studied in detail.

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IL-5

Enzymes as an attractive tool for Chemical transformation

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In the 21st century the chemists / biotechnologists are paying attention to carry out the organic transformations as natures do. In other words focus research for obtaining value added products using the cost effective, ecofriendly green tools. The last decay has seen a major transformation in the field of biocatalysis in pharmaceutical industry. Indeed it opens an opportunity to explore the use of enzymes (Nature's tool) as an attractive ways in drug manufacturing organizations. Numerous chiral alcohols / amines are obtained in high enantiomeric purity from the corresponding ketones / imines . Just for discussion take an example of the complex synthesis of vitamin B2. In the past so many years the molecule was manufactured in 8 steps from glucose. But now the same is being manufactured through biocatalysis in two steps. The total production cost has been reduced to 40 % and industrial wastage has been reduced to 95 %. Always the selectivity and reactivity of the enzyme varies to the substrate. The global use during last year is increased by ~20 % against the previous year. I sense an all-pervasive mood of optimism and

buoyancy as biocatalysis 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 use of biocatalysis in the lower affordable cost.

IL-6

Challenges and Opportunities in drug discovery for malaria

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Medicines have played a key role in controlling malaria historically since the application of cinchona bark during the 16th century. However, even in the 21st century, malaria continues to take an enormous toll on human health accounting for an estimated 2.5 billion people affected and 1 million deaths annually. Of the four recognized *Plasmodium* species causing disease in humans, *Plasmodium falciparum* causes most mortality and *Plasmodium vivax* causes most morbidity besides harbouring a dormant reservoir of latent infection that hampers total cure. While the access to medicines is clearly a major challenge, there are several reasons why new antimalarials are urgently needed. First, the emergence of drug resistance to any infectious disease treatment is inevitable. Artemisinines representing the last class of widely efficacious drugs are also getting compromised today with the reports suggesting increased sensitivity levels for *P falciparum* parasites. The recent reports of delayed PCT are an early warning that treatment failure could be just a few years away. Secondly, the elimination of long lasting reservoirs of infection represented by hypnozoites has become a major challenge and drugs targeting relapses are urgently needed as part of the eradication strategy. Owing to the intrinsic difficulties in discovering and developing new antimalarials, no new class of drugs has been introduced in the clinical practice since 1996. In the search for new medicines to combat malaria there have been two major technological steps forward over the last ten years. First the parasite genomes have been sequenced allowing a systematic analysis of all the essential and druggable genes, This has allowed assays to be set up for screening with the hope of finding new starting points for chemical programmes. Secondly advances in automation technologies have facilitated setting up

of quicker and reproducible screening assays with live parasites. Moreover compound collections from several pharma companies are now available to be screened at the discovery end of the pipeline. Antimalarial drug discovery can broadly be separated into three areas as (i) treatment of blood stage resistant malaria, (ii) radical cure killing dormant hypnozoites in the patients infected by *P vivax* and (iii) blocking the transmission from host to the vector and vice versa. With the advancing technologies and sustained investment, the next 10 years should ensure availability of diversified portfolio of malaria drugs to mitigate the human sufferings and eventual eradication of this dreadful disease.

IL-7

Microwave Assisted Green Protocols in Organic Synthesis

Krishna Nand Singh

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Within the past decade, green chemistry has attained the status of a major scientific discipline. The investigation and application of green chemistry principles has led to the development of cleaner and more benign chemical processes, with many new technologies being developed each year. In today's world, synthetic chemists in both academia and industry are constantly challenged to consider more environmentally benign methods for generation of the desired target molecules. Among the 12 principles of green chemistry, the desire for utilizing "safer solvents" and to "design for energy efficiency" can be considered two key principles of relevance to synthetic chemists.

Microwave has emerged as a novel and benign source of energy for chemical reactions and microwave assisted organic synthesis (MAOS) has been extensively investigated during recent years. Compared to conventional thermal heating, the use of microwave provides chemical processes with special attributes, such as enhanced reaction rates, higher yields, enhanced product purity, better selectivity, improved ease of manipulation, rapid optimization of reactions and several eco-friendly advantages.

Solvent usage is often an integral part of a chemical or manufacturing process. The unavoidable choice of a specific solvent for a desired chemical reaction can have profound economical,

environmental, and societal implications. The pressing need to develop alternative solvents to some extent originates from these implications and constitutes an essential strategy under the emerging field of green chemistry. Toward this end, considerable efforts have been devoted to develop and use nontraditional solvents for chemical synthesis. Such unconventional media include, among others, solvent-free conditions, supercritical carbon dioxide, ionic liquids, and last but not the least water.

In view of the above and as a part of our ongoing research interest, some green protocols on microwave assisted multicomponent strategies and transition metal catalyzed organic reactions will be discussed.

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2Highly efficient one-pot synthesis of primary amides catalyzed by scandium (III) triflate under controlled MW,Bharat Kumar Allam and Krishna Nand singh
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. **9**Eco-friendly and facile one-pot multicomponent synthesis of acridinediones in water under microwave,**Satish Kumar Singh and** Krishna Nand Singh
J. Heterocyclic Chem, 48 (**2011**) 69-73.

IL-8

Efficient Drug Design by Structural Biology Protocols

Surat Kumar

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In present times, the modern nD-NMR and powerful computational techniques are available as drug design tools. In a number of cases, these methods have been demonstarted to be used for structural biological investigations as well as furnishing drug design. Ease with which, these tools have been employed in last 2 decade has facilitated phenomenal growth and development of these techniques. The structural parameteres needed for snug-fit binding of drug candidates onto the receptor site were deciphered with the x-ray, 2D-NMR and structural refinement methods. These parameters have furnished the efficient design of potential drug candidates with potent biological activities. Meticulous investigations and bioinformatics devices/software tools have only strengthened this approach of effective drug design. An overview of a few such studies will be presented.

IL-9

Design and Synthesis of Novel 1,2,4-Oxadiazoles as Tubulin Inhibitors

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Microtubules are the components of cell structure, which take part in a variety of crucial cellular functions [1]. The key role of microtubules in cell division makes them a well validated target for cancer chemotherapy [1].Chemotherapeutic agents those are able to modulate the microtubule network either by inhibition of tubulin polymerization or by blocking microtubule disassembly, are of great interest in anti-cancer therapy [2]. The 1,2,4-oxadiazole is a five-

membered nitrogen and oxygen containing heterocycle which has been commonly used as a privileged scaffold to produce various novel therapeutic molecules [3]. A recent study of 3,5-diaryl-1,2,4-oxadiazoles [3]have revealed their selective cytotoxicity against breast and colorectal cancer cell lines by arresting cell cycle in G_1 phase. Their further explorations to ameliorate the activity led to the preparation of 5-furyl-1,2,4-oxadiazoles which exhibited good in vivo efficacy in animal studies [3]. In our efforts to identify novel and selective anticancer agents, we have synthesized a new series of 3,5-disubstituted-1,2,4-oxadiazoles and tested against a panel of human cancer cell lines [4]. The preliminary tubulin polymerization studies of some 3,5-disubstituted-1,2,4-oxadiazoles have shown significant inhibition. Design, synthesis and anticancer activity of novel 1,2,4-oxadiazoles will be discussed during the presentation.

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IL-10

Driven to Death: Monastrol induced geranylgeranyltransferase inhibition in *Leishmania*

Neeloo Singh

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Visceral Leishmaniasis (VL) is caused by the parasite *Leishmania donovani.* Ninety percent of VL occurs in seven countries: India, Bangladesh, Nepal, Sudan, Ethiopia, Kenya and Brazil. The disease is fatal if left untreated. Discovering, developing and commercializing safe and affordable therapeutics for VL continues to engage the attention of leishmaniacs worldwide. Our

laboratory is engaged in target based drug discovery for leishmaniasis and has identified monastrol as a potent oral antileishmanial. Monastrol having dihydropyrimidine (DHPM) pharmacophore, is a small inhibitor of mitotic kinesin Eg5 and currently in use for cancer therapy. In the present study, microarray experiments were conducted on Affymetrix GeneChip® HG-U133 Plus 2.0 array to determine the genes that encode proteins related to pathological alterations of cell signaling pathways in intracellular *Leishmania* amastigotes in response to the oral antileishmanial agent, monastrol. Monastrol, the investigational compound, with antileishmanial activity targeting pteridine reductase (PTR1) in *Leishmania* parasites, induced unprenylated Rap1A when exposed to this anticancer drug at IC_{50} of 10 µM. Monastrol is known to cause mitotic arrest in cancer cells, inhibited Rap1A prenylation (geranylgeranylation) in intracellular *Leishmania* which results in blockade at the G1 phase of the cell cycle. Regulators (unprenylation) of cell signaling pathways can be exploited in *Leishmania* parasites as novel therapeutic tools. We propose the development of antiparastic drugs to 'piggyback' on the development of inhibitors for cancer research targeting farnesyltransferase and geranylgeranyltransferase.

IL-11

Synthetic Case Studies: An Industrial Perspective

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Ever increasing global demand for environmentally friendly pharmaceutical processes and products requires the development of non-infringing and cost-effective approaches to pollution prevention. One of the most attractive concepts for pollution prevention is green and sustainable chemistry, which is best defined as *the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture, and applications of chemical products.*[1] Appropriate utilization of these Green Principles frequently requires the redesign of chemical products or processes from fundamental perspective. Driven by improved process conditions and economics, constantly increasing environmental controls and social

pressure, incorporating green chemistry into the synthesis of active pharmaceutical ingredients (APIs) and intermediates with "get it right at the first place" approach, has steadily been gaining priority in the pharmaceutical industry and has evolved into an institutionalized practice among major pharmaceutical companies. There will be few case studies discussed with the emphasis of related non-infringing chemistry, process and scalability aspects.

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IL-12

Synthesis of novel heterocyclic compounds employing multicomponent reactions and evaluation of their Src kinase inhibitory activity

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Protein kinases play a pivotal role in the signal transduction pathways. Expression of c-Src, a member of Src family kinases (SFKs), is frequently elevated in a number of epithelial tumors including colon, breast, prostate, lung, ovary and pancreas compared with the adjacent normal tissues. Because of this inhibition of Src kinases has become an attractive therapeutic strategy for several diseases. A large amount of small molecules that target the ATP-binding pocket in the catalytic domain of c-Src have been identified. However, due to conserved nature of catalytic domain in kinases synthesis of novel heterocyclic molecules that can selectively inhibit catalytic domain of a protein kinase is still desirable.

Multicomponent reactions (MCRs) have become important tool in drug discovery as they allow assembly of molecular arrays with high molecular diversity. In continuation of our interest in development of Src kinase inhibitors, we have synthesized several novel heterocyclic compounds by employing multicomponent reactions and evaluated them for their potential to inhibit c-Src kinase. The compounds were also evaluated for their anti-proliferative activities for different cancer cell lines in which c-Src is found to be elevated.

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IL-13

Macromers as Targeted Nano Delivery Materials: Opportunities and Challenges

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Macromolecular and nano-scopic forms of materials are being engineered for delivery of bioactives in the form of prodrug conjugates, depots (liposomes, nanoparticles), polyplexes (complexes), and micelles (self assemblies). The talk will highlight various forms of synthetic polymers and their associated chemistry in tuning for suitable biological applications. Furthermore, the opportunities and challenges in designing such polymeric macromers as multi-component delivery systems in targeting cancer, and *in vitro* and *in vivo* imaging.

IL-14

Antitubercular molecules with "Hydrazide linkers" with/without spacer attached to small heterocycles"

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In Past few years, several efforts are made towards the development of new chemical entities related to Antitubercular activity.Our revelation of using the "hydrazide linkers" in various capacities as a attachment to small heterocyclic systems has given very promising results, where several molecules are identified as potent Antitubercular against *mycobacterium tuberculosis (H$_{37}$Rv)*. The mechanistic pathway for this activity may attribute similar to isoniazide through mycolic acid.
The mini review of work will be presented.

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IL-15

Pyrazolo[3,4-*d*]pyrimidine core based models for studying π–π interactions in flexible propylene and butylidene linker compounds at molecular and supramolecular level

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In addition to stabilization of DNA/RNA structures, arene interactions are known to play an important role in chemistry and biology particularly in molecular recognition, crystal engineering, foldamers, molecular tweezers/clips and drug development. Arene interactions studies based on **pyrazolo[3,4-*d*]pyrimidine** core, which is isomeric with purine system found in adenine and guanine two of the nucleic acid bases, in flexible *propylene* and *butylidene* linker compounds will be discussed for better understanding of π–π interactions at molecular and supramolecular level. Extensive use of X-ray crystallography and ^{1}H NMR spectroscopy for such studies to understand molecular recognition will be highlighted.

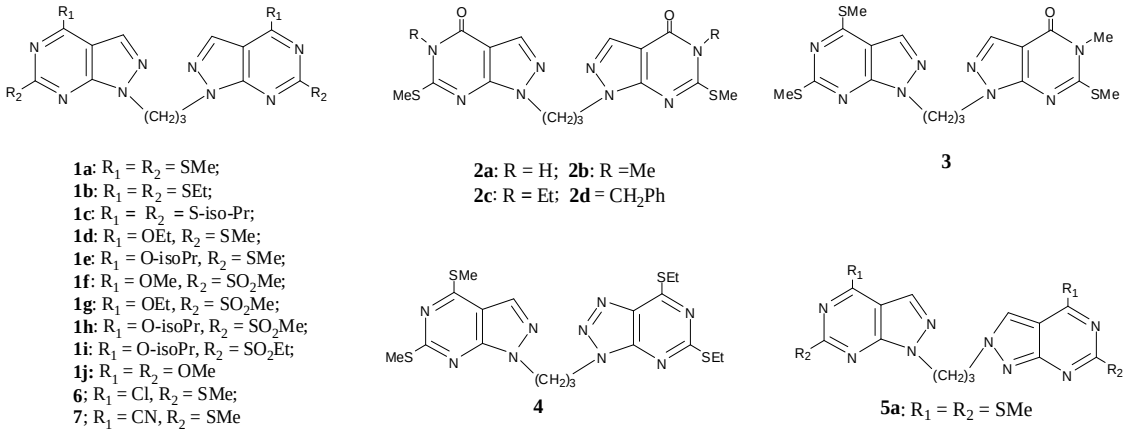

Figure 1: Pyrazolo[3,4-*d*]pyrimidine core based *propylene* linker compounds.

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*Author is grateful to DST, New Delhi, India for financial support (grant no. SR/S1/OC-14/2010).

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IL-16

Intricacy in selective targeting of CNS disorders: Rational approach to Design Antiparkinsonian agents.

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The brain is the control center of body and is involved in regulation of of thoughts, memory, speech and movement. Drug discovery and development for CNS drugs, that complete clinical trials and win regulatory approval—especially drugs in the CNS area, such as Alzheimer's and Parkinson's disease is challenging. The vast majority of drugs fail to cross the BBB in successful development of CNS drug candidates. The development of small- and large-molecule drugs, that can efficiently cross the BBB are associated with undesirable side effects due to overlapping pathways to control biochemical and pharmacological functions in brain. The attempt has been made to exercise rational approaches to overcome these difficulties, to some extent, for development of anti-Parkinsonian agents.

O1

Vanadium-Based Sulfonamide derivatives of Medicinal Relevance: Studies on Some Oxovanadium(IV) Complexes in O, N-Donor Coordination Matrix of Sulfa Drug Schiff Bases Derived from a 2-Pyrazolin-5-one Derivative

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During the past two decades the frequencies and types of life-threatening infections have increased. Besides the usual cases, there is an increase of immunocompromised patients as well as patients undergoing more invasive medical procedures among others. A big associated problem is that the incidence of drug resistant isolated bacterial strains in the community has become quite alarming. For these reasons the demand for new and better chemotherapic compounds has increased and nowadays the search for new chemicals with antimicrobial activity is an important field of research.

Specially, sulfonamide derivatives exhibit a range of bioactivities, including anti-angiogenic, anti-tumor, anti-inflammatory and anti-analgesic, anti-tubercular, anti-glaucoma, anti-HIV, cytotoxic, anti-microbial and anti-malarial agents. The sulfonamide derivatives are also known to exhibit a wide variety of pharmacological activities through exchanges of different functional groups without modification of the structural –S(O)2N(H)– feature. The pharmacological activity of these types of molecules is often enhanced by complexation with metal ions.

The pyrazolone derivatives have been reported to possess strong antibacterial, antihistaminic and antifungal, analgesic, antipyretic, anti-inflammatory and anti-rheumatic activities. They also show antidiabetic, anticancer and antineoplastic properties.

Vanadium plays an important role in life and one of its most relevant properties identified thus for, is its capacity to act as insulin-enhancing agent, either in the form of its inorganic salts or complexes with organic ligands. Besides the antidiabetic action, vanadium complexes are known to possess potent anticancer activity, which deserve increasing attention for application to biomedical sciences. Some oxovanadium(IV) complexes {[$VO(N_4)$] type} have recently been evaluated for their inhibitory effects on HIV-1(BaL) (a Human Immunodeficiency Virus) replication in Hut/CCR5 cells.

In view of the above, the present paper reports the synthesis and characterization of some new oxovanadium(IV) complexes of composition $[VO(L)_2(H_2O)]\cdot H_2O$, where LH = N-(4'-butyrylidene-3'-methyl-1'-phenyl- 2'-pyrazolin-5'-one)sulfadiazine, N-(4'-butyrylidene-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one)sulfaguanidine, N-(4'-butyrylidene-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one)sulfanilamide and N-(4'-buty-rylidene-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one)sulfamerazine. These complexes were prepared by the reaction of vanadyl sulfate pentahydrate with the said Schiff bases in 1:2 metal-ligand ratios, in ethanol. The compounds so obtained were characterized by different physicochemical studies, *viz.*, elemental analyses, molar conductance and magnetic measurements, thermogravimetry, cyclic voltammetry, infrared, electron spin resonance and electronic spectral studies. The 3D molecular modeling and analysis for bond lengths and bond angles have also been carried out for one of the representative compounds, $[VO(bumphp\text{-}sdz)_2(H_2O)]\cdot H_2O$ (**1**) to substantiate the proposed structure. The pharmacological studies of these compounds are in progress.

O2

Activity optimisations of biologically active plant constituent

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Increasing popularity of herbal preparation in managements of conical disorders at global level may be attributed to the lesser side effects. Development of the spectroscopic and analytical

technique has led to the discovery and development of several bioactive molecules. Recently, some of the compounds isolated from the plants are in clinical use and even not having any synthetic substitute viz. taxol isolated from the bark of *Taxus bravifolia is a prominent anticancer drug* [1] *and artemisinin was isolated from Artimisia annua has been found to be more effective for the treatment of drug resistant malaria* [2]. Identification and characterizations of bioactive plants constituents increases their versatile uses in the modern clinical system. Furthermore, after the identification of lead molecule it is then subjected to lead optimizations by the preparation of suitable derivatives. Here, in this paper detailed isolation procedure and structural elucidation of active constituent and optimizations of the its activity will be discussed.

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O3

Synthesis and Biological evaluation of 1-[2,4-dimethyl-5-(5-aryl-1,3,4-oxadiazol-2-yl) - 1H-pyrrol-3-yl]ethanones as potent Antitubercular and Antibacterial Agents

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A new series of 1-[2,4-dimethyl-5-(5-aryl-1,3,4-oxadiazol-2-yl)-1*H*-pyrrol-3-yl]ethanones was synthesized by acid catalyzed condensation between 4-acetyl-3,5-dimethyl-1*H*-pyrrole-2-carbohydrazide and different aromatic carboxylic acids. The structures of all the synthesized compounds were confirmed by 1H NMR, IR, Mass spectral analysis. The newly synthesized compounds were screened for their anti-tubercular and antibacterial activity. The screening result suggested that compounds **6c**, **6f**, **6i**, **6k**, **6m** and **6n** have shown promising anti-tubercular activity against *Mycobacterium tuberculosis* H37Rv strain with 88%, 70%, 84%, 81%, 83% and 70% inhibition respectively at <6.25 μM concentration, where as compounds **6c**, **6f**, **6h** and **6j**

revealed broad spectrum anti-bacterial activity with the minimum inhibitory concentration up to 18μg/mL.

O-4

Hydroaminomethylation of olefins using Rhodium polyether diphosphinite complex anchored in polyethylene glycol as an efficient homogeneous recyclable catalyst

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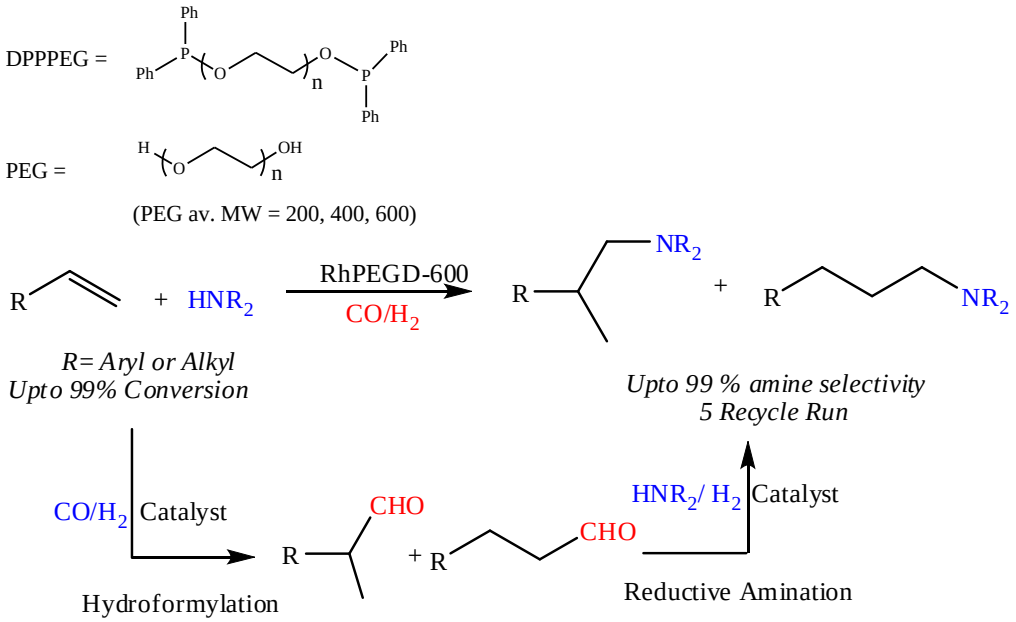
Hydroaminomethylation is an atom economic and efficient one-pot process for the synthesis of amines from olefins and primary or secondary amines. This domino reaction consists of initial hydroformylation of an olefin to an aldehyde and subsequent formation of an enamine (or imine) followed by hydrogenation (Scheme 1). Hydroaminomethylation of various olefins with primary and secondary amines using rhodium polyether diphosphinite complex anchored in polyethylene glycol [RhPEGD] has been studied. The system was optimized with respect to various reaction parameters and showed wider applicability for hydroaminomethylation of different aromatic, aliphatic and cyclic olefins to corresponding amines. During the course of reaction, catalyst was soluble with reactants/products while could be quantitatively separated from reaction media in biphasic form by addition of anti-solvent on completion of reaction. The catalyst exhibited remarkable activity and was subsequently recycled up to five consecutive cycles.



Scheme 1. Hydroaminomethylation of olefins

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P-1

EVALUATION OF GENOTOXICITY OF SMA-DMSO COMPLEX BY AMES TEST & INVITRO CHROMOSOMAL ABERRATION ASSAY

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Genotoxic assessment of RISUG (complex of Styrene maleic anhydride and Dimethyl sulphoxide) was done using Bacterial Reverse muation assay (AMES test) and Chromosomal aberration assay.

Histidine auxotrophic strains of Salmonella typhimurium TA98, TA 100 and TA102 were tested for mutagenicity after application of SMA-DMSO in dose range of .1 mg to 1 mg by AMES test as per the OECD guidelines 471. Results obtained in presence of test compound were compared with positive control (mutagen CP and mitomycin) and negative control(untreated bacterial strains grown in presence of DMSO) and it was found that SMA-DMSO exhibited no genotoxicity in the observed concentration range.

Subsequently, Inviro Chromosomal aberration assay was performed as per OECD guidelines 473 to assess genotoxicity of SMA- DMSO further using CHO cell line.The *in vitro* chromosome aberration test is employed to identify agents that cause structural chromosome aberrations in cultured mammalian cells. CHO cells were treated with SMA-DMSO in the concentration range of 0.01 M to 5 M and Ethyl methanesulfonate was used as positive control. Cells were arrested in metaphase stage after 4 hrs of treatment and were then observed for chromosomal aberrations. A total of around 200 metaphases per concentration of SMA-DMSO

was observed. Analysis of Mitotic index and chromosomal strands with & without gaps showed that SMA- DMSO is not genotoxic upto the concentration of 1 M but above this concentration, it showed significant genotoxic results

P-2

Microwave Assisted Synthesis of flourochloro Benzimidazolo substituted Thiazolidinone derivatives for Antimicrobial activities

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Benzimidazole is an antiprotozoal agent, was found as anthelmintics by Gregory in 1992, also used as anticancer agent by inhibiting Poly (ADP-ribose) Polymerase (PARP). To synthesize some novel flourochloro Benzimidazolo substituted thiazolidinone derivatives by establishing microwave assisted methods for synthesis of the proposed derivatives and confirm the various structures by spectral and elemental analysis. Evaluation of synthesized derivatives for their Biological activity is done. Further the Benzimidazolo-thiazolidinone derivatives have been reported for antimicrobial activity with one gram positive and one gram negative staphylococcus aureus and E coli agents. Thiazolidinone derivatives have been used as antidiabetic agent in view of the above and in continuation of search we have prepared benzimidazolo-thiazolidinon derivatives**.**

P-3

Synthesis and anti-HIV activity of novel N-((1, 3-substituted diphenyl-*1H*-pyrazole-4-yl) methylene)-2-methylindoline-1-amine derivatives using MTT method.

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A novel series of novel N-((1, 3-substituted diphenyl-1H-pyrazole-4-yl) methylene)-2-methylindoline-1-amine derivatives has been synthesized by microwave assisted green chemical approach. All the synthesized compounds were evaluated for their anti-HIV activity using MTT method. Most of the compounds shown moderate to potent activity against two strains of Human Immunodeficiency virus (HIV-I and HIV-II). Among all compounds, three compounds **5c**, **5d**, **5e, 5j, 5m and 5o** shown potent activity (5c, IC_{50} = 9.07 µg/ml), (5d, IC_{50} = 12.55 µg/ml), (5e, IC_{50} = 8.05 µg/ml), (5j, IC_{50}= 8.01 µg/ml), 5m, IC_{50}= 10.09 µg/ml), 5o, IC_{50}= 8.21 µg/ml), while **5f, 5i** and **5n** shown moderately active against MT-4 cells.

P-4

Oxaheterocycles: Di- and Trioxabenzo[3,4]cyclohepta[1,2-*a*]naphthalene-6,7-diones and Dibenzo[*a,c*]cycloheptene-3-carbonitriles

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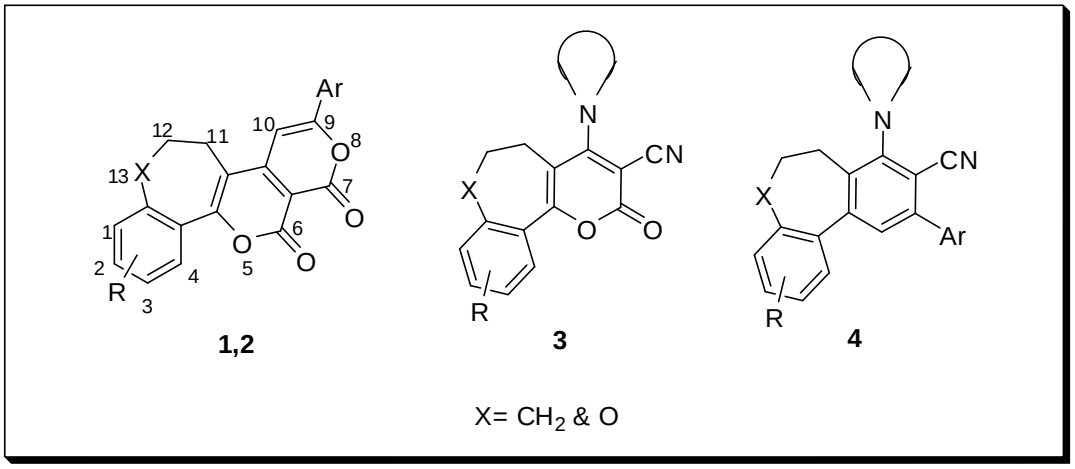
An efficient and convenient synthesis of 9-aryl-11,12-dihydro-13*H*-5,8-dioxabenzo[3,4]cyclohepta[1,2-*a*]naphthalene-6,7-diones (**1**, X=CH_2) and its oxygen analog (**2**) has been delineated through base catalyzed condensation-cyclization of 4-methylsulfanyl-2-oxo-2,5,6,7-tetrahydro-1-oxadibenzo[*a,c*]cycloheptene-3-carbonitriles and 4-methylsulfanyl-2-oxo-5,6-dihydro-2*H*-1,7-dioxadibenzo[*a,c*]cycloheptene-3-carbonitriles with aryl methyl ketone separately. We have also synthesized 2-aryl-4-*sec*-amino-6,7-dihydro-5*H*-dibenzo[*a,c*]cycloheptene-3-carbonitriles (**4**, X=CH_2) through ring transformation of 4-*sec*-amino-2-oxo-2,5,6,7-tetrahydro-1-oxadibenzo[*a,c*]cycloheptene-3-carbonitriles (**3**, X=CH_2) with aryl methyl ketones in the presence of a base.



Reference:

1. Tandon, V. K.;* Maurya, H. K.; Kumar B.; Kumar, B.; Ram, V. J.* *Synlett.* **2009**, 2992 *and the references cited therein*.

P-5

Pentacyclic Helicenes: An innovative concise synthesis of naphthoxepino-pyrano pyrans

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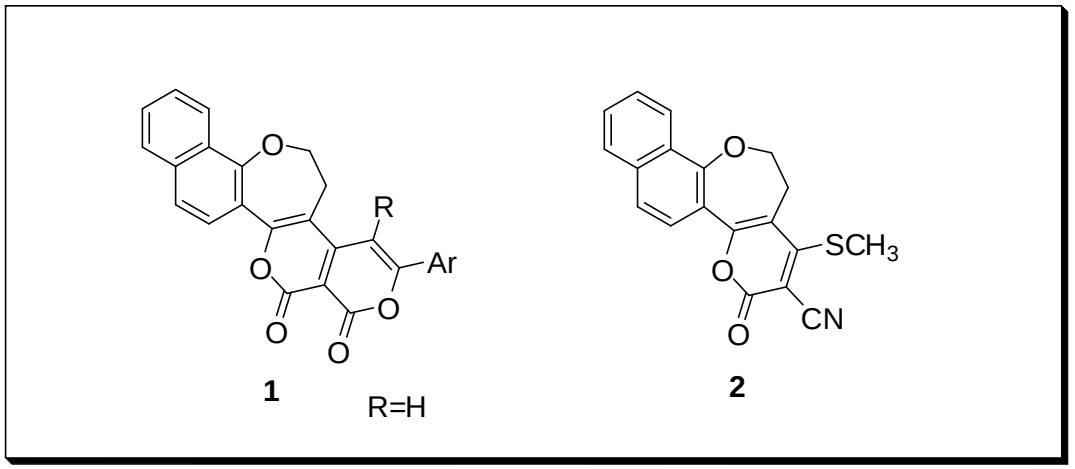
An innovative concise synthesis of naphthoxepino-pyrano pyrans (**1**) has been delineated through base catalyzed condensation cyclization of naphtho-pyrano-oxepines (**2**) with arylakyl ketones in presence of base.



Reference:

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P-6

On-Water": Synthesis of potential antimicrobial hetero-1,4-naphthoquinones

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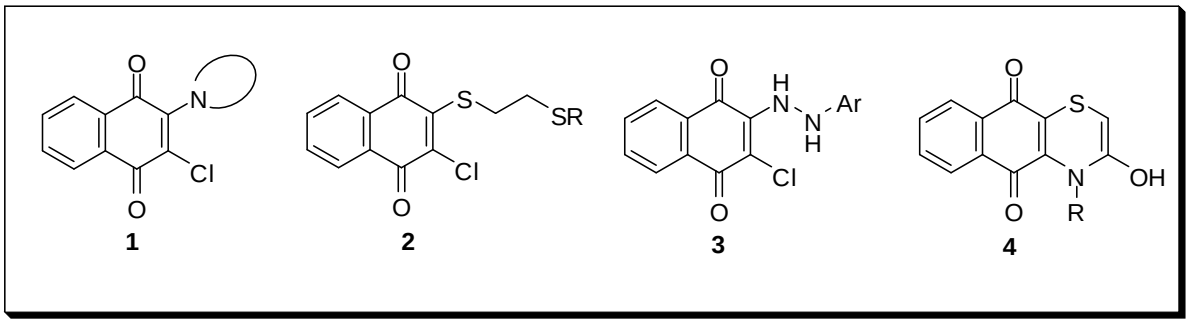
2-Chloro-3-(sec-amino)naphthalene-1,4-dione (**1),** 2-chloro-3-(2-mercaptoalkylthio)naphthalene-1,4-dione (**2**), 2-chloro-3-(2-arylhydrazinyl)naphthalene-1,4-dione (**3**), 3-hydroxy-4-alkyl-4*H*-naphtho[2,3-*b*][1,4]thiazine-5,10-dione (**4**) have been synthesized by a green methodology approach using water as solvent and evaluated for their antifungal and antibacterial activity



Reference:

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P-7

Micelles catalyzed chemoselective synthesis of potent antifungal 1,4-naphthoquinones

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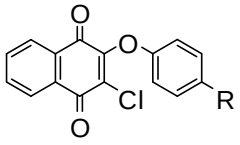
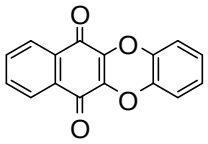
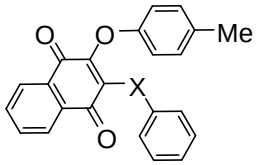
Various oxygen containing 1,4-naphthoquinone derivatives have been synthesized chemoselectively by an economical, viable green methodology approach using water as solvent with surfactants SDS/ LD (laundry detergent) and evaluated for their *in vitro* antifungal and antibacterial activity. The antifungal profile of various synthesized compounds indicated that compounds **1-3** have potent antifungal activity compared to clinically prevalent antifungal drugs Fluconazole and Amphotericin-B against *Sporothrix schenckii*, *Trichophyton mentagraphytes* and *Candida parapsilosis*.



1a:R=H
1b: R=Me



2



3a:X=S
3b:X=NH

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P-8

Carbonylative synthesis of *N*-substituted phthalimides using Palladium on carbon as a phosphine free, heterogeneous and reusable catalyst

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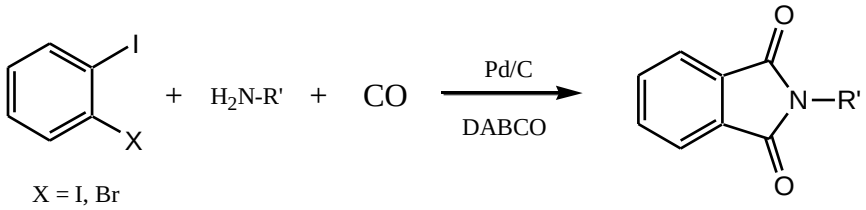
Phthalimides are key structural units of a variety of biologically important compounds, many of which are pharmaceutically significant. Recently they are used in treatment of acquired immunodeficiency syndrome (AIDS), leprosy, and other diseases. Owing to the increasing biological and industrial importance of cyclic imides especially phthalimides and their

derivatives, synthesis of these molecules via new methodology has emerged as a topic of interest for synthetic chemist. In 1991, Perry and co-workers reported phthalimide synthesis from *o*-dihaloarenes using homogeneous Palladium catalyst. Since then various palladium based catalytic systems have been developed, however reported methods suffer from one or more drawbacks.



Scheme 1. Pd/C catalyzed carbonylative synthesis of *N*-substituted phthalimides.

Double carbonylation of *o*-dihaloaryls with amines providing excellent yield of *N*-substituted phthalimides in shorter reaction time was investigated using inexpensive palladium source i.e. Pd/C (Scheme 1). Furthermore, scope of the developed protocol was applied for synthesis of verity of aromatic, aliphatic and heterocyclic *N*-substituted phthalimides via single step carbonylative cyclization reaction. Furthermore the catalyst was efficiently recycles for eight consecutive cycles without loss in catalytic activity.

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P-9

Purification of Mn-peroxidase from *Musa paradisiaca* stem juice

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Mn-peroxidase has been purified from a plant source, *Musa paradisiaca* stem juice, using concentration by ultra filtration and anion exchange column chromatography on diethyl amino ethyl cellulose. The purified enzyme gave a single protein band in sodium dodecyl sulphate polyacrylamide gel electrophoresis corresponding to molecular mass 43 kDa. The native polyacrylamide gel electrophoresis of the purified enzyme gave a single protein band confirming the purity of the enzyme. The *K*m values using $MnSO_4$ and H_2O_2 as the variable substrates for the purified enzyme were 21.0 μM and 9.5 μM respectively. The calculated k_{cat} value for the purified Mn-peroxidase using Mn(II) as the substrate in 50 mM lactate buffer *pH* 4.5 at 25^0C was $6.7s^{-1}$ giving a k_{cat}/ *K*m value of 0.32 $\mu M^{-1}s^{-1}$. The *pH* and temperature optima of the purified enzyme were 4.5 and 25 ^{0}C respectively. The k_{cat} value for the Mn-peroxidase catalyzed reaction has been found to be dependent of the Mn(III) chelator molecules malonate, lactate and oxalate indicating that the enzyme oxidizes chelated Mn(II) to Mn(III). The purified enzyme in combination with H_2O_2 liberates bromine and iodine respectively in presence of KBr and KI indicating that it can be used as a reagent in organic bromination reactions.

P-10

Design and synthesis of nitrogen and sulphur containing fused heterocycles for their potential biological significance

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Nitrogen, oxygen and sulphur containing heterocycles play vital role in medicinal chemistry and have special synthetic interest not only because many of them have been displayed diverse biological activity [1-3] but also because they posses different reaction centers to create the structural diversity and hence makes immense help for the generation of the lead molecules. These properties make them prominent starting material in medicinal chemistry as valuable building blocks for the cyclisation reactions to create heterocycles of various ring sizes. In our continuous effort to design and synthesis of heterocycles of biological importance [4-6] recently, we have synthesized a series of some novel fused pyrimidines. Here detailed biological activity, synthetic procedure, isolation, characterization by the analysis of various spectral data and

mechanism of ring closure reactions leading to the synthesis of fused heterocycles will be discussed.

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P-11

3D QSAR Study of Thienopyridine Derivatives as Anticancer agents

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Chk1 is a cell cycle kinase that is involved in regulation of cell cycle through G_2/M checkpoint.Chk1 is activated by the ATR kinase in response to DNA damages that stall replication fork progression. After activation Chk1, phosphorylates cdc25, thus halting the transition of cells from G2 to M phase. Several Chk1 inhibitors are in clinical trials as anti neoplastic agents (Tse et al,[1] and Zhou et al,[2]). These inhibitors are currently used in combination with DNA damaging agents like cisplatin, fluorouracil, topotecan and cytarabine (Chen et al, [3]). We have developed CoMFA and CoMSIA model of Thienopyridine class of inhibitors (Zhao et al,[4]) using 56 molecules, out of which 46 were kept in training set and 10 in test set. Models showed good Predictive ability having $R2_{pred}$>0.5 in both CoMFA and CoMSIA. 3D- qsar is a computational method in drug designing, which relies on molecular fields of aligned molecules. In summary, we have carried out 3D- qsar ofThienopyridine class of human chk1 inhibitors. This study can be useful in predicting and designing novel inhibitors of Human chk1 as anticancer agents.

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P-12

Translationally controlled tumour protein homolog (TCTP): The artemisinin target protein in *Plasmodium*

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Malaria is one of the most widespread infectious diseases of our time. The global malaria map has been shrinking over the past 50 years, but today ~ 40% of the world's population live in countries where the disease is endemic and ~247 million people suffer from the disease every year [1]. Malaria is caused by protozoan parasites of the genus *Plasmodium* that infect and destroy red blood cells, leading to fever, severe anaemia, cerebral malaria and, if untreated, death. Drug resistant malaria is a major public health problem. The main factors contributing to resurgence of this disease are the development of parasites' resistance to effective and inexpensive drugs. Artemisinin derivatives based therapies are currently the preferred treatment for malaria. The mechanisms of action attributed to artemisinin include interference with parasite proteins [2], disruption of parasite mitochondrial functions[3,4] and modulation of host immune function [5]. Alkylation of plasmodium TCTP is believed to be a major target for Artemisinin derivatives [6]. To gain a better understanding of the mode of action of artemisinin in *Plasmodium*, we have Isolated, cloned and over-expressed TCTP homolog of*P. vinckei* in *Escherichia coli*. The PviTCTP contained 516 bp that encoded 171 amino acids and shared a 99% sequence identity with TCTP from other *Plasmodium* species. The recombinant enzyme monomer had an approximate molecular mass of 20 kDa. The significant sequence homology of PviTCTP with other *Plasmodium* TCTP indicates that they may have similar molecular structures. Studies with TCTP of *P.vinckei* to elucidate mechanism of Aremisinin and physiological role of TCTP in malaria parasite will be discussed.

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P-13

Expression, Purification and Characterization Studies of Rv3001c

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Mycobacterium tuberculosis, the causative agent of tuberculosis (TB), kills more than 2 million people per year and has infected an estimated 2 billion people worldwide. It is the leading cause of mortality due to infectious diseases. Metabolic adaptation to the host niche is a defining feature of the pathogenicity of *Mycobacterium tuberculosis* (Mtb). Many of the unique properties of *tuberculosis* are attributable to its metabolism, which is a significant determinant of the *Mycobacterium tuberculosis* (Mtb) survival in the host. Knowledge of the metabolic pathways used by Mtb during infection is therefore important for understanding its pathogenicity, and can also guide the development of new drug therapies. The branch chain amino acid (BCAA) pathway offers an attractive source of targets as this pathway is not found in humans. The Rv3001c is annotated to code for ilvC, a probable ketol-acid reductoisomerase (EC 1.1.1.86) or acetohydroxy-acid isomeroreductase and is supposed to catalyze second step of isoleucine, and valine biosynthesis. This is an essential gene for Mtb survival as has been revealed by Himar1-based transposon mutagenesis in H37Rv. To characterize the Rv3001c encoded protein, we PCR amplified and cloned it in pET expression system. The initial expression studies suggested that protein was being distributed in both soluble and insoluble fractions. The insoluble fraction was further used to refold the expressed protein. The refolded protein was purified using Ni-IDA resin and analyzed using SDS-PAGE. The details of the study will be discussed.

P-14

Metalic Thiophile Catalyzed Chemoselective one pot synthesis of 3-amino-1,2,4-oxadiazoles : potent inhibitors of NF-KB and AP-1

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1,2,4-Oxadiazoles are important class of small heterocyclic compounds due to their wide range of applications as tyrosine kinase inhibition,[1] muscarinic agonism,[2] histamine H_3 antagonism,[3] anti-inflammation,[4] antitumor,[5] and monoamine oxidase inhibition [6]. Oxadiazoles are found to have anti-cancer activity.

In addition to this, NF-kB proteins are a class of 'rapid-acting' transcription factors that regulate the expression of more than 400 target genes and play a pivotal role in several important physiological processes including immune and inflammatory responses. Inhibition of NF-kB and AP-1 are known to inhibit cancer [7].

In order to obtain structurally diverse molecules with better biological activity, we have designed and synthesized various 3-amino-1,2,4-oxadizaole compounds using a one-pot synthesis approach. An efficient one pot synthesis of 3-amino-1,2,4-oxadiazoles from the simple starting materials like isothiocyanates, amidines/guanidines and hydroxylamine (**Scheme-1**) was carried out. The reaction is facilitated by thiophile assisted desulfurization of in-situ formed amidino/guanidinothioureas to give chemo selectively N-hydroxyguanidine intermediate which on intramolecular cyclization elicit exclusively diverse 3-amino-1,2,4-oxadiazoles in good to excellent yields [8]. The reaction mechanistic pathway may be proceeding through an intramolecular *5-exo-trig* cyclization. These molecules were then subjected for the screening of NF-kB and AP-1 in-vitro biological assay.

All the synthesized compounds were screened for NF-kB and AP-1 transcriptional activation in-vitro in human embryonic kidney cell lines. Some compounds have shown reasonably good inhibition of both these transcription factors. The results suggest that compounds PMCHJ-3D, PMCHJ-26D, PMCHJ-31D and PMCHJ-32D are inhibiting both NF-kB (56, 45, 58 & 60%) and AP-1 (59, 62, 78 & 55%) as dual inhibitors, while compound PMCHJ-12D was inhibiting mainly AP-1 (79%).

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P-15

In vitro antileishmanial activity of synthetic tetrazole tethered β –carbolines

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Visceral leishmaniasis (VL), a chronic infection caused by haemoflagellate obligate intracellular protozoan belonging to the genus *Leishmania* is transmitted by the bite of phlebotomine sand fly. VL causes bouts of fever, substantial weight loss, swelling of the spleen and liver, and anemia and

is fatal, if not treated. Although the disease is endemic in more than 60 countries, around 59,000 deaths, with 200 million people at risk, 90% of the 500,000 cases per year happen in five countries: India, Bangladesh, Nepal, Sudan and Brazil. The chemotherapy of VL has several limitations including resistance and toxicity of the existing drugs. The emergence of *Leishmania* /HIV co-infection as a new disease entity makes current chemotherapy inadequate and has triggered a continuous search for novel chemotherapeutic agents.

In continuation of our drug discovery program on antileishmanial agents, we developed a versatile, efficient route for synthesis of new β –carbolines with tethered tetrazole, for the first time using Ugi 4CC reactions. The antileishmanial activities of 24 synthesized tetrazole tethered β-carbolines were evaluated *in vitro* against intramacrophagic amastigotes of *Leishmania donovani*. Amongst them, six compounds displayed promising antiamastigote activity with IC_{50} ranging from 2.48 to 11.96 µM. These compounds displayed better *in vitro* activity compared to the existing antileishmanials, sodium stibogluconate and miltefosine in respect to $IC_{50.}$ Based on Selectivity Index (SI), all the six compounds were selected for *in vivo* trial in *L. donovani*/ Hamster model.

P-16

Isolation of novel hexasaccharide from donkey's milk

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In recent times carbohydrates and carbohydrate containing molecules have developed themselves as a new source for medicines under the umbrella of glycobiology.Various glycosides,glycoconjugates and oligosaccharides have come in light in form of medicines and vaccines.Various natural sources have been taped for isolation of these glycocompounds.During the course of studies milk of various sources have been investigated for their oligosaccharide content. During the studies and with back up of Ayurveda,Donkey's milk was chosen for its

oligosaccharide content. As it showed immunostimulant activities,it was worth to isolate and characterise its oligosaccharides. On investigation and processing of Donkey's milk by Kobata and Ginsburg method followed by its chromatography by Gel filteration and HPLC a novel hexasaccharide Famiose -$C_{42}H_{71}N_3O_{31}$ $[\alpha]_D$+330 was isolated. It gave positive phenol sulphuric acid test, Fiegl test, Morgon- Elson test, showing the presence of normal and amino sugar in it .HSQC spectrum of acetylated Famiose showed 7 cross peaks in the anomeric region of carbon and proton at 6.259x89.19, 5.509x90.04, 4.731x95.18, 4.582x100.93 4.517x101.01, 4.508x100.93 and 4.49x104.17 confirming it to be a hexasaccharide in its reducing form. It also showed 6 cross peaks at 3.85x81.81, 3.82x77.19, 4.08x76.18, 3.87x77.19,4.11x76.67, 3.82x76.18 for glycosidialy linked proton and carbon. Further on the basis of chemical degradation, chemical transformation, mass spectrometry data and NMR(1H,13C,COSY,TOCSY,HSQC) the structure of Famiose was confirmed as under

GlcNAc (1-6) β GalNAc (1-4) β Glc (1-3) β Gal (1-4) Glc (1 - 6) GlcNAc

P-17

Isolation of Novel Pregnane Oligoglycoside of 2,6di-deoxy sugar from *Dregea lanceolata*

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Since the Science emmemorial the natural products were the basis of medicinal chemistry which is providing lead for newer medicines .In search for new compounds from natural sources it was found that a compound containing carbohydrate in them shows varied biological activities. The sugar moieties present in them not only increases the water solubility but also decreases the toxicity . The carbohydrate containing compound are present either as free sugar or as glycosides. In search for new glycosides *Dregea lanceolata* was taken for its chemical constituents. A novel pregnane glycosides was isolated from 4:1 $CHCl_3$-EtOH Extract .This

novel compound was named as **Ceoside, m.p.148o-151o C,[α]D +16.27, $C_{52}H_{82}O_{21}$.** It gave positive xanthydrol and Keller Killiani reaction for 2,6 dideoxy sugars and also gave positive test in the Partridge reagent for normal sugars. It also responded positively to Liebermann Burchardt test for steroids and tetranitro methane test for double bond indicating it to be steroidal glycoside. The HSQC spectrum shows four cross peaks in carbon and hydrogen in the anomeric region at 114.15x 4.48, 99.61x 4.75, 99.61x 4.79 and 95.85x 4.81 confirming it to be a tetraglycoside. It also contain proton and carbon signal for steroidal moieties. Further on mild acid hydrolysis the Ceoside gave 11, 12-di-O-acetyl Drevogenin P, cymarose and galactose. Showing the presence of these moieties in them. The structure of 11, 12-di-O-acetyl Drevogenin P was confirmed by 1-H, 13-C, COSY and HSQC NMR experiments. The position and sequence of sugar and genin were confirmed by chemical degradation mass spectrometry and NMR (1-H, 13-C, COSY, HSQC). Based on the pattern of chemical shift of 1-H, 13-C, HOMOCOSY, TOCSY and HSQC NMR experiments in the light of forgoing evidence, the structure of novel substance Ceocide was established as 11, 12-di-O-acetyl Drevogenin P-3-O-β-D-cymaropyranosyl-(1→4)-O-β-D cymaropyranosyl-(1→4)-O- β-D- cymaropyranosyl--(1→4)-α-D-galactopyranoside.

P-18

POTENTIATING METRONIDAZOLE SCAFFOLD AGAINST RESISTANT TRICHOMONAS

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Metronidazole (MTZ), the FDA approved drug [1] against *Trichomonas vaginalis*, is being challenged seriously by drug resistance; while its inertness to sperm makes it ineffective as a vaginal contraceptive. Thirteen piperidine dithiocarbamate hybrids of 2-(2-methyl-5-nitro-1H-

imidazol-1-yl) ethane were designed (Fig. 1) to potentiate the MTZ framework against drug-resistance and sperm. New compounds were 1.2 – 12.1 times more effective against MTZ-susceptible and MTZ-resistant strains of *Trichomonas vaginalis*. Six compounds irreversibly immobilized the human sperm at 1% concentration. All the compounds exhibited high safety towards cervical (HeLa) cells and *Lactobacillus*. Thirty eight compounds were synthesized [2] and scrutinized by CoMFA and CoMSIA techniques of 3D–QSAR. Good predictive r_{pred}^2 values for CoMFA and CoMSIA models reflected the robustness of the predictive ability. This was validated by designing of five new analogues, which were potently microbicidal (3-10 and 10-20 times against MTZ-susceptible and MTZ-resistant TV, respectively) and spermicidal.

Fig. 1

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P-19

Pharmacokinetics of anti-tuberculosis azolyl phenyl cyclopropyl methane, S010-399, in rats

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Tuberculosis (TB) is more prevalent in the world today than at any other time in human history. In 2009, there were an estimated 9.4 million incident cases of TB globally (equivalent to 137 cases per 100000 populations). Most of the estimated number of cases in 2009 occurred in Asia

(55%) and Africa (30%). India alone accounts for an estimated one fifth (21%) of all TB cases worldwide [1,2]. The compound S010-399 has potent anti-tuberculosis agent. 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 were collected. An HPLC assay method was developed and validated and then applied for quantitative analyses of S010-399 in serum samples. Pharmacokinetic parameters were calculated from noncompartmental models using WinNonlin program.

The lower limit of quantification for the analytical method was 10 ng/ml of S010-399 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 2 h and could be monitored up to 24 h. The clearance (0.003 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-20

In-vitro production and estimation of cardiac glycosides using Ultra-High Performance Liquid Chromatography Electrospray Ionization Tandem Mass Spectrometry

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Cardiac glycosides (CG) are secondary metabolites produced by plants and animals, which are generally used as anti-arrhythmic agents and to treat congestive heart failure. However, during last few years CGs are reported to have antiproliferative activity on tumor cell lines and are targeting for cancer chemotherapy. *Calotropis gigantea* (L.) Ait.under the family Asclepiadaceae,one of the important medicinal plants normally found in waste land in Lower Bengal, Himalayas, Punjab, Assam, South India, Ceylon, Singapore, Malay Island and South China, is a rich source of many CGs. The present work deals with the standardization of callus induction and growth from the various explants of *C. gigantea* for CGs production and estimation through Ultra-High Performance Liquid Chromatography Electrospray Ionization Tandem Mass Spectrometry. Among the various hormonal combinations tried, the best one was the NAA (3µm) and FAP (4.6µm) in MS basal media (Murashige and Skoog, 1962) for callus induction and then transferred to MMS media (Modified Murashige and Skoog) supplemented with NAA (2.69µm) and BAP (4.44µm) for callus growth and CGs production. The MMS media supplemented with NAA (2.69µm) and FAP (2.32µm) also proved effective for CGs production. This is a preliminary study of such kind, which may turn into valuable therapeutic option for discovery of new antiproliferative agents without disturbing the wild populations of the original plant.

Key Words: Cardiac glycoside, *Calotropis gigantea*, callus culture

P-21

Validated RP-HPLC method for determination of Marmin, Bioactive Coumarin derivative from Aegle marmelos.

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An isocratic, reversed phase, high-performance liquid chromatographic (HPLC) method was developed for the determination of the marker Marmin in alcholic extracts of different parts of Aegle marmelos from two different locations. Marmin is bioactive coumarin from Aegle marmelos and its separation was achieved on a LiChospher® RP-18, 5µm, 250mm X 4mm i.d.

column with a mobile phase consisted of a mixture of acetonitrile and Water (60:40 v/v), at a flow rate of 0.5 ml/min. The retention time of Marmin was about 7.4 mins, and the effluents were monitored at 320 nm. The calibration curves were linear over the concentration ranges of 0.78-100µg/ml for Marmin. The limit of detection was 0.39 µg/ml. The accuracy and precision in all cases were less than 5% in the calibration range. The assay was successfully applied to determine Marmin in various extract from different parts of the plant, Aegle marmelos.

P-22

Design and synthesis of the hybrid quinazolinone-chalcone/pyrimidine/tetrazole as antileishmanial agents

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Chemotherapy against leishmaniasis is unsatisfactory because it is mainly based on antimony agents like sodium stibogluconate and meglumine antimoniate, amphotericin B, miltefosine, and paromomycin and the modeofaction of thesecompounds are poorly understood [1]. Leishmaniasis is a disease caused by infection with human protozoan parasites belonging to the *Leishmania* [2]. Recently, the emergence of drug resistantance has led to treatment failures for many infectious diseases, including malaria and leishmania. There is therefore a pressing need for the development of new drugs to treat leishmaniasis. Natural products are being explored to generate new leads in the chemotherapy of leishmaniasis. Compounds of both synthetic and natural origin comprising a diverse group of chemical structures, include mostly the nitrogen heterocycles such as quinolines [3], pyrimidines [4] and other classes of compounds include chalcones [5], quinines [6] amino acid esters and amides have been reported as antileishmanial agents. Biochemical targets are also under investigation in which Dihydrofolate reductase (DHFR) [7] is being used to design the novel compounds. A number of compounds having pteridine, quinazoline and pyrimidine moieties are reported to be potent inhibitors of DHFR in Leishmania. Based on these observations we report the quinazolinone based novel compounds having antileishmanial activity.

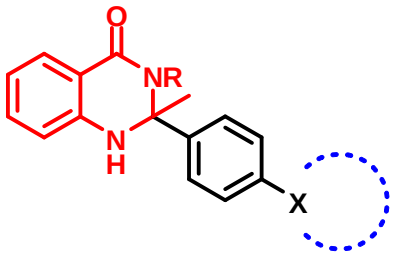

Fig. Hybrid of Quinazolinone-chalcone/pyrimidine/tetrazole

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P-23

Synthesis of β-carboline derivatives based on natural product and their biological evaluation

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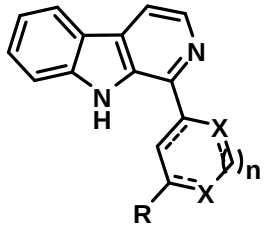
Natural and synthetic β-carbolines and tetrahydro-β-carbolines alkaloids are well-known compounds that possess a variety of biological properties. In 1998, a tetrahydro-β-carboline alkaloid buchtienin was isolated from *Kopsia griffithii* and found to have good antileishmanial activity ($0.30 < IC_{50} < 1.56$ ng/ml) against *L. donovan* [1]*i.* Later, annomontine, a pyrimidine-β-carboline alkaloid, isolated from the bark of a Brazilian tree *Annona foetida* [2], was also reported to be active against leishmania. A number of naturally occurring β-carbolines alkaloids have shown good activity against various cancer cell lines [3]. Recently, a new 1-imidazoyl-3-

carboxy-6-hydroxy- β-carboline alkaloid, named hyrtiocarboline, isolated from a Papua New Guinea marine sponge, *Hyrtios reticulates* has shown selective antiproliferative activity against H522-T1 non-small cell lung, MDA-MB-435 melanoma, and U937 lymphoma cancer cell lines [4].

As part of our continuing efforts toward the design and synthesis of novel nitrogen heterocylces anti-infective and anticancer agents, our group has identified some synthetic analogues of β-carboline potent against leishmania and cancer [5]. Herein, we propose to synthesize natural product based β-carboline derivatives to develop more efficacious biologically active molecules.



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P-24

Synthesis and antimalarial activity of new heterocyclic hybrids based on chloroquine and rhodanine scaffolds

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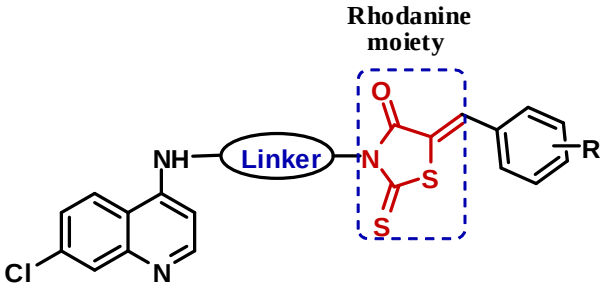
Malaria, a parasitic disease, affects roughly 250 million people and causes over 8, 00,000 deaths annually[1]. There are four major species of the malaria parasite *plasmodium; P. falciparum, P. vivax, P. malariae* and *P. ovale* that are responsible for the spread of the disease in humans [2]. Among these species, *P. falciparum* remains the most problematic [3]. Quinoline containing compounds are still attractive models for treatment of malaria. The success of the antimalarial aminoquinoline drug and chloroquine (CQ) has been based on its excellent clinical efficacy, limited host toxicity, ease to use and simple cost-effective synthesis [4]. The spreading resistance of Plasmodium falciparum to existing antimalarials including chloroquine, antifolates, and artemisinin has resulted in a pressing need to discover new chemotherapeutic agents against this disease [5].

In effort to synthesize a library of new series of effective compounds against both chloroquine-sensitive and chloroquine-resistant strain of malaria, we envisioned rhodanine moiety attached to 4-aminoquinoline pharmacophore through linker. It is well established that basic nature of the linker joining the 4-aminoquinoline is crucial for accumulation of the drug within acidic food vacuole of the parasite along the pH gradient. As a part of our continuing efforts in malaria chemotherapy and to address the urgent need of new antimalarial agents here we further optimized derivatives of **Chloroquine-Rhodanine** hybrid as antimalarial agents.



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P-25

A green synthesis of 2,3-dihydroquinazolin-4(1H)-ones derivatives

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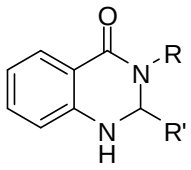
2,3-dihydroquinazolinones class of compounds has been reported as antibiotic, antidefibrillatory, antispermatogenic, vasodilatory, and analgesic [1]. In addition, these compounds can be further oxidized to their quinazolin-4(3H)-one analogues, an important class of biologically active heterocyclic compounds [2] that is also found in some natural products [3]. The unique biological significance of the 2,3-dihydroquinazolin-4(1H)-one skeleton stimulated several research groups to develop new synthetic procedures. However, various improved protocols for the synthesis of 2,3-dihydroquinazolin-4(3H)-ones have been reported in the literature [4], but many of these methods are not environmentally friendly. As development of a clean and environmentally benign synthetic procedure has become crucial demand in modern research, there is still a need to develop a simple and convenient approach for the synthesis of 2,3-dihydroquinazolinones. In the context of our interest in the synthesis of biologically important heterocycle, 2,3-dihydroquinazolinone in an environmental friendly manner, we have developed such green methodology that ensures us to minimize the use and generation of hazardous substances and to be proved environmentally friendly.



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P-26

First synthesis towards natural product Perspicamide analogues and their bioevaluation as antileishmanial agents

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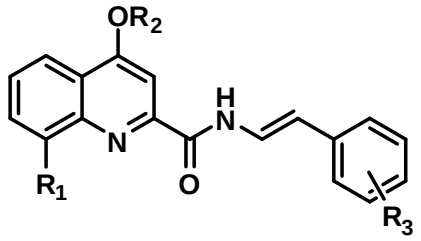
Leishmaniasis, serious tropical disease is caused by parasitic protozoa of the genus Leishmania among them visceral leishmaniasis(VL) is most severe form ,called Kala-azar or black fever, can have a fatality rate as high as 100% within two years if left untreated . From WHO reports in 2010 ,Leishmania threatens 350 million people in 88 countries found throughout the intertropical and temperate regions and current remedies is depends on heavy matals based drugs and other are toxic enough for long time treatment.[1] Quinoline based natural products have established landmark for their application in medicinal chemistry ,showing broad range of biological activities. In search of this, the metabolite perspicamide A & B having quinoline core nucleus along with secondary enamide sidechain, were first isolated from the Australian ascidian Botrylloides persipicuum Herdman 1886 (Styelidae) in 2005 by Matthew J. McKay etal.[2] Enamides are important structural motif present in a large number of functionalized molecules with a wide variety of uses, including applications in medicinal chemistry, materials science, and several reaction intermediates. Enamide natural products salicylihalamide A and B, lobatmide A-F, apicularen A, Oximidines I and II , TMC-95A-D are already proven for their cytoxic activity .[3] Among the emerging methods, for the synthesis of C-N bond formation, metal catalysed reactions found their application in the synthesis of biologically active natural products. Particularly Copper catalysts have significant role, because it is very cheap, non-toxic & mostly efficient in catalytic amount. Copper-catalyzed coupling reaction of amides with vinyl halides

has received increasing attention because they are highly Diastereoselective have functional tolerance and equally effective in prior as well as at a late stage in the synthesis.[4] Since long time our interest to synthesized quinoline based molecules as anti-infective activity, We report the first synthesis towards Perspicamide analogues, which were tested for their bioactivity and few synthesised compounds showed moderate to good Antileishmanial activity[5].



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P-27

A convenient desulfitative dimethylamination of the 2-Thiohydantoin scaffold using N,N-dimethylformamide

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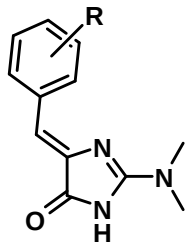
There is no dearth of compounds containing a dimethylamino functionality in nature as well as in the organic chemist's arsenal.[1] For example, taxoids, a series of anti-cancer drugs, which inhibit cell growth by interacting with microtubules, often contain a dimethylamino moiety as part of the pharmacophore.[2] The dimethylamino moiety is also found in a number of active

tetracyclines. [3] Similarly, a compound like austrospicatine, bearing a dimethylamino function, has shown promising insecticidal activity. [4] Moreover, many of the dimethylamino substituted heterocyclic compounds represent important drugs like, e.g., ampyzine, triampyzine, and methadone. [5] Here we will comment on an unprecedented and convenient dimethylamination of 2-Thiohydantoins applying a mixture of DMF/H_2O (1:1) in the presence of potassium carbonate in excellent yields.



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P-28

Synthesis of novel tetrazole derivative of 4-aminoquinoline as potent antimalarials

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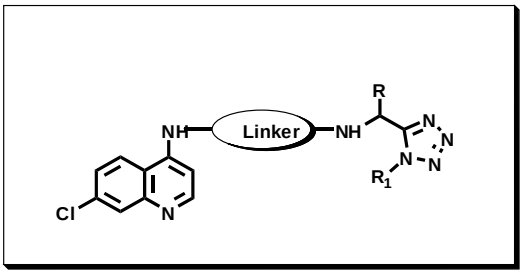
Combinatorial chemistry has in the recent past emerged as a powerful tool for the rapid identification, generation and optimization of lead compounds in the drug discovery

process[1,2]·Multi-component reactions (MCRs),have in this regard been used to efficiently generate chemical diversity. Several MCRs are known to date among which the Ugi 4-component variants remains, by far, the most documented and most versatile.

In the context of our on-going research[3], we wished to synthesize novel compounds for screening against malaria parasites .So we have designed and synthesized novel diverse tetrazole compounds via Ugi reactions built around the 7-chloro-4-aminoquinoline unit, a known antimalarial pharmacophore and evaluated for its antimalarial activity.



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P-29

Generation of tetrahydro-β-carbolinediketopiperazines ring system via Ugi-4-CR followed by tandem deprotection-cyclization/Pictet-Spengler reactions in one pot

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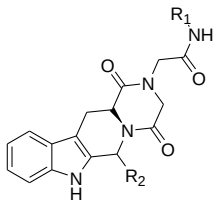
The tetrahydro-β-carbolinediketopiperazines ring system is a common motif frequently encountered within a large family of indole alkaloids [1]. This alkaloids family have attracted much attention due to their wide-ranging biological activities; complex molecular structure and limited availability in nature [2]. We have documented an expedient approach towards the

synthesis of tetrahydro-β-carbolinediketopiperazines ring system present in various natural products. This synthetic strategy involved an Ugi reaction followed by tandem deprotection-cyclization/ Pictet-Spengler reaction, with all the processes in same reaction flask. We believe that this novel strategy not only provides the approach for the generation of new and pharmacologically active tetrahydro-β-carbolinediketopiperazines derivative, but it can be also used to efficiently assemble indole alkaloids type natural product [3, 4].



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P-30

Profiling and Fingerprinting Studies of *Gloriosa superba* using DART MS Technique

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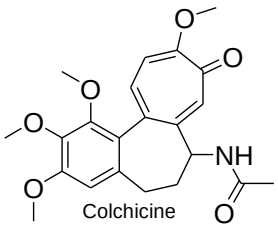
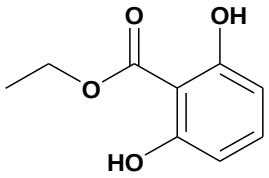
Gloriosa superba L. family Liliaceae is a semi-woody herbaceous climber found throughout India upto an altitude of 6000 ft. locally it is known as Kalihari having number of medicinal properties like antitumor, abortifacient, antiinflammatory, antimitotic, and antifibrotic. Plant species is well known for its high content of colchicine and used for the treatment of cancer. One of the other alkaloids (Gloriosine) isolated from the tuber of this plant are used for the treatment of gout and rheumatism. Due to its imprudent harvesting, the plant species is kept under endangered category (IUCN Red Data Book) and became verge of extinction. It is one of the most important seven upavishas (semi-poisonous drug) used in Indian System of Medicine

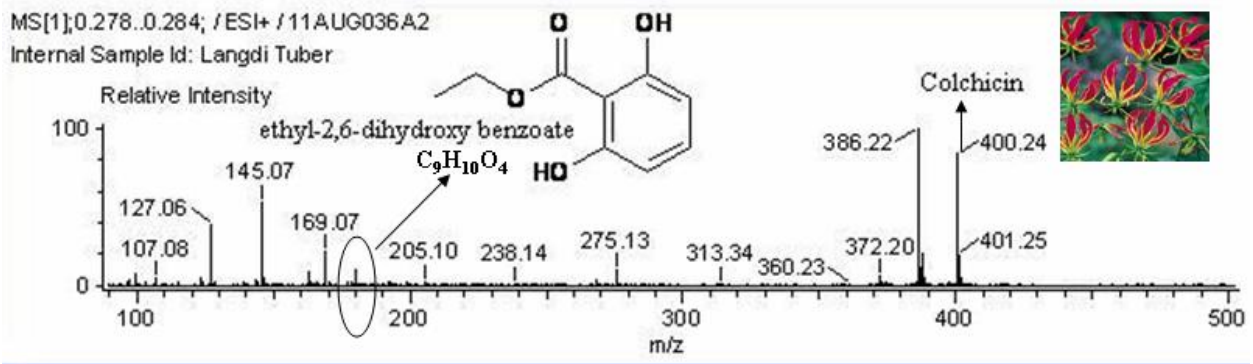
(ISM), which cure many ailments. Some time higher doges' revealed fatality in many cases. The main active compound colchicine was also reported in tubers of some other species of this genus. During chemical investigations one of its important compound monoethyl ester of 2, 6-dihydroxybenzoic acids was isolated from the extract of *G. superba* and pharmacologically found active against snake venom. In the present work DART MS technique is used for Phytochemical investigation and profiling of *Gloriosa superba* plant part.



Colchicine
$C_{22}H_{25}NO_6$
Exact Mass: 399.16819



ethyl - 2, 6-dihydroxy benzoate
$C_9H_{10}O_4$
Exact Mass: 182.05791



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P-31

Phytochemical investigation of *Ajuga bracteosa using* DART MS and Q-TOF LCMS (HRMS) techniques

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*Ajuga bracteosa wall benth. (*Neelkanthi) is an Indian medicinal plant used in many Ayurvedic preparations and distributed in subtropical and temperate regions from Kashmir to Bhutan. The present study deals with the profiling and fingerprinting studies of different plant parts of *Ajuga bracteosa* using advance mass spectrometric techniques like DART HR MS and HPLC-ESI Q-TOF HRMS. DART MS of *A. bracteosa* leaf and root were recorded directly from leaf and root without any sample preparation. HPLC –Q TOF based profiling of *A. bracteosa* shows clear differentiation of leaf and root. This is first report of profiling of *A. Bracteosa* plant part using latest HPLC-ESI Q-TOF combination. Compounds reported and calculated from A. bracteosa leaf and root is Bracteosin C, Bracteosin A, Lupulin A, Dihydroclerodin, Ajugarin -1, Hexadecanoic acid. Exact mass of major compounds calculated using HR Q-TOF analysis. "Lupulin A" exhibit COX-1 and COX-2 inhibitory effect and is calculated in *A. bracteosa* leaf so it gives the projection of anti-inflammatory effect in *A. bracteosa* leaf. Chemical profiling is also important for quality control and efficacy of herbals.

P-32

Rapid Identification of bio-flavonoids using electrospray ionization tandem mass spectrometry with MS/MS library

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Flavonoids are polyphenolic compounds that are ubiquitous in nature and are categorized, according to chemical structure, into flavonols, flavones, flavanones, isoflavones, catechins, anthocyanidins and chalcones. Due to the increasing understanding of the health benefits and chemopreventive properties of flavonoids, there continues to be significant effort dedicated to improved analytical methods for characterizing the structures of flavonoids. We are reporting the identification of bio-flavonoids by utilizing searchable web-based MS/MS spectra library (www.tmsdatabase.org) constructed using the electrospray ionization (ESI) tandem mass spectrometry (MS/MS).

P-33

Mass fingerprinting analysis of Berberis aristata, Berberis asiatica, Coscinium fenestratum and Mahonia borealis using LC-QTOF HRMS Techniques

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Berberis aristata is the most important medicinal plants used extensively for treating several ailments in almost all of the indigenous systems of medicine in India. Berberis asiatica, Mahonia borealis and Coscinium fenestratum having similar constituents to Berberis aristata and hence are often used to adulterate Berberis aristata and their herbal products. QTOF MS have been used for profiling the constituents of Berberis aristata, Berberis asiatica, Mahonia borealis and Coscinium fenestratum found in India. Different parts like root, stem and leaf are included in the study. QTOF mass spectrometric technique has been applied for the first time for the profiling of Berberis aristata, Berberis asiatica, Coscinium fenestratum and Mahonia borealis. Chemical profiling of leaf, stem and root has been done successfully. Mostly the Berberine is found in root and stem of Berberis species. It is also observed that there is significant difference in mass spectra obtained from the leaf, stem and root of Berberis aristata, Berberis asiatica, Coscinium fenestratum and Mahonia borealis. This will help in identification and characterization of genuine part used for drug preparation and for the effective quality control and efficacy of drug candidate in future.

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P-34

Galactolipids from *Bauhinia racemosa* as a new class of antifilarial agents against human lymphatic filaria parasite, *Brugia malayi*

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Lymphatic filariasis, is a mosquito-borne disease that is endemic in 81 countries worldwide with 1.2 billion people at risk and an estimated 120 million infected [1]. The currently used drugs are mainly microfilaricidal, thus more effective treatment regime is needed which could be effective on both forms (adult and mf) of parasite [2]. *Bauhinia racemosa* Lam. (family- Caesalpiniaceae) is known to show various biological activities [3] and is traditionally used for diarrhoea, dysentery, malaria and headache [4]. In the present study, the crude ethanolic extract of the leaves of *B. racemosa* showed 80% reduction in the motility of lymphatic adult filarial parasite *B. malayi in vitro.* It was further fractionated into hexane, chloroform and butanol fractions which were subjected to *in vitro* assays and only butanol fraction showed promising activity. Bioassay guided purification of active butanol fraction led to the isolation of galactolipid and catechin class of the compounds (**1**-**7**). Of all the tested compounds, only galactolipids **1**-**3** showed activity and **1** emerged as the lead molecule that killed both adult and mf forms of *B. malayi* with IC_{50} values of 1.25 and 1.607 µg/ml respectively. Active compounds were evaluated *in vivo* in primary screening model (adult *B. malayi* i.p. transplanted jird) at the dose of 50 mg/kg i.p. for 5 consecutive days. **1** was found to be the most potent compound with 58.3± 8.33%, adulticidal activity over control, which was found to be better than the standard drug diethyl carbamazine (DEC) in terms of dose and efficacy.

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P-35

Production of extracellular L-glutaminase from *Pseudomonas* sp.

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Enzyme L-Glutaminase has received enough commercially significant attention recently owing to its potential applications in medicine as an anticancer agent and in food industries as flavor enhancer. L-Glutaminase (L-Glutamine amidohydrolase EC 3.5.1.2) is the enzyme which deaminates the L-Glutamine to L-Glutamic acid and ammonia. We have studied the production of L- Glutaminase using a bacterial strain of *Pseudomonas* sp. isolated from soil sample and developed in our laboratory. Although L- Glutaminase can be derived from plant as well as animal sources also, microbial enzymes are the more important source for meeting the industrial demands. The microbe was cultivated in complex medium at 28^0 C for 20-96 hours and the fermented broth was found to have glutaminase activity. It was observed that *Pseudomonas* sp. produce extracellular glutaminase under submerged fermentation conditions.

Crude extracellular protein content of broth was estimated to be 2.4mg/ml with specific enzyme activity 14.2 IU/mg. The enzyme was purified by 60% ammonium sulphate precipitation followed by Gel filtration column chromatography. A total of 17 fold purification was obtained with a specific activity 240IU/mg. Production medium was optimized by substrate concentration, inoculums size, salt (NaCl) concentration and other sources like carbon nitrogen and amino acids. Culture show maximum enzyme production activity at some specific concentrations of above factors. Maximum enzyme activity was estimated with 2% (v/v) inoculums size, 0.7% (w/v) substrate concentration, carbon source Trisodiumcitrate (1%w/v),nitrogen source casein (1%w/v) 1.5% (w/v) of NaCl concentration, at pH 7.0 and Temperature 30°C.

P-36

Antimicrobial peptide: A prospect of alternate antibiotics

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Increasing pathogen resistance against conventional antibiotics triggered interest to explore the antimicrobial substances which have great propensity to wipe out pathogenic microbes, and confer no chance to develop resistance property. Unlike conventional antibiotics antimicrobial peptides are generally synthesized employing natural amino acids over induction of pathogens. Usually antimicrobial peptides are 10-100 amino acids long, possess net positive charge ranging from +2 to +9 and are amphipathic in nature. During last two decades more than 1500 antimicrobial peptides has been discovered in bacteria, insects, fish, amphibians, birds, plants and even in humans. Several methods have been used to determine the mechanisms of antimicrobial peptide activities like Microscopy, Fluorescent dyes, Ion channel formation, Circular dichroism, Dual Polarization Interferometry, Solid-state NMR spectroscopy, Neutron diffraction etc. The modes of action of antimicrobial peptides explained till date include inhibition of cell wall formation, pore formation in the cell membrane resulting in the disruption of membrane potential with eventual lysis of the cell and, finally, inhibition of nuclease activity involving RNase and/or DNase activity. Antimicrobial peptides exhibit broad spectrum of activity which include bacteria, viruses, fungi, protozoan and even cancer/tumor cells. This extensive range of activity is the major attraction towards these types of molecules to be developed as novel potent anti-microbial agents. However toxicity and stability is the major obstacle to adapt these antimicrobial peptides as a drug. Therefore the most emerging issue in this field is to design antimicrobial peptides with reduced toxicity maintaining similar antibacterial activity. For that reason identifying the structural parameters or sequence elements which are responsible for the toxic activity of antimicrobial peptide can provide a useful tool to design novel molecules with high therapeutic index.

P-37

Non specific binding interaction of vinblastin on base specific DNA sequences

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A number of small molecules bind directly and selectively to DNA, acting as chemotherapeutic agents by inhibiting replication, transcription or topoisomerase activity. Two common binding modes for these small molecules are intercalation or groove-binding. Sequence and structure-specific molecular recognition of DNA by Indole alkaloid is an important goal in biophysical chemistry and drug discovery. The binding of Vinblastin containing indole group to nucleic acids is of great interest for the control of gene expression and other nucleic acid mediated processes. In the present study, we have studied the influence of Vinblastin with four DNA decamer sequences having base-specific central core by fluorescence spectroscopy. These spectroscopic profiles of Vinblastin bound to different DNAs showed non specific interaction with the purine-pyrimidine bases. This binding influence of the drug molecule reside in the H-bond donor/acceptor atoms in the DNA binding site of the molecules. In addition, docking study reveals the presence of van der Waal's forces facilitates the interaction between the Vinblastin and the DNA. In this study, we have evaluated the DNA binding constants obtained for Vinblastin and its analogue are in the range of 10^4-10^5 per mole.

P-38

Antimalarial potential of aryl cyclopropyl methanones

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Malaria is a major public health problem in the developing world. The existing armamentarium of drugs for the treatment of malaria is limited either due to the drug resistance or unacceptable toxicity. Identification of new targets, discovery of compounds that act through specific pathways and concept of combination therapy are the current strategies to fight against malaria. Fatty acid biosynthesis is an essential process for the survival of the malaria parasite and interestingly the parasite has type II fatty acid synthase complex (FASII) while human's

posses type I. It is therefore suggested that inhibitors designed against FASII will be potent and safe antimalarials.

Considering the above facts, a series of alkylamino aryl cyclopropyl methanones as possible FASII inhibitors were synthesized and evaluated *in-vitro* against *Plasmodium falciparum* 3D7 strain for their antimalarial activity and also against mammalian cell line (Vero cells) to determine their safety. Out of 29 new alkylamino aryl cyclopropyl methanones, 10 compounds showed potent antimalarial activity as well as high degree of selectivity indices. Their IC_{50} values were in range of 0.035-0.76µg/ml having selectivity range of 6948-9.25. The present study reveals that alkylamino aryl cyclopropyl methanones may prove as potent and safe antimalarials if their activity confirms in animal model.

P-39

Neurotoxicity of Tributyltin

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Due to their biocidal property, tributyl-tins are widely incorporated in antifouling paints, heat stabilizers, biocides,etc . The use of Tributyltin (TBT), although banned from paints in the European Union from 2003, remains in high levels in foods, particularly fish and shellfish. Several studies demonstrate immunotoxicty, hepatotoxicity and genotoxicity by TBT, but very few reports are available illustrating the effects of TBT on nervous system. Depending on Evans blue staining at 24hrs invivo of different brain region administered with 50mg/kg TBTC by iv route, for studying blood brain disruption by TBTC, we selected caudate nucleus (120%),cerebellum (208%),hippocampus(137.9%) and hypothalamus(197.2%) for early biochemical perturbations (glutathione and calcium), cell death and GFAP expression levels in primary cell culture.

Various doses of TBT(30, 300 and 3000nM) were tested and 300nM conc. of TBT reduced the cell viability (by MTT) in caudate neurons by 30% at 18hrs. against 10% in. Sharp decline in glutathione at 3hrs and a substantial fall in mitochondrial membrane potential supported mitochondrial contribution in cell death. In cerebellum glutathione levels tend to rise initially at 3 and 6hrs and decline only at 18hrs. This data suggests that GSH depletion appears critical for the fate of neurons to undergo apoptosis. The pattern of intracellular Ca^{2+} in caudate primary

culture over a period of 60min. exposure shows a constant rise, whereas in cerebellum primary culture the levels fell at 60 min..

The above preliminary data suggest that caudate region appear more sensitive than other brain regions.

P-40

Sulforaphane-mediated protection against toxicity of CuO nanoparticles in mouse embryonic fibroblasts (BALB 3T3) cells

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Despite the great interest in nanoparticles safety, no comprehensive test paradigm has been developed. Oxidative stress has been implicated as an explanation behind the toxicity of nanoparticles. It is reported that sulforaphane (SFN) present in cruciferous vegetables like cauliflower and broccoli has potential to protect cells from oxidative damage and inflammation. However, protective role of SFN in nanotoxicity is not explored. We investigated the protective effect of SFN against the toxic response of CuO nanoparticles (NPs) in mouse embryonic fibroblasts (BALB 3T3). Results showed that CuO NPs induced dose-dependent (5-15 µg/ml) cytotoxicity in BALB 3T3 cells demonstrated by MTT and LDH assays. CuO NPs were also found to induce oxidative stress in dose-dependent manner indicated by induction of reactive oxygen species (ROS) and lipid peroxidation (LPO) and depletion of glutathione and glutathione reductase. Co-treatment of BALB 3T3 cells with SFN (6 µM) significantly attenuated the cytotoxicity, ROS generation and oxidative stress caused by CuO NPs. We found a significant increase in the activity of GR enzyme and GSH in SFN treated BALB 3T3 cells. Enhancement of antioxidants-GR and GSH- in BALB 3T3 cells could be one of the mechanisms offering protection by SFN against CuO NPs toxicity. We believe this is the first report showing that SFN significantly protected the BALB 3T3 cells from CuO NPs toxicity, which is mediated through generation of oxidants and depletion of antioxidants. Consequently, protective mechanism of SFN against CuO NPs toxicity should be further investigated.

Key words*:* CuO Nanoparticles; Cytotoxicity; ROS; Oxidative stress; Sulforaphane; Protection

P-41

Assessment of hOGG1 Ser326Cys polymorphism and DNA Damage in head and neck squamous cell carcinoma in North India

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Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer in world [1]. In India, it accounts for 21 % of total cancer burden and here we tested the role of hOGG1 ser326cys polymorphism and oxidative DNA damage in HNSCC patients in North India hOGG1 8-oxoguanine DNA glycosylase, one of the key members of base excision DNA repair pathway , eliminates the mutagenic base oxidation product 8-oxoguanine, which is produced as a result of exposure to reactive oxygen species[2, 3]. The tobacco products have clastogenic and carcinogenic effects and are capable of generating free radicals during auto oxidation of polyphenols in saliva of tobacco users[4]. Genomic DNA from human salivary cells and whole blood of 40 controls and equal number of HNSCC cases was isolated and the polymorphism of hOGG1 was studied by PCR-RFLP method . Blood and salivary DNA adduct (8-OHdG) was measured by ELISA base colorimetric assay. The results indicated no difference in hOGG1 polymorphism in both blood and saliva samples. However, more apurinic sites was evident in salivary DNA adduct(8-OHdG) than in blood. Direct interaction of salivary cells to tobacco product exposures could be one of the reasons . The study suggests that salivary DNA adduct is a better indicator of DNA damage in HNSCC patients. The result also suggests that DNA adduct (8-OHdG) is more predominant in oral reason that neck region.

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P-42

In process quality control and stability studies on centchroman, a non-steroidal contraceptive agent

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Centchroman, (INN: Ormeloxifene hydrochloride, I.P.) is once a week non-steroidal oral contraceptive. In this paper, we report validated isocratic HPLC method for in-process quality control of centchroman. This method is capable of base line separation of its cis isomer, the process intermediates with the parent compound. HPLC separation was achieved on C18 column, at a flow rate of 2ml/min with detection wavelength 280 nm & 255 nm, using two different solvent system comprising of acetonitrile: TDW: tetramethyl ammonium hydroxide, pH adjusted to 7.6 with orthophosphoric acid (80:20:0.4%) for intermediate steps III, IV, V, VI, cis isomer and trans centchroman and second one is acetonitrile:TDW:tetramethyl ammonium hydroxide, pH adjusted to 7 with orthophosphoric acid (50:50:0.2%) for steps I, II and starting material resorcinol. Validation parameters such as limit of detection (LOD), limit of quantitation (LOQ), linearity, precision, accuracy, specificity & preformulation studies were conducted according to new guidelines of International Conference on Harmonization (ICH). Stability data was generated for determination of optimal storage and packaging conditions for bulk lots of the material and formulations. Forced degradation studies were also conducted. These stability studies revealed that the centchroman is a quite stable drug.

P-43

Preparation and optimization of Arteether nanoemulsion with the use of high pressure homogenizer

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Arteether (ART) is a second line drug for malaria which is a lipid soluble drug and has a very poor bio-availability. The present study was aimed to prepare the ART nano-emulsion to improve the bio-availability when administered orally. Arteether nanoemulsion was prepared by dissolving ART in ground nut oil (10%) at a temperature between 40-50^{0}C and subjected to pre-

milling with ultra-turrax in presence of 2% of tween 80:span 80 (68:32). The formulation was optimized in terms of pressure and number of cycles using high pressure homogenizer. The optimized formulation was found to have 93.2% of ART loading and the particle size was around 124nm with a zeta potential of around -22mv. The developed formulation was stable up to 3 months in terms of particle size and size distribution. The *invitro* release profile of the nanoemulsion showed 82% drug release in 12 hours. Arteether nano formulation is expected to improve the bio-availability which can be given to a convenient route of administration (oral).

P-44

A new formulation of centchroman

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The aim of the present work was to prepare depot injectables of centchroman by loading it in ethylcellulose (EC) microsphere (MS) and to evaluate the influence of different pH of external phase, viscosity of internal phase, drug: EC ratio and EC: water soluble polymers associations on the physiochemical characteristics of the microspheres, % loading and encapsulation, *in vitro* dissolution and biocompatibility tests. The physicochemical compatibility of the drug and the polymers were performed by Differential scanning calorimetry (DSC) and Fourier transform infrared (FTIR) spectroscopic technique. Three water soluble polymers have been associated with EC: hydroxyl ethylcellulose (HEC), hydroxypropyl methylcellulose (HPMC) and polyvinyl pyrrolidone (PVP) in order to adjust the water permeability of EC and to achieve a zero order release of centchroman for more than 7 days. Compatibility studies suggested that there were no significant interaction between the drug and polymers used. Results indicated that when the pH of external phase was kept at 7.0, centchroman showed lowest solubility in it and therefore microsphere resulted in maximum loading. Viscosities of the internal phase also have major effects on size, shape and drug loading of the microsphere. Association of the hydrophilic polymers (HPMC and HEC) with EC resulted in zero order release kinetics with r^2>0.915 and it was also found that the formulation is protecting the damage caused by the drug to erythrocytes and 3T3 mouse embryonic Fibroblasts (MEF) up to concentration of 10 mg/ml (with respect to drug).

P-45

Synthesis of 3-substituted-1-quinolin-4-yl-propan-1-one as potential spermicidal agents

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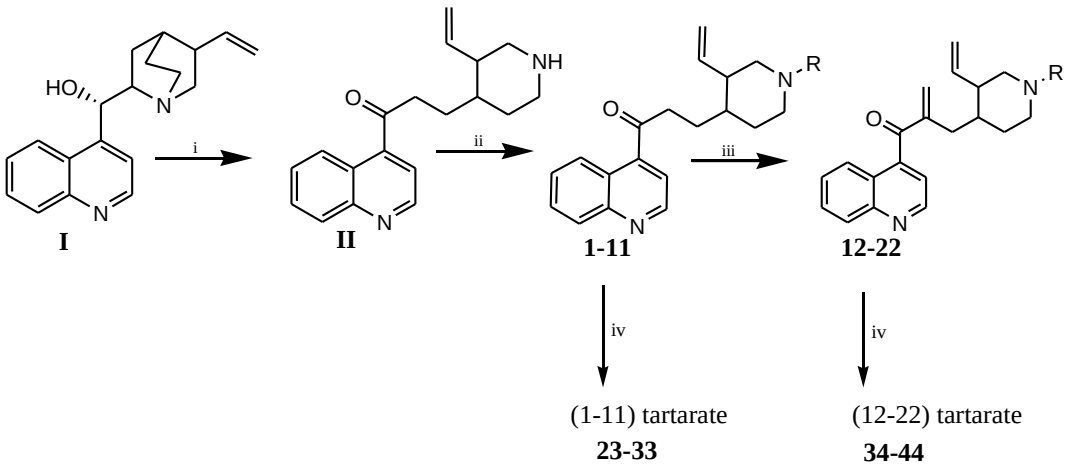
A series of twenty two novel derivatives of 1-Quinolin-4-yl-3-(3-vinyl-piperidin-4yl)-propan-1-one (Cinchotoxin) and their tartarate salts were synthesized from naturally abundant Cinchonine (I) and were evaluated for their spermicidal activity. Most active compounds showing spermicidal activity (24, 27, 34, 36, and 38) were further tested against different strains of *Trichomonas valinalis*, HeLa cell lines for cytotoxity and *Lactobacillus jensenii* for eco-safety. Tartarate salt of 3-(1-Pentyl-3-vinyl-piperidin-4-yl)-1-quinolin-4-yl-propan-1-one (27) was found to be more active spermicidal agent than nonoxinol-9.

SCHEME-1



R= ethyl, n-propyl, n-butyl, 2-butyl, n-pentyl, n-hexyl, n-octyl, N, N-dimethylaminopropyl, pyrrolidinoethyl, piperidinoethyl, morpholinoethyl.

P-46

Folic acid Conjugated Guar Gum Nanoparticles for Targeting Methotrexate to Colon Cancer

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A newly synthesize conjugated polymer drug system holds promising aspects for development of better and effective drug delivery system. It was envisaged to develop Folic acid (FA) functionalized Guar Gum Nanoparticles (FA-GGNP) charged with methotrexate (MTX) to target specifically to colon. The MTX loaded FA-GGNP [MTX-FA-GGNP] was prepared by emulsion crosslinking method. These surface modified nanoparticles were compared with unmodified one (MTX-GGNP). The developed formulations were evaluated for size and size distribution, zeta potential, Differential Scanning Calorimetry, release profile and uptake studies. The nanoparticles have been found to have average size of 325 nm in diameter having polydispersity index (PDI) 0.177 indicating mono-disperse particles. The zeta potential of the particles was found to be -36.9 mV. The percent growth inhibition of MTX-FA-GGNP was found to be better than MTX-GGNP when tested in Caco 2 cells indicating folate receptor mediated uptake. The

MTX-GGNP protect the release of MTX in upper gastrointestinal tract while maximum release of MTX occurred in simulated colonic fluids of pH 6.8. The *in vivo* uptake studies revealed preferential uptake of nanoparticles in the colon. These studies provide evidences that MTX-FA-GGNP holds promise to address colorectal cancer over-expressing folate receptors. This prototype formulation enjoys dual advantage of having propensity to release the drug in the colon and in the conditions of colorectal carcinoma; it could be better localized and targeted with improved therapy due to over-expression of folate receptors.

P-47

Stability indicating high-performance liquid chromatographic method for estimation of ar-turmerone in HM-oil and its formulation.

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A validated stability indicating method has been developed for the estimation of ar-turmerone in HM oil and capsules as per ICH guide lines. Forced degradation studies of ar-turmerone in pure form, bulk HM oil and HM capsule formulation were performed under conditions of hydrolysis, oxidation, photolysis, temperature and humidity. The chromatography was performed using a C-18 (250x4.6 mm, 5 μm, Lichrocart, Lichrosphere, MERCK) column using isocratic elution by acetonitrile and water in the ratio of 70:30 v/v, pumped at flow rate 1.0 mL/min and UV detection at 220 nm with total run time 20 minutes. The column was maintained at 30±2 °C throughout the analysis. The method was linear for ar-turmerone in the range of 2– 10 μg/mL. Stability indicating capability is established by forced degradation experiment. The method was applied successfully in stability testing of HM-oil/capsules. This newly developed method was capable in better resolution of Ar-Turmerone as compared to earlier reported method. The results indicated that ar-turmerone was found to be susceptible for oxidative, photolytic and heat conditions. An alternate equation has been developed for estimation of α,β-turmerone (another major constituent of HM, the reference standard of which is not very stable after isolation) using calibration curve of ar-turmerone.

P-48

Evaluation of chromium toxicity in North Indian tannery workers with special reference to genotoxicity

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In North India, Kanpur is one of the biggest leather tanning center. Trivalent Chromium is a toxic chemical, extensively used in leather tanning industry. Tannery workers working in these tanning industries, continue to suffer both acute and chronic health problems, which appear to be associated with exposure to chromium (Cr). Therefore, a cross-sectional study was design to evaluate the toxicological effect of Cr in tannery workers with special reference to DNA damage. The study was comprised of 100 male tanners in the exposed group and 100 healthy male (no history of Cr exposure) in the comparable control group. Baseline characteristics including age, smoking, alcohol consumption habits and duration of exposure were recorded via interviewing the subjects. Blood Cr level (measured by atomic absorption spectrophotometry), DNA damage (measured by comet assay) were measured in both groups. As a result of statistical analysis, the significant mean difference was found to be higher in blood Cr level ($p< 0.0001$) and DNA damage ($p< 0.0001$), when compared with controls. Smoking, alcohol consumption habits and age had no significant effect ($p>0.05$) on DNA damage in both groups. In simple and multiple correlation analysis, DNA damage showed significant positive correlation with Cr level and duration of exposure in exposed group. The finding of the present study revealed that chronic occupational exposure to Cr in tannery workers may have hazardous effects in terms of DNA damage.

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Natural products from biodiverse organisms in drug discovery

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In recent years, natural products from biodiverse organisms have yielded a considerable number of drug candidates. Curacin A is a potent, anti-mitotic algal natural product obtained from strains of the tropical marine cyanobacterium *Lyngbya majuscula*. It exerts its potent cell toxicity through interaction with the colchicine drug binding site on microtubules and inhibits tubulin polymerization in cells. Dolastatin 10, isolated from the Indian Ocean sea hare *Dolabella auricularia*, is a natural, cytotoxic peptide with microtubule-inhibitory and apoptotic effects. The dolastatin family also possesses anti-neoplastic,

bactericidal and fungicidal properties. The structurally-related γ-lactams salinosporamide A, omuralide and lactacystin, of bacterial origin, inhibit proteasome activity and are of interest as lead compounds for the development of anticancer agents. Salinosporamide A, a novel marine natural product, produced by an obligate marine bacterium *Salinispora tropica,* found in ocean sediment, is a potent proteasome inhibitor used as an anticancer agent. Squalamine lactate, a novel anti-angiogenic aminosteroid, isolated from the dogfish shark *Squalus acanthias,* is targeted for the treatment of ovarian cancer. Bovine lactoferrin, an antimicrobial component of colostrum and milk, helps in the protection of infants from gastrointestinal infections. Porcine pepsin cleavage of native lactoferrin produces low molecular weight peptides inhibitory to some Gram- negative and Gram-positive bacteria. Hydrolysis of native lactoferrin at pH 2 and 120°C produces active peptides that are bactericidal.

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Comparative antimicrobial study of clove oil & its extract for its role as bio-preservatives

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A comparative study was carried out on the antimicrobial activity of clove oil and its extract prepared in 50%v/v ethanol for their role as natural antimicrobial agents on some selected food spoilage bacteria. The antimicrobial activity was tested against ten bacteria (seven Gram positive & three Gram negative) and seven fungi commonly associated with food spoilage by agar well diffusion assay. The clove oil was found to be better antagonistic agent as compared to its extract counterpart by inhibiting both the groups of bacteria and fungi. The oil produced inhibition zones of diameter (IZD) ranging between 15-24mm and produced widest zone against *Bacillus cereus* and *Listeria monocytogenes* with an IZD of 24.0mm and 21.0mm respectively and a lowest minimum inhibitory concentration (MIC) of 2.5% (v/v). The fungi, *Aspergillus niger* followed by *Penicillium sp.* was found to be highly sensitive to the oil with an IZD of 42.0mm and 40.0mm respectively and a lowest minimum inhibitory concentration of 2.5% (v/v) for each fungal species. On the other hand, for clove extract inhibition zones against bacteria ranged between 12.0- 26.0nm and for fungi between 20.0- 30.0mm. Sodium propionate (standard food preservative) was used as a positive control in the present study. Clove oil was found to be a better antagonistic agent as compared to both clove extract and standard preservative. This study shows clove oil to be a promising candidate as a future bio-preservative.

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