11th ISCB CONFERENCE (1SCBC-2007)

International Conference

on

Advances in Drug Discovery Research

February 24-26, 2007 (Saturday-Monday)

Jointly Organized by

Indian Society of Chemists & Biologists

CDRI, Lucknow, India

&

Dr. Babasaheb Ambedkar Marathwada University Aurangabad, India

at

Welcom Hotel Rama International
Chikalthana, Aurangabad Maharashtra (India)

Website: www.iscbindia.com

Scientific Program

Saturday 24th February, 2007

8.30 – 10.00 AM	Registration	
10.00- 11.00 AM	Inaugural Session	
	Welcome Address:	**Dr.R.A .MANE,Secretary,ISCBC-2007**
	About ISCB:	**Dr. P.M.S. Chauhan, Secretary, ISCB.**
	Presidential Address:	**Professor Nagnath Kottapalle**, **Vice-Chancellor, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad**
	Address by Chief guest	**Dr.Vasant Gobarikar**
	Key note address	***David J. Triggle***, *State University of New York, Buffalo, New York USA* **Drug Discovery in the 21st Century: The Intersection of Biological and Chemical Space**
	Vote of Thanks:	**Dr. M.S. Shingare Convener ISCBC-2007**
11.00-11.30	High-Tea	
.		

SESSION – I

Chairpersons: **David J. Triggle and Dr.G.C.Saxena**

PL-1,11.30– 12.10 PM	**Dr. A.V. Rama Rao,** *Avra Laboratories Pvt. Ltd.Avra House, 54 Sai Enclave,Habshiguda Hyderabad - 500 007*
PL-2,12.10 – 12.50 PM	**M. Iqbal Choudhary** ***H. E. J Research Institute of Chemistry, Karachi, Pakistan*** **Excitement and Importance of Natural Product Chemistry in Natural Drug Development**
PL-3,12.50-1.30	**A. Ganesan** *School of Chemistry, University of Southampton and Karus, UK* **Natural Products Inspiring Drug Discovery: A Case Study with Histone Deacetylase Inhibitors**

Lunch,

1.30 PM **PM- 2.OO PM**

[Parallel] SESSION – II & SESSION – III

SESSION – II [Parallel]

Chairpersons:
Prof.M. Iqbal Choudhary and Prof A. Ganesan

PL-4, 2.00 –2.40 PM	**Mukund K. Gurjar** Deputy Director & Head,Organic Chemistry Technology,National Chemical Laboratory Pune-411 008(India)
PL-5 2.40 -3.20PM	**Dr. Somesh Sharma** *Nicholaspiramal, MUMBAI* **Progress Towards Developing NCEs In India For World-wide Markets**
IL-1, 3.20PM-3.40	**Satya P. Gupta** *Department of Chemistry, Birla Institute of Technology and Science, Pilani - India* **QSAR Studies on Calcium Channel Blockers**
IL -2, 3.40PM-4.00PM	**Geronikaki Athina** *Aristotle University of Thessaloniki, Thessaloniki, Greece* **Novel 3-((Furan-2-Yl)Methyl)-2-Phenyl Thiazolidin-4-One Derivatives As Ptp 1b And Shp-2 Inhibitors. Potent Future Drugs**
IL -3, 4.00PM-4.420PM	***Virinder S. Parmar*** *Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi – 110 007(India)* **Studies on an Array of Bioactive Heterocyclic Compounds as New Pharmacophores**

SESSION – III [Parallel]
Chairpersons: Prof. Ashok D. B. Vaidya and Dr. Mukund Chorghade

PL-6 2.00 –2.40 PM	Virendra N. Pandey, Ph.D ***University of Medicine and Dentistry of New Jersey*** Development of Genome Targeted Inhibitors for blocking HIV-1 replication
PL-7 2.40 -3.20PM	**Akhil B. Vaidya, Ph.D**. *Drexel University College of Medicine, Philadelphia, USA*
IL-4 3.20PM-3.40	**PMS Chauhan,,** *Central Drug Research Institute,Lucknow-226001* **Combinatorial chemistry of Heterocycles of biological interest**
IL 5, 3.40 PM-4.00PM	Kamlakar Avasthi

	Central Drug Research Institute, Lucknow **Pyrazolo[3,4-*d*]pyrimidine core: A versatile heterocycle for studying 'arene interactions' in flexible compounds**
IL -6, 4.00 PM- 4.20 PM	**Ramesh C. Gupta** *Torrent Research Centre, Village: BHAT, Ta. & Dist. Gandhinagar – 382428, Gujarat, INDIA* **Recent Advances in Dipeptidyl Peptidase IV Inhibitors : An Overview**

4.20 PM - 4.30 PM Tea Break

[Parallel] SESSION – IV & SESSION – V

SESSION – IV[Parallel]
Chairpersons: Dr.Yetendra Kumar Dr.Rajesh Thakarey

O-1, 4.30 PM -4.40PM	**Anil Kumar,** Chemistry Group, Birla Institute of Technology & Science Pilani, 333031 Rajasthan, INDIA, **Design, Synthesis and SAR of Peptide Analogs of CIYKYY as Src Tyrosine Kinase Inhibitors**
O-2, 4.40PM - 4.50 PM	**Rajiv Dahiya** Chattikara, Mathura, India **Synthesis And Biological Potential Of A Natural Cyclopeptide – Segetalin D**
O-3, 4.50 – 5.00 PM	**S.S. Pandit** Padmashree Vikhe Patil College Pravaranagar, Tal- Rahata Dist- Ahmednagar-413713 **One Pot Multicomponent Reactions Catalised By Cyanuric Chloried Synthesis Of Benzopyran Derivatives Under Mild Conditions**
O-4 5.00 PM - 5.10PM	**J. S. Biradar** **Gulbarga University. Gulbarga Karnataka, India** **Synthesis of Novel Pyrazoles by Microwave and Conventional methods**
O-5 5.10PM – 5.20 PM	**Arvind K. Srivastava** *Central Drug Research Institute, Lucknow-226001* *A Journey Towards The Search for New Antidiabetic Agents*
O-6 5.20 – 5.30 PM	**Ms S.R. Mahalle**, *Dr. Babasaheb Ambedkar Marathwada University, Auranbgabad-India.* Synthesis and Antidiabetic Evaluation of New Thiazolidinediones**.**

O-7 5.30-5.40PM	**S B Munde** *Dr. Babasaheb Ambedkar Marathwada University, Auranbgabad-431 004 (M.S.) India.* **.Synthesis of New Benzopyrano{4,3-d]-2-toluene sulfonamido pyrimidines**
O-8 **5.40-5.50**	**Manobjyoti Bordoloi** Regional Research Laboratory Jorhat-785006, Assam, INDIA **Bioactive Molecules from the Flora of North East India : Phytochemical Investigations at RRL, Jorhat**

SESSION – V [Parallel]
Chairpersons:DR..Satish patil and Dr.Kesav Deo

O-9, 4.30 PM -4.40PM	A. Dandia *University of Rajasthan, Jaipur-302 004* **Green chemical alternatives from synthons to biodynamic heterocycles: Selectivity under microwaves**
O-10 4.40PM - 4.50 PM	**M.N.WARE** *Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, India* DBU Catalyzed One-Pot Synthesis of 2-amino-4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile Derivatives Under Solvent-Free Conditions
O-11 4.50 – 5.00 PM	**Dalip Kumar** *Chemistry Group, Birla Institute of Technology and Science, Pilani India* **Synthesis and DNA Cleavage Studies of Novel Heterocyclic Aza-enediynes**
O-12 5.00 PM - 5.10PM	**Neeloo Singh** *DTDD Division, Central Drug Research Institute, Lucknow* **Exploring *Leishmania donovani* pteridine reductase 1 as a therapeutic drug target**
O-13 5.10PM – 5.20 PM	**S. D. Srivastava** *Dr. H. S. Gour University, Sagar* **Arylated substituted azino/azolo acetylamino-1,3-thiazolidin-4-ones and azetidinones : Novel Chemistry and potential use in medicine.**
O-14 5.20 – 5.30 PM	**K. Anil Kumar** *Department of Biotechnology, IIT, Chennai, India* **Experimental and theoretical studies on podophyllotoxin derivatives as effective cytotoxic and anti-fungal agents.**

O-15 5.30-5.40PM	**R. V. Chaudhari** *National Chemical Laboratory, Pune, India* Cobalt Chloride Containing Indicator Grade Silica Gel as a Cheap, Efficient and Reusable Catalyst for Aerobic Oxidation of *p*-Cresol to *p*-Hydroxybenzaldehyde
O-16 5.40-5.50PM	Pradeep K. Srivastava ***Central Drug Research Institute, Lucknow*** Biodiversity Hotspot of Northeast India: Urgent Need for Conservation Using Triple Helix Approach

5.50 PM **-7.30 PM Poster session-I [1-60]**

7.30 – 8.30 PM **Cultural Programmee.**
8.30 – **Dinner**.

Suinday 25th February, 2007

SESSION – VI
Chairpersons Prof.S.P.Gupta and Dr.Y.S.AGSIMUNDIN

PL-8 9.30 – 10.10 am	**Tsann-Long Su** *Institute of Biomedical Sciences, Academia Sinica, Taipei 115, Taiwan.* **Potent Antitumor Agents, DNA-Directed Alkylating N-Mustards**
PL-9 10.10 AM– 10.40 AM	**Prof.Mauro Panunzio** , University of Balogna ,**Italy**, mauro.panunzio@unibo.it **Use Of Azadienes For Production Of Pharmaceutically Interesting Scaffolds**
PL-10 10.40 AM -11.20 AM	**Ashok D. B. Vaidya** MD, PhD *Medical & Research Director, SPARC, Mumbai* Reverse Pharmacology Path for Drug Discovery Research
PL-11 11-20AM-12.00	**Bharat Trivedi,** *Wockardrt Research Center, Aurangabad* **Opportunity & Challenges for Drug Discovery in India**
PL-12 12.00-12.40 P.M	**Prof.Salvatore Guccione, Italy**
IL-7 12.40 - 1.20 PM	**Anamik Shah** Department of Chemistry,Saurashtra University, Rajkot- 360 005 **Development of Novel Dihydropyridines as MDR Reverting Agents- A New Look for Lead Optimization**

Tea in between
1.2 0 – 2.00 PM Lunch
[Parallel] SESSION – VII & SESSION – VIII

SESSION – VII [Parallel]

Chairpersons: Prof. Anamik Shah and Prof. R.S.Mali

IL-8 02.00-02.20 PM	**Veela B Mehta, Phd** *Department Of Surgery, Center For Perinetal Research, Children's Research Institute, Columbus, Ohio, 43205, USA* **Regulation Of Endothelial Cell Wound Healing And Angiogenesis By Heparin Binding Egf-Like Growth Factor (Hb-Egf)**
IL-9 02.20 PM -02.40 PM	**Shiv K. Agarwal** *Divisions of Medicinal Chemistry, Dabur Research Foundation, India* Sesquiterepene Lactone Derivatives: Synthesis and Their Cytotoxicity
IL-10 02.40-03.10 PM	K. S. Jain *Sinhgad College of Pharmacy, Pune* **Reactions of Nitriles under acidic conditions: An Efficient technique for synthesis of drug substances and bioactive heterocycles**
IL-11 03.10- 03.30 PM	**F.G.Kathawala** *Retired,Executive Director,Sandoz/Novartis,39 Woodland Avenue, Mountain Lakes, NJ USA* **The Metabolic Syndrome, Need To Find New Drugs For Its Treatment?**
IL-12 03.30-3.50 PM	**Shyam Sunder Chatterjee** Stettiner Str. 1; D 76139 Karlsruhe; Germany **Novel therapeutic potentials of hyperforin and other acyl-phloroglucinol derivatives**
IL-13 3.50PM-4.10PM	**Asit K. Chakraborti** *National Institute of Pharmaceutical Education and Research, India* **The Nucleophilic and Electrophilic Activation Strategies: Applications in Developing Reactions used for the Preparation of Drug Molecules**
IL-14 4.10PM-4.30 PM	**Ashok K. Prasad** *University of Delhi, Delhi-110 007* **Greener Biocatalytic Synthetic Route to Unnatural Nucleosides of Biological Importance**

[Parallel] SESSION – VIII & SESSION – IX

SESSION – VIII[Parallel]

Chairpersons: Prof. Tsann-Long Su and and Prof.D.B.Ingle

IL-15	**Dr.Satish Patil, IISC, BANGLORE**

02.00-02.20 PM	
IL-16 02.20 PM -02.40 PM	**S. B. Katti** *Central Drug Research Institute, Lucknow* **Design and synthesis of new class of antimalarial agents from 4-aminoquinoline**
IL-17 02.40-03.10 PM	**J. K. Saxena** Central Drug Research Institute,Lucknow-226001 **Parasitic enzymes as chemotherapeutic targets for antiparasitic drug discovery**
IL-18 03.10- 03.30 PM	**Anil Singh,** *Indian Institute of Technology, Mumbai, India*
IL-19 03.30-3.50 PM	**Pulakesh Mukherjee** BASF India Limited, Mumbai, 400 052, India **Biocatalysis at BASF: An Elegant Path to Pharmaceutical Intermediates**
IL-20 3.50PM-4.10PM	**W. Haq** *Central Drug Research Institute, Lucknow* **Novel strategies for vaccine construct towards enhanced immunogenicity and HIV recognition**
IL-21 4.10 PM-4.30 PM	**Prof.M.M.Salunkhe** *Vice -chancellor ,Shivaji University Kholapur*

4.30-4.40 Tea Break

[Parallel] SESSION – IX & SESSION – X

SESSION – IX [Parallel]

Chairpersons:Dr. Shyam Sunder Chatterjee and Prof.Asit K. Chakraborti

IL-22 4.40-5.00PM	**Joydeep Kant** Ranbaxy Research Laboratories, Haryana India **Chemistry of Novel Paclitaxel Analogs**
IL-23 5.00-5.20 PM	Arun K. Shaw Central Drug Research Institute, Lucknow **Studies on glycal derived 2, 3-epoxy alcohols and their application towards syntheses of trisubstituted THF derivatives**
IL-22 5.20-5.40 PM	**S. K. Srivastava** Dr. H. S.University, Sagar-470003, India **Synthesis of several new series of heterocyclo-thiazolidin-arylidine and thiadiazolyl-azetidines: Biological active molecules**
O-17	**Barbhaiya HC**

5.40-5.50 PM	Natural Remedies Pvt. Ltd., Bangalore, India **A double blind placebo controlled study of BacoMind™ on cognition enhancement in elderly volunteers**

SESSION – X [Parallel]

Chairpersons: ***Dr. S. K.Agarwal & Dr. Veela B Mehta***

IL-24 4.40-5.00PM	**Ram A. Vishwakarma** *Nicholas Piramal Research Centre,Mumbai India* **Phosphatidylinsitol kinases/phosphatases as drug targets for Inflammation and Cancer**
IL-25 5.00-5.20 PM	K. K. Bhutani *National Institute of Pharmaceutical Education and Research Punjab (India).* **Joys of Natural Molecules for Drug Discovery and Rationalising Indian Traditional Medicines**
IL-26 5.20-5.40 PM	**Srinivas Nanduri** *Dr. Reddy's laboratory, Hyderabad, India* **Design and Synthesis of Novel Kinase Inhibitors**
O-18 5.40-5.50 PM	**A .J.Joshua** Natural Remedies Pvt. Ltd., Bangalore, India ***In vivo* safety evaluation of Zigbir, a hepatoprotective polyherbal formulation in rats**

5.40 PM **-7.30 PM Poster session-II (Poster 60 -120)**

7.30 – 9.30 Dinner

Monday 26th February, 2007

SESSION –XI
Chairpersons
Prof. Virinder S. Parmar and Dr. F.G.Kathawala

PL-13 9.30 AM -10.10 AM	**Rakesh Kumar** *University of Alberta, Edmonton, AB, Canada* **Design and Investigation of New Classes of Nucleosides as Potential Anti-Tuberculosis Agents**
PL-14 10.10 AM -10.50 AM	**Michael Giardello** *President, CEO, CTO, MATERIA, Pasadena, CA USA*
LL-27	**Shyam Sunder Chatterjee**

10.50 AM -11.30 AM	*Stettiner Str. 1; D 76139 Karlsruhe; Germany* **A versatile strategy for evaluating herbal remedies**
IL-28 11.30 AM -11.50 AM	Prasad K Deshpande ***Wockhardt Research Centre, Aurangabad, India.*** WCK 1152: A Novel Fluoroquinolone for the Treatment of Respiratory Infections

SESSION –XII
11.50PM - 01.20 PM
Poster session-II (Poster 120 onward)

Lunch 1.20 onward
2.0
Award session 2.00-230PM
Valedictory Session :3.00

Sight seeing 3.00

5.30 PM- 6.30 PM ISCB GENERAL BODY MEETING

Key Note

Drug Discovery in the 21st Century: The Intersection of Biological and Chemical Space

David J. Triggle, *State University of New York, Buffalo, New York USA.*

Until the middle of the 20th century available dugs were largely natural products. Even today a significant fraction of available agents are either naturally occurring molecules or have been derived by structural modification of such molecules. This is not surprising. Nature's molecules are derived from a set of building blocks that are survivors of Darwinian evolution and have been forged in that crucible for biological fitness.

Nature utilizes, in fact, a very small region of chemical space. A typical protein of 300 residues of the 20 naturally occurring amino acids can have $>10^{390}$ permutations and it has been calculated that the number of small molecules of <500 daltons is in excess of 10^{60}. There is not enough mass in the universe to create even a single molecule of each species! Similarly, the number of genes in species has been found to be surprisingly small - ~ 22,000 for humans – and nature generates biological complexity through variations on a simple theme. Finally, it is worth observing that the minimal gene set – the number of genes to satisfy the requirements for a living cell – is also surprisingly small. Thus, nature is parsimonious with respect to her use of chemical space. The challenge for drug discoverers is how to discover and work in the subset of chemical space that is biologically relevant.

The issues of defining useful space will be illustrated with reference to privileged structures and master keys, pharmacodynamic and pharmacokinetic space, as well as the possibilities of expanding the genetic code [and thus expanding biologically useful space] and the question of whether there exists a universal chemical language necessary for life.

References

M. Weatherall, In Search of a Cure. Oxford University Press, 1990.
J. B. Taylor and D. J. Triggle, Comprehensive Medicinal Chemistry, Second Edition. Elsevier, London. 2006.
C. M. Dobson, Chemical Space and Biology, Nature 432: 824, 2004.
D. J. Triggle, Drug targets in the voltage-gated calcium channel family: why some are and some are not. ASSAY and Drug Development Technologies, 1: 719-733, 2003.

PL-1
A. V. Ramarao, Hyderabad
Abstract awaited

Plenary-2

Excitement and Importance of Natural Product Chemistry in Natural Drug Development

M. Iqbal Choudhary and Atta-ur Rahman
H. E. J Research Institute of Chemistry, International sources for Chemical and Biological Sciences ,University of Karachi, Karachi-75270,Email: hej@cyber.net.pk

World of nature is full of surprises. The wonders of the nature not only fascinate and excite humanity but are equally important for the long term human survival on planet Earth. The most complex manifestation of the nature is in living organisms, be animals or plants or even small microorganisms. Each one of them contains a fascinating array of natural products.

Natural product chemistry is a tool to discover the chemical diversity hidden in biodiversity. This is a science which encounters unexpected chemical structures and unimaginable biological properties on daily basis. It is known that only a fraction of living organisms have been explored for their bioactive chemicals. The journey of discovery of fascinating molecular leads is yet to begin and excitement of natural product chemistry is seemingly an endless voyage.

The study of natural products has many advantages over synthetic drug designing as it leads to materials having new structural features and with novel biological activity. Not only do higher plants and marine invertebrates continue to serve as important sources of new drugs, but chemicals derived from them are also extremely useful as lead structures for synthetic modifications and optimization of bioactivity. The starting materials for about one–half of the medicines we use today come from natural sources. Virtually every pharmacological class of drugs includes a natural product prototype. The future of natural products as sources of medicinal agents for use for over 9.0 billion population in 2050 and in the investigation, prevention, and treatment of new emerging diseases is very promising.

In our search of natural products with biological properties from medicinal herbs, we have discovered a large array of structurally novel and biologically potent molecules. This include potent antioxidants from *Harungana madagascariensis*, *Lindelofia stylosa*, *Iris germenica* and *Climaeoptera obtusifolia.* Several series of potent enzyme inhibitors against the enzymes thymidine phosphorylase, acetylcholinesterase, butyrylcholinesterase, α-glucosidase, phosphodiesterase and lipoxygenase were also identified. Structures of some of these compounds were modified by using microorganisms (bacteria and fungi) and structure-activity relationships were extensively studied by computational as well experimental methods. This plenary presentation will describe the results of some of our recent work in the field of natural products based drug development.

Plenary-3

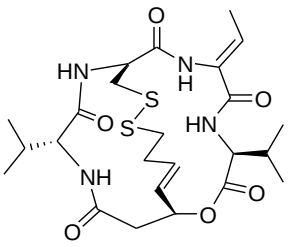
Natural Products Inspiring Drug Discovery: A Case Study with Histone Deacetylase Inhibitors

A. Ganesan
School of Chemistry, University of Southampton and Karus Therapeutics, Southampton SO17 1BJ, United Kingdom email: ganesan@soton.ac.uk, Fax: +44 (0)23 8059 3781

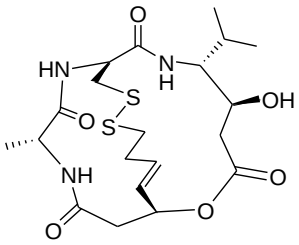
Eukaryotic DNA is tightly packaged around histone and non-histone proteins in a dynamic manner. Post-translational modifications of histones are largely responsible for these interactions and represent an 'epigenetic code' that ultimately controls gene transcription. Modulation of the enzymes responsible for histone post-translational modification is hence an attractive strategy for addressing disease states of aberrant gene transcription and cell proliferation. Among these enzymes, histone deacetylases (HDACs) are at the most advanced stage in drug discovery.

The human genome contains eleven class I/II HDACs. These enzymes are metallohydrolases containing an active site zinc, and catalyze the hydrolysis of acetyl-lysine sidechains back to lysine. Substrate mimics containing a zinc-binding group have proven to be efficient inhibitors and one, SAHA, has recently received FDA approval as an anticancer agent. Most first-generation HDAC inhibitors, including SAHA, are non-selective. Notable exceptions are FK228 and spiruchosatin A, bicyclic depsipeptide natural products discovered by Astellas in Japan. These compounds have exceptional potency (IC_{50} ~ 1 nM) and high selectivity between HDAC isoforms. Although FK228 is currently in Phase II clinical trials, there are no analogues known due to the difficulty of modifying these complex natural products.

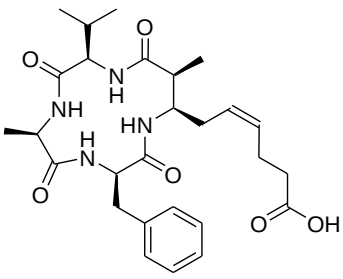
We have optimized total synthesis routes for the preparation of FK228 and spiruchostatin A, and the recently discovered azumamides. These have enabled us to prepare the first synthetic analogues and derive SAR on these compounds. In the presentation, we will review the chemistry and biology, including data on isoform selectivity, ADME/T assays and proof of efficacy in animal models.



FK228



spiruchostatin A



azumamide E

PL-4

Mukund K. Gurjar
Deputy Director & Head,Organic Chemistry Technology,National Chemical Laboratory Pashan Road,Pune-411 008(India) Tel.:+91-20-25893614 Fax:+91-20-25882456
E-Mail:mk.gurjar@ncl.res.in, URL:www.ncl-india.com

PL-5

Progress towards developing NCEs in India for world-wide market

Somesh Sharma
Nicholaspiramal, MUMBAI

PL-6

Development of Genome Targeted Inhibitors for blocking HIV-1 replication

Virendra N. Pandey, Ph.D.
Associate Professor Center for the Study of Emerging and Re-emerging Pathogens Department of Biochemistry and Molecular Biology,New Jersey Medical School (MSB, Room # A920K) University of Medicine and Dentistry of New Jersey 185 South Orange Avenue,Newark, NJ 07103 Tel: 973-972-0660

PL-7

Akhil B. Vaidya, Ph.D.
Professor, Department of Microbiology and Immunology,Director, Center for Molecular Parasitology,Drexel University College of Medicine,2900 Queen Lane, Philadelphia, PA 19129,Phone: 215-991-8557,Fax: 215-848-2271

PL-8
Potent Antitumor Agents, DNA-Directed Alkylating N-Mustards

Tsann-Long Su
Laboratory of Bioorganic Chemistry, Institute of Biomedical Sciences, Academia Sinica, Taipei 115, Taiwan.

DNA alkylating agents have played an important part in cancer therapy. A variety of DNA alkylating agents are currently using for the treatment of cancer patient including nitrogen mustards. A drawback of using DNA-alkylating agents includes their high reactivity resulting in loss of drug's therapeutic activity against malignancy by reacting with other cellular components such as proteins, thiols or genes, and producing genotoxicity. However, linking the DNA alkylating agents, such as N-mustards, to a carrier molecule having an affinity for DNA, could ameliorate many of these drawbacks. The use of sequence-specific carriers should direct the pattern of alkylation sites on the DNA and ultimately provide specific targets to certain genes. Recently, we have designed and synthesized a series of N-mustards linked to

DNA-affinic molecules (9-anilinoacridines, DNA-intercalating agents and Topoisomerase II inhibitor) either on the anilino ring or/and acridine chromophore with various lengths of spacer. All of the new N-mustard derivatives exhibited significant cytotoxicity in inhibiting a variety of human tumor cell growth in vitro with IC_{50} values of 2–50 nM and did not exhibit cross-resistance against vinblastine-resistant (CCRF-CEM/VBL) or taxol-resistant (CCRF-CEM/taxol) cells. Study on the mechanism of action showed that these agents are DNA cross-linking agent, but not a topoisomerase II inhibitor. Remarkably, nude mice bearing various human tumor xenografts were treated with the selected derivatives resulted in complete tumor remission or significant suppression. Detailed structure-activity relations as well as the therapeutic efficacy of these compounds will be discussed.

PL-9

Dr. Mukund Chorghade
President and CSO,D&O Pharmachem, Pharmaceuticals Sciences Division , USA
Abstract awaited

PL-10

Reverse Pharmacology Paradigm In Drug Discovery Research For Cancer

Ashok D. B. Vaidya, M.D., Ph.d., Ashok Amonkar, Ph.D.
Bharatiya vidya Bhavan's Swami Prakashananda Ayurveda Research Centre, Mumbai – 400 049. sparcles @gmail.com

Six million people die of cancer annually and that too with an unbearable burden of suffering. The morbidity due to cancer is compounded by the adverse effects and hazards of radical surgery, radiotherapy and cancer chemotherapy. Despite significant advances in the basic biology and genomics of cancer, the impact on human morbidity and mortality is not as expected. There is an urgent need for a paradigm shift in anticancer drug discovery research. Conventional cancer treatments cover a huge list of agents under diverse categories: antimetabolites, alkylating agents, angiogenesis and topoisomerase inhibitors, anthracyclines, antibiotics, hormones/antihormones, enzymes and inhibitors, immuomodulation and last but not the least natural products of diverse chemical groups. Most of chemical drugs and natural products are primarily meant to be cytotoxic to the malignant cells. The paradigm shift has to focus on how the host tumour-survelliance eliminates transformed cells. It is about time we also ask why and how spontaneous tumour regression occurs even in patients with metastatic cancer. Is nature trying to whisper her secret of cancer control in these rare clinical phenomena?

Reverse Pharmacology involves robust experiential documentation of unusual clinical responses to diet, drugs, medicinal plants etc. in cancer patients. This has to be then followed up by relevant *in vitro* and *in vivo* models to evolve a lead from the clinical hit. Once a lead is evolved the stage of experimental research would develop the lead into a candidate drug, by state-of-the art preclinical and clinical research. This novel path has led to many drug discoveries in several fields in the past. But that was in an unorganized and tardy manner. Now the Reverse Pharmacology paradigm is being employed in India, in a systematic manner, by ICMR, CSIR and CCRAS for diabetes, arthritis hepatitis and malaria. However, less attention has been paid to anticancer drug discovery except for arsenic bhasma in acute promyeloid leukemia.

The choice of natural products for the Reverse Pharmacology discovery path has to be based on well-developed selection criteria and the degree of biological plausibility. The spontaneous regression of cancer after uretero-sigmoidostomy and retine, *Curcuma longa* and precancerous oral submucous fibrosis, *Semicarpus anacardium* for oesophgeal cancer, *Withania somnifera* and breast cancer, *Tinospora cordifolia* and ovarian cancer etc. offer potential for novel anticancer modalities through Reverse Pharmacology. The natural molecules may not be always cytotoxic but may provide novel activities in host to regress or control cancer. There is an urgent need to netwok for such drug discovery research, at national level, to expedite the proof of clinical hits and even to identify novel structures for combinatorial chemistry and high throughput, vis-à-vis cancer therapy.

PL-11
Henk Timmerman, Netherland

PL-12
Salvatore Guccione, Italy

PL-13
Ganesh Pandey,
National Chemical Laboratory, Pune India

PL-14
Anil Singh,
Indian Institute of Technology, Mumbai, India

Pl-15
Design and Investigation of New Classes of Nucleosides as Potential Anti-Tuberculosis Agents

Rakesh Kumar[1]*, Chris Tse[1], Nancy Desroches[1], Tracey Manning[1], Naveen C. Srivastav[1], Dennis Kunimoto[2] and Babita Agrawal[3].
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Mycobacterium tuberculosis, *M. bovis* and *M. avium* infections cause the most important mycobacterioses leading to increased mortality in patients with AIDS. Various 5-substituted 2'-deoxyuridines, arabinouridines, arabinocytidines and 2'-arabinofluoro-2'-deoxyuridines were synthesized and evaluated for their *in vitro* inhibitory activity against *M. tuberculosis* (H37Ra and H37 Rv), *M. bovis* and *M. avium*. Several 5-substituted acyclic pyrimidine nucleosides containing 1-(2-hydroxyethoxy)methyl and 1-[(2-hydroxy-1-(hydroxymethyl) ethoxy)methyl] acyclic moieties were also investigated against these mycobacteria. Among 5-substituted pyrimidine nucleosides possessing furanose moiety, 5-(C-1 substituted)-2'-deoxyuridine derivatives emerged as potent inhibitors of *M. avium* (MIC_{50} = 1-10 □ g/mL range); 5-(1-azidovinyl)-2'-deoxyuridine being the most active (MIC_{50} = 1-5 □ g/mL range). In the series of acyclic nucleosides studied, 1-(2-hydroxyethoxy)methyl-5-(1-azido-2-haloethyl or 1-azidovinyl) analogs, 1-[(2-hydroxy-1-(hydroxymethyl)ethoxy)methyl]-5-decynyluracil and 1-[(2-hydroxy-1-(hydroxymethyl) ethoxy)methyl]-5-dodecynyluracil exhibited significant *in vitro* activity against *M. tuberculosis*, *M. bovis* and *M. avium*. The nature of C-5 substituents appeared to be a determinant of anti-mycobacterial activity in these classes of nucleosides.

Pl-16
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I-1

QSAR Studies on Calcium Channel Blockers

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Calcium channel blockers (CCBs) have got potential therapeutic uses against several cardiovascular and non-cardiovascular diseases. For the vasospastic angina, CCBs have been found to be the most effective drugs. These drugs selectively inhibit Ca^{2+} influx into heart muscles by blocking slow inward channels for Ca^{2+} or inhibit Ca^{2+} influx into vascular smooth muscles. The result is negative inotropism of smooth muscle relaxation, which is translated into hypotension. The three principal structural classes have been found to act as potent calcium channel blockers and they are phenylalkylamines, 1,4-dihydropyridines (DHPs), and benzothiazepines. Recently, a few more classes of CCBs have been studied. We intend to present a comprehensive review on quantitative structure-activity relationship (QSAR) studies on all kinds of CCBs. These QSAR studies lead to highlight the essential structural features and physicochemical properties that the compounds should possess to act as potential CCBs and vividly describe the mechanism of interaction of CCBs with the calcium channel.
Invited

I-2

Novel 3-((Furan-2-Yl)Methyl)-2-Phenyl Thiazolidin-4-One Derivatives As Ptp 1b And Shp-2 Inhibitors. Potent Future Drugs

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During the last decade, protein kinases and phosphatases have been extensively studied and members of both enzyme families have been proved to be related with various diseases.
Interaction of insulin with its receptor results in the phosphorylation of three tyrosine residues of the receptor. This is the first step of a cascade of sequential events causing glucose uptake. PTP1B is a protein tyrosine phosphatase that terminates this cascade by dephosphorylating insulin receptor. Thus, PTP1B inhibition, resulting in prolonged maintenance of the phosphorylated state, enhances insulin effect. Consequently, effective and selective PTP1B inhibitors can be potent drugs for the treatment of type 2 diabetes and obesity.
HSP-2 is one of the classical non-transmembrane PTPs. A mutation in the gene, making HSP-2 continuously active results in Noonan syndrome, a developmental disorder that may lead to a higher risk for certain cancers, such as juvenile myelomonocytic leukaemia. HSP-2 selective inhibitors may be potent drugs for the treatment of Noonan Syndrom patients.
In the present study, we synthesised a number of 3-((furan-2-yl)methyl)-2-phenyl thiazolidin-4-one derivatives and tested their PTP1B and HSP-2 inhibitory activity. Many of the

derivatives showed good inhibitory action. All inhibitory actions were tested using human recombinant phosphatases. In all cases p-nitro-phenyl-phosphate was used as substrate.

Bibliography

1. Rob Hooft van Huijsduijnen, Wolfgang H. B. Sauer, Agnes Bombrun, and Dominique Swinnen. Prospects for Inhibitors of Protein Tyrosine Phosphatase 1B as Antidiabetic. Drugs. J. Med. Chem. 2004, *47*, 4142-4146.
2. Liwei Chen, Shen-Shu Sung, M. L. Richard Yip, Harshani R. Lawrence, Yuan Ren, Wayne C. Guida, Said M. Sebti, Nicholas J. Lawrence, and Jie Wu. Discovery of a Novel Shp2 Protein Tyrosine Phosphatase Inhibitor. J. Biol. Chem. vol. 281, No. 10, pp. 6785–6792, 2006

I-3

Studies on an Array of Bioactive Heterocyclic Compounds as New Pharmacophores

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Heterocyclic compounds arose on our planet long before the first living creatures. Together with other classes of organic compounds, heterocyclic compounds promoted the formation of life on Earth. Heterocyclic compounds are widely distributed in nature and are essential to life; they play a vital role in the metabolism of all living cells. There are a vast number of pharmacologically active heterocylic compounds, many of which are in regular clinical use. There is no doubt that the chemistry of heterocylics will continue to grow for the creation of new drugs, agrochemicals, novel material, etc.

In our laboratory, we have synthesized a large variety of heterocylic compounds which have exhibited interesting anti-inflammatory activity of importance in treating asthma and alzheimer's disease; antioxidant activity against the initiation of lipid peroxidation in rat liver microsomes; antiinvaise activity against human MCG-7/6 mammary carcinoma cells; antifungal activity against two deadly lung fungal infections; antiviral activity as non-nucleoside HIV-I reverse transcriptase inhibitors (NNRTIs) and antimycobacterial activity against *Mycobacterium tuberculosis.*

Recently a number of publications and reviews have advocated the use of microwave technology in synthesis of heterocyclic compounds catalysed by transition metals. Microwave radiation generally results in enhanced reaction rates and higher product yields as compared to those by conventional heating. In view of above, we have synthesized spiroisoxazolidines (by the reaction of indolylidene acetate with a series of nitrones); dihydropyridines and tetrahydropyridine-2-ones (by Bignelli cyclocondensation of ethy1/methy1 acetoacetate and different aldehydes); pyrazinones (by using Cross still reaction, Chan-Lam and Liebes kind-Srogl protocol) in one-pot reaction sequence using microwave radiation. Spiroisoxazolidines exhibited interesting anti-tubercular and anti-invasive activities against MCF 7/6 cancer cells, while the dihydrophyridines and tetrahdropyridine-2-ones showed promising antifungal activity against *Aspergillus fumigatus* and *Candida albicans.*

Details of synthetic studies and activity data of all these compounds will be discussed in the lecture.

Recent Key References:

1. Raunak, V Kumar, S Mukherjee, Poonam, AK Prasad, CE Olsen, SJC Schaffer, SK Sharma, AC Watterson, W Errington and VS Parmar. Microwave mediated synthesis of spiro-(indoline-isoxazolidines): mechanisitic study and biological activity evaluation. *Tetrahedron* **61**, 2005, 5687-5697.

2. S Kumar, BK Singh, N Kalra, V Kumar, A Kumar, AK Prasad, HG Raj, VS Parmar and B Ghosh. Novel thiocoumarins as inhibitors of TNF-α induced ICAM-1 expression on human umbilical vein endothelial cells (HUVECs) and microsomal lipid peroxidation. *Bioogranic and Medicinal Chemistry* **13**, 2005, 1605-1613.

3. BW Vanhoecke, HT Depypere, AD Beyter, SK Sharma, VS Parmar, DD Keukeleire and ME Bracke. New anti-invasive compounds: Results form the Indo-Belgian screening program. *Pure and Applied Chemistry* **77**, 2005, 65-74.

4. MC Foti, SK Sharma, G Shakya, AK Prasad, G Nicolosi, P Bovicelli, B Ghosh, HG Raj, RC Rastogi and VS Parmar, Biopolyphenolics as antioxidants: Studies under an Indo-Italian CSIR-CNR project. *Pure and Applied Chemistry* **77**, 2005, 91-101.

5. SV Slambrouck, VS Parmar, SK Sharma, BD Bondt, F Fore, P Coopman, BW Vanhoecke, T Boterberg, HT Depypere, G Leclercq and ME Bracke. Tangeretin inhibits extracellular-signal-regulated kinase (ERK) phosphorylation. *FEBS Letters* **579**, 2005, 1665-1669.

6. A Kumar, BK Singh, R Tyagi, SK Jain, AK Prasad, HG Raj, RC Rastogi, AC Watterson and VS Parmar. Mechanism of biochemical action of substituted 4-methylcoumarins. Part 11: Comparison of the specificities of acetoxy derivatives of 4-methylcoumarin and 4-phenylcoumarin to acetoxycoumarins: protein transacetylase. *Bioogranic and Medicinal Chemistry* **13**, 2005, 4300-4305.

7. S Kumar, P Arya, C Mukherjee, BK Singh, N Singh, VS Parmar, AK Prasad and B Ghosh. Novel aromatic ester from *Piper longum* and its analogues inhibit expression of cell adhesion on endothelial cells. *Biochemistry* **44**, 2005, 15944-15952.

8. AK Chhillar, P Arya, C Mukherjee, P Kumar, Y Yadav, AK Sharma, V Yadav, J Gupta, R Dabur, HN Jha, AC Watterson, VS Parmar, AK Prasad and GL Sharma. Microwave-assisted synthesis of antimicrobial dihydropyridines and tetrahydropyrimidin-2-ones: Novel compounds against aspergillosis: *Bioogranic and Medicinal Chemistry* **14**, 2006, 973-981.

9. P Khurana, R Kumari, P Vohra, A Kumar, Seema, G Gupta, HG Raj, BS Dwarakanath, VS Parmar, D Saluja, M Bose, A Vij, NK Chaudhary, JS Adhikari, YK Tyagi and E Kohli. Acecoxy drug: protein transacetylase catalyzed activation of human platelet nitric oxide synthase by polyphenolic peracetates. *Bioogranic and Miedicinal Chemistry* **14**, 2006, 575-583.

10. HG Raj, R Kumari, Seema, G Gupta, R Kumar, D Saluja, KM Muralidhar, A Kumar, BS Dwaraknath, RC Rastogi, AK Prasad, SA Patkar, AC Watterson and VS Parmar. Novel function of calreticulin: Characterization of calreticulin as a transacetylase mediating protein acetylator independent of Acety1 CoA using polyphenolic acetates. *Pure and Applied Chemistry* **78**, 2006, 985-991.

11. BK Singh, P Atppukktan, S Claerhout, VS Parmar and EV Eycken. Copper (II)-mediated cross-coupling of arylboronic acids and 2(1*H*)-pyrazinones facilitated by microwave irradiation with simultaneous cooling. *Organic Letters* **8**, 2006, 1863-1866.

I-4

Combinatorial chemistry of Heterocycles of biological interest

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Combinatorial chemistry has been aggressively explored both in academia and in the pharmaceutical industry during the last 15 years. There has not only been an exponential increase interest from academic groups and small bio teach companies, but also the genesis of some quite impressive projects by large pharmaceutical companies. This reflects both the scientific and commercial attractiveness of combinatorial chemistry.
Dramatic changes in accessing vast arrays of synthetic compounds , in the guise of combinatorial libraries , have broken old paradigms of drug discovery and development. Among the many factors which have contributed to such rapid progress in combinatorial chemistry are the scientific hunger for understanding and exploiting molecular diversity and a rebirth of solid phase organic synthesis. Drug lead discovery has been literally revolutionized by combinatorial chemistry method. We have concentrated our attention mainly on nitrogen heterocycles [1-11] Since many drugs contain the nitrogen heterocylic component and nitogen heterocycles posses a high order of structural diversity. Solid phase and solution phase synthesis of Novel heterocycles their combinatorial chemistry will be discussed.

REFERENCES:

1. Arun Kumar, Sanjay Babu Katiyar, Suman Gupta and **Prem M. S. Chauhan,** ***European Journal of Medicinal Chemistry,*** **2006,** 41 ,106–113,
2. Sharad Porwal, Rishi Kumar,[b] Prakas R. Maulik,and **Prem M. S. Chauhan, Tetrahedron Letters** ,**2006** , 47,5863–5866
3. Sanjay Babu Katiyar, Arun Kumar and **Prem M. S. Chauhan, Synthetic communications,** 36(20), **2006 ,**2963-73
4. Naresh Sunduru, Anu Agarwal,Sanjay Babu Katiyar,Nishi, Neena Goyal,,Suman Gupta and Prem M.S. Chauhan, ***Bioorganic and Medicinal Chemistry***, 14,**2006**,7706-7715
5. Anu Agarwal and **Prem M. S. Chauhan**,, **Letters in Organic Chemistry**,3,2006,712-714
6. Anu Agarwal, Kumkum Srivastava, S.K. Puri, S. Sinha and Prem M.S. Chauhan ,***Bioorganic and Medicinal Chemistry Letters*** 15 (2005) 4923–4926
7. Anu Agarwal, Kumkum Srivastava, S.K. Puri, S. Sinha and **Prem M.S. Chauhan** , *Bioorganic and Medicinal Chemistry Letters* 15 (2005) 5218-5221

8. (A)Srivastava, S. K.; Chauhan, P. M. S.; Agarwal, S. K.; Bhaduri, A. P.; Singh, S. N.; Fatima, N.; Chatterjee, R. K.; Bose, C. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2623-2628. (B) Srivastava, S. K.; Agarwal, A.; Chauhan, P. M. S.; Agarwal S. K.; Bhaduri, A. P.; Singh, S. N.; Fatima, N.; Chatterjee, R. K. *J. Med. Chem.* **1999**, *42*, 1667-1672. (C) Srivastava, S. K.; Agarwal, A.; Chauhan, P. M. S.; Agarwal, S. K.; Bhaduri, A. P.; Singh, S. N.; Fatima, N.; Chatterjee, R. K. *Bioorg. Med. Chem.* **1999**, *7*, 1223-1236. (D) Srivastava, S.K.; Chauhan, P.M.S.; Bhaduri, A.P.; Fatima, N.; Chatterjee, R. K. *J. Med. Chem.* **2000**, *43*, 2275-2279. (E) Tiwari, S; Chauhan, P.M.S.; Bhaduri, A.P.; Fatima, N.; Chatterjee, R. K. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1409-1412.
9. Srivastava, S.K.; Haq, W.; Murthy, P. K.; Chauhan, P.M.S. Murthy, P.K. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1885-1888.
10. (A)Chauhan, P.M.S.; Kumar, A. *Comb. Chem. Highthroughput Screening* **2002**, *5*, 93-95. (B) Kumar, A.; Sinha, S.; Chauhan, P.M.S. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 667-669. (C) Srivastava, S.K.; Haq, W.; Chauhan, P.M.S. *Comb. Chem. Highthroughput Screening* **1999**, *2*, 33-37.
11. Srivastava, S.K.; Haq, W.; Chauhan, P.M.S. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 965-966.

I-5

Pyrazolo[3,4-*d*]pyrimidine core: A versatile heterocycle for studying 'arene interactions' in flexible compounds

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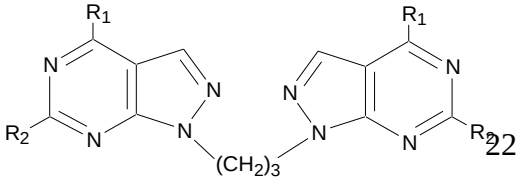
Arene interactions are known to play an important role in chemistry and biology particularly in molecular recognition, stabilization of DNA/RNA structures, crystal engineering, foldamers, molecular tweezers/clips and drug development. Since Hunter and Sanders paper (*JACS*, **1990**, *112*, 5525) this area has witnessed hectic activity, however, the nature of π–π interactions is still not well understood. The offset stacked geometry is the most common geometry for **arene interactions**, but the least well studied (*JACS*, **2002**, *124*, 1860). Potential of flexible polymethylene especially **trimethylene linker** for studying *intramolecular* **arene interactions** in nucleic acid bases was first demonstrated by Leonard (*JACS*, **1968**, *90*, 7302). In **1995**, we at *CDRI, Lucknow*, started, for the first time, use of pyrazolo[3,4-*d*]-pyrimidine core, which is isomeric with biologically significant purine system, for studying **arene interactions**. Thus, we reported first synthesis of 1,3-bis(4,6-dimethylsulfanyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)propane (**1a**, Fig. 1) in order to develop new flexible model for studying *intramolecular* aromatic π–π interactions. X-Ray crystallographic studies on **1a** confirmed *intramolecular stacking* and in addition revealed *intermolecular stacking*. Robustness of the unusual **U-motif** in compound **1a** formed due to *intramolecular stacking* has been further demonstrated in ethyl- (**1b**) and iso-propyl- (**1c**) analogs by X-ray crystallography. Symmetrical structures (**1d** & **1e**; Fig. 1) related to **1a** but having 4-alkoxy group in place of 4-methylsulfanyl group, also show similar folded conformation.

Figure 1



1a: $R_1 = R_2 =$ SMe;
1b: $R_1 = R_2 =$ SEt;
1c: $R_1 = R_2 =$ S-iso-Pr;
1d: $R_1 =$ OEt, $R_2 =$ SMe;
1e: $R_1 =$ O-iso-Pr, $R_2 =$ SMe

I-6

Recent Advances in Dipeptidyl Peptidase IV Inhibitors : An Overview

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Diabetes is one of the most challenging health problems of the 21st Century. The rapidly increasing prevalence of diabetes is a significant cause for concern. The number of diabetics is increasing by 4-5 % per year. The highest rate of diabetes prevalence is to be found in the North American Region, followed by the European Region. Unfortunately the million of people worldwide are unaware that they have the disease. Since the signs of diabetes are not immediately obvious, diagnosis can be preceded by an extended period of impaired glucose tolerance resulting in the prevalence of beta-cell dysfunction and microvascular complications. The treatment of diabetes is being aggressively combated through treatment for lowering circulatory blood glucose and inhibiting postprandial hyperglycemic spikes.

Current strategies to treat diabetes include reducing insulin resistance using glitazones, supplementing insulin supplies with exogenous insulin, increasing endogenous insulin production with sulfonylureas and meglitinides, reducing hepatic glucose production through biguanides and limiting postprandial glucose absorption with alpha-glucosidase inhibitors. The current medicines are not yet capable of more efficiently prevent or reverse progression of the disease and its complications. Although promising biological targets like PTP-1B, Glycogen Synthase Kinase 3 (GSK3), Inhibitors of glucoseneogenesis like Pyruvate Dehydrogenase Kinase (PDH) inhibitors, Lipolysis Inhibitors, fat oxidation including carnitine palmitoyltrasferase (CPT) I & II inhibitors and DPP-IV inhibitors are also explored in various laboratories worldwide. Treatment of type-2 diabetes that is based on enhanced and sustained action of insulinopropic incretin hormones such as GLP-1 have received much attention in the recent years. Treatment strategies include administration of GLP-1 analogs that are resistant to degradation by the serine protease DPP-IV and small molecules DPP-IV inhibitors that are able to provide sustained action of endogenous GLP-1 again by preventing its degradation. The advances and developments in small molecules as DPP-IV inhibitors will be presented

I-7

Regulation Of Endothelial Cell Wound Healing And Angiogenesis By Heparin Binding Egf-Like Growth Factor (Hb-Egf)

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Background: Angiogenesis, the formation of new blood vessels from pre-existing vascular bed, plays an important role in a number of physiologic and pathologic processes, including reproduction, wound repair, inflammatory diseases, and tumor growth. Angiogenesis involves

sequential steps that are triggered in response to angiogenic growth factors released by inflammatory, mesenchymal, or tumor cells that stimulates endothelial cells. Stimulated cells detach from neighboring cells and migrate, proliferate, and form tubes. HB-EGF is believed to be a regulator of angiogenesis, but the molecular mechanisms by which HB-EGF regulates angiogenesis are unknown.

Objective: The present study investigated the role played by the PI3-kinase, P38 MAPK and ERK pathways in HB-EGF-mediated wound healing and angiogenesis in human umbilical vein endothelial cells (HUVEC).

Design/Methods: Design/Methods: EC wound healing was assessed by subjecting HUVEC to scrape wounding. Monolayers were pretreated with either the PI3-kinase inhibitor wortmannin, the Mek inhibitor UO126, the EGF receptor (EGFR) inhibitor AG1478 or p38 MAPK inhibitor prior to stimulation with HB-EGF. A scrape wound was created using a pipette tip and photographs taken at 0h and 18h following wounding. The number of migrated cells across the wounded edge were counted. An *in vitro* tube formation assay for angiogenesis was performed by culturing HUVEC on basement membrane extract (BME)-coated plates in the presence or absence of HB-EGF and the above inhibitors, with tube length measured 18h later. Lastly, a 3-D angiogenesis assay was performed. Tube formation in the 3-D culture is reasonably faithful to the *in vivo* situation, and the formation of tight junctions can be confirmed by microscopy. The 3-D assay was performed by mixing EC with BME at final concentration 6 mg/ml. The mixture was then added to the wells and allowed to gel, and was then overlayed with medium containing either HB-EGF, epidermal growth factor (EGF) or vascular endothelial growth factor (VEGF) and the inhibitors listed above. Angiogenesis was assessed 72 h later.

Results: HB-EGF-induced activation of PI3-kinase triggered activation of Akt. The PI3-kinase inhibitor wortmannin blocked Akt activation and HB-EGF-induced cell migration. The EGFR inhibitor AG1478 and the Mek inhibitor UO126 also blocked HB-EGF-induced wound healing in HUVEC. When grown on BME, we found that HUVEC formed tube-like structures closely resembling *in vivo* capillary tube formation. HB-EGF treatment significantly increased tube formation by 2-fold, and was found to be EGFR-, PI3-kinase-, p38MAPK and ERK1/2 dependent.

Conclusions: These data demonstrate that HB-EGF is a potent angiogenic factor that induces EC migration and capillary tube formation via activation of the p38MAPK pathway. The role played by HB-EGF in stimulating physiologic processes such as wound healing *in vivo* may be dependent, in part, on its ability to promote angiogenesis.

I-8

Sesquiterepene Lactone Derivatives: Synthesis And Their Cytotoxicity

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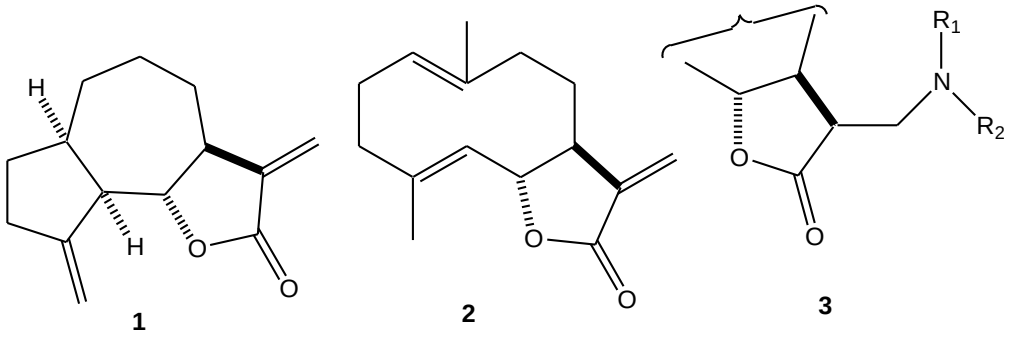
A number of sesquiterepene lactones have been isolated from the natural plants and several of them have shown a variety of biological activities [1]. Sesquiterpenes are known to have antitumour activity by triggering apoptosis in human leukemia cells [2]. Costunolide (1) and dehydrocostus lactone (2), sesquiterpene lactones, are being considered as a potential candidates for various types of tumors [1, 3-6]. Thus it appeared of interest to prepare derivatives of costunolide (1) and dehydrocostus lactone (2) in order to improve their cytotoxicity and establish the meaningful structural activity relationship.
In our laboratory, a number of costunolide and dehydrocostus lactone derivatives (3) were synthesized and evaluated for their *in vitro* cytotoxicity. The details would be presented.



REFERENCES:

1. Sun c-h.; syu, w-j.; don, m-j.; lu j-j.; lee, g-h. *J. Nat. Prod*. 2003, *66*, 1175-1180.
2. Hibasami h.; yamada y.; moteki h.; katsuzaki h.; imai k.; yoshioka k; komiya t. *International journal of molecular medicine*, 2003, *12*, 147 –151.
3. Okugawa, h.; ueda, r.; matsumoto, k.; kawanishi, k.; kato, a. *Phytomedicine* 1996, 147-153.
4. Bocca c.; gabriel l.; bozzo, f.; miglietta, a. *Chemico-biological interactions* 2004, *147*, 79-86.
5. Lee, m-g.; lee, k-t.; chi, s-g.; park, j-h. *Biol. Pharm. Bull*, 2001, *24(3)*, 303-306.
6. Zhang, s.; won, y-k.; ong, c-n.; shen, h-m. *Curr. Med. Chem.-anti-cancer agents* 2005, *5*, 239-249.

I-9

Reactions of Nitriles under acidic conditions: An Efficient technique for synthesis of drug substances and bioactive heterocycles

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Reaction of nitriles under the influence of dry HCl gas with a variety of the *o*-amino carbonyl compounds to yield 2-substituted-4-oxo/amino/choloropyrimidines and condensed pyrimidines has been thoroughly exploited by Shishoo *et. al.*. Through the proper selection of nitriles as well as *o*-aminocarbonyl substrate, a variety of condensed pyrimidines, bearing benzene, thiophene, furan, pyridine or pyrimidine, *etc*. rings fused to the pyrimidine ring have been prepared.

Further, by subtly manipulating the reaction conditions and reagents the 4-substitution can be a 4-oxo, 4-chloro, or 4-amino group. Also, the transient amidine intermediates have also been isolated and converted to the corresponding 4-oxo, 4-chloro and 4-amino-2-

substitutedpyrimidines and condensed pyrimidines, by subtly manipulating their cyclization conditions.
A total overview of this novel but hitherto not reviewed or much reported reaction till date; including the underlying mechanisms shall be discussed.
Interestingly, this novel and interesting reaction has been nicely explored by us to prepare a variety of drugs and drug intermediates, through almost one pot condensations and good yields as well as purity.
Secondly, the reaction has also been modified suitably in its reaction condition to be exploited and used for high throughput synthesis of compound libraries for New Drug Discovery.
References: *Shishoo et al., various references in J.Het.Chem. & Tet. Letters.*

I-10

The Metabolic Syndrome, Need To Find New Drugs For Its Treatment?

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The Metabolic Syndrome is a serious medical condition affecting millions of individuals all over the world. The Metabolic Syndrome is associated with sets of factors leading to AN INCREASED RISK FOR ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) and DIABETES.The core risk factors of the metabolic syndrome are Atherogenic

Dyslipidemia, Elevated Plasma Glucose, Vascular Dysfunction, Vascular Inflammation and Prothrombotic state.The underlying cause(s) of the Metabolic Syndrome is being studied intensively and is hotly debated. Recent developments for treating the Metabolic Syndrome have led to newer drugs which treat separately each of the risk factors associated with the Metabolic Syndrome. This approach forces the unfortunate patient to take as much as ten different drugs.Challenge remains for Drug Discovery and Development scientists to develop safe and effective SINGLE drugs that treat multiple risk factors associated with the Metabolic Syndrome.

I-11

Novel therapeutic potentials of hyperforin and other acyl-phloroglucinol derivatives

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Hyperforin, a prenylated bi-cyclic poly-ketide, is quantitatively the major non-nitrogenous secondary metabolite isolated to date from *Hypericum perforatum*. Numerous properly controlled clinical trials have consistently reconfirmed therapeutic usefulness of this herb for treatment of mild to moderately severe depression. However, diverse other medicinal uses of this herb have been known since centuries. Concentrated efforts made to identify its other possible therapeutic potentials revealed that hyperforin is indeed the most prominent bio-active extractable component of the herb, and that its therapeutically interesting pharmacological activity profile is not like any known therapeutically used antidepressant or other drugs. Therefore, hyperforin was considered to be a lead suitable for identifying structurally and functionally novel drug candidates.

Results of initial pharmacological screening conducted with hyperforin, several of its derivatives and analogues and a few other naturally occurring cyclic poly-ketides, indicated that the acyl-phloroglucinol moiety could represent the essential pharmacophore of hyperforin. Consequently, numerous acyl-phloroglucinol derivatives were synthesised and pharmacologically screened in a battery of experimental models for their hyperforin like bioactivities. These efforts led not only to the identification of several therapeutically interesting pharmacological properties of acyl-phloroglucinols, but also one such easily accessible molecule (DIVP) with activity profile almost identical to that of hyperforin. Since hyperforin is a labile molecule, and it is difficult to obtain and handle in pure form, DIVP was chosen as a useful experimental tool for identifying potential mode(s) and site(s) of action(s) of hyperforin. Main aim of this communication is to summarise progress made to date in these efforts, and to point out some novel therapeutic potentials of hyperforin and DIVP revealed by our efforts.

The reported observations add further experimental evidence in support of the conviction that facilitation of vesicular release processes is involved in its neuronal-function modulating effects and reveal further that DIVP represents a novel type of insulin releasing agent. Since structurally unique secondary metabolites of diverse medicinal plants are acyl-phloroglucinol derivatives, and their diverse reported bio-activities are like those of hyperforin or DIVP, evaluation of such plants in light of the findings reported here seems warrantable.

I-12

The Nucleophilic and Electrophilic Activation Strategies: Applications in Developing Reactions used for the Preparation of Drug Molecules

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Synthesis plays the central/key role in the drug discovery and development process. The various chemical transformations required in the synthesis of drug molecules can be broadly classified into two types: constructive and modifying. The chemistry currently used in drug development in the pharmaceutical industry indicates significant gaps in synthetic methodologies. The increasing awareness and need of sustainable chemistry development and the regulations imposed by EPA on chemical processes has induced a change in the drug development process. These redefine the expertise and training required in the discipline of medicinal chemistry. The present deliberation will demonstrate the utilization of electrophilic[1]/nucleophilic[2] activation strategies and the concept of atom economy[3] in the context of sustainable chemistry[4] for the development of reactions used in drug synthesis.

References

1. A. K. Chakraborti, Shivani *J. Org. Chem*. **2006**, *71*, 5785. A. K. Chakraborti, R. Gulhane *Synlett* **2004**, 627. A. K. Chakraborti, R. Gulhane, Shivani *Synthesis* **2004**, 111. A. K. Chakraborti, R. Gulhane, Shivani *Synlett* **2003**, 1805. A. K. Chakraborti, L. Sharma, R. Gulhane, Shivani *Tetrahedron* **2003**, *59*, 7661. A. K. Chakraborti, R. Gulhane *Tetrahedron Lett*. **2003**, *44*, 6749. A. K. Chakraborti, R. Gulhane *Chem. Commun*. **2003**, 1896. A. K. Chakraborti, R. Gulhane *Tetrahedron Lett*. **2003**, *44*, 3521. S. V. Chankeshwara, A. K. Chakraborti, *Synthesis* **2006**, 2784. A. K. Chakraborti, S. V. Chankeshwara, *Org. Biomol. Chem.* **2006**, *4*, 2769. S. V.

Chankeshwara, A. K. Chakraborti, *J. Mol. Cat. A: Chem*. **2006**, *253*, 198. S. V. Chankeshwara, A. K. Chakraborti, *Tetrahedron Lett*., **2006**, *47*, 1087.
2. A. K. Chakraborti, L. Sharma, M. K. Nayak *J. Org. Chem*. **2002**, *67*, 2541. M. K. Nayak, A. K. Chakraborti *Chemistry Lett*. **1998**, 297.
3. A. K. Chakraborti, A. Basak (née Nandi), V. Grover *J. Org. Chem*. **1999**, *64*, 8014. A. Basak (née Nandi), M. K. Nayak, A. K. Chakraborti *Tetrahedron Lett*. **1998**, *39*, 4883.
4. S. V. Chankeshwara, A. K. Chakraborti *Organic Lett*. **2006**, *8*, 3259. G. L. Khatik, R. Kumar, A. K. Chakraborti *Organic Lett*. **2006**, *8*, 2433.

I-13

Greener Biocatalytic Synthetic Route to Unnatural Nucleosides of Biological Importance

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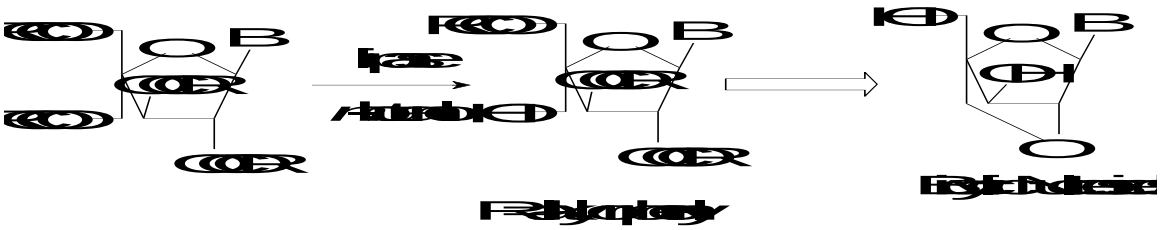
Synthesis of modified, unnatural nucleosides has become important because of their applications as antiviral agents and also because of their use as precursor for the synthesis of modified oligonucleotides of different utility. During the synthesis of targeted nucleosides and their derivatives, selective manipulation of different hydroxyl functions in sugar moiety is always sought. It is at this juncture that the nature's catalysts "ENZYMES" come into the picture. The use of enzymes in synthetic sequences provides unique advantages of efficiency, regioselectivity, stereoselectivity and environment friendliness.

We have developed an efficient synthesis of different modified, unnatural nucleosides under a research program of synthesis of modified nucleosides as potential antiviral agents and as oligonucleotide monomers to be used for chemical etiological studies suing lipases in one of the crucial steps. Further, a method of selective benzoylation of nucleosides of both, ribo- and deoxy- ribo series using benzoyl cyanide in ionic liquid have been developed, which may find application in selective manipulation of different hydroxyl groups in nucleoside monomer during oligonucleotide synthesis. Detailed results will be presented in the meeting.



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Key References:

1. Wengel, J. *Acc. Chem. Res*. **1999,** *32*, 301.
2. Prasad, A.K.; Kumar, V.; Maity, J.; Sanghvi, Y.S.; Ravikumar, V.T.; Parmar, V.S. *Nucleosides, Nucleotides & Nucleic Acids* ***2005,*** *77*, 237.
3. Prasad, A.K.; Kumar, V.; Malhotra, S.; Ravikumar, V.T.; Sanghvi, Y.S.; Parmar, V.S. *Bioorg. Med. Chem.* **2005**, *13*, 4467.

4. Prasad, A.K.; Husain, M.; Singh, B.K.; Gupta, R.K.; Manchanda, V.K.; Olsen, C.E.; Parmar, V.S. *Tetrahedron Lett.* **2005,** *46,* 4511.
5. Prasad, A.K.; Roy, S.; Kalra, N.; Wengel, J.; Olsen, C.E.; Cholli, A.L.; Samuelson, L A.; Waterson, A.C.; Parmar, V.S. *Tetrahedron* **2003***, 59,* 1333.
6. Sharma, S.K.; Roy, S.; Kumar, R.; Parmar, V.S. *Tetrahedron Lett* **1999***, 40,* 9145

I-14

Design and synthesis of new class of antimalarial agents from 4-aminoquinoline

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Malaria is one of the foremost public health problems in developing countries affecting nearly 40% of the global population. Historically 4-aminoquinoline based entities, particularly chloroquine (CQ), have remained the first choice in the malaria chemotherapy. The mechanistic investigations demonstrate that this class of compounds enter the food vacuole and inhibit the parasite growth by forming complex with haematin thereby inhibiting the haemozoin formation. However, development of resistance has severely limited the choice of available antimalarial drugs, which clearly highlights the urgent need of novel chemotherapeutic agents for the treatment of malaria. Contemporary biochemical studies suggest that a close analogue of CQ and its derivatives are active against CQ-resistant parasites. It highlights that the mechanism of resistance does not involve any change to the target of this class of drug but involves a compound specific resistance. Based on this observation a number of groups have developed short chain analogues of 4-aminoquinoline, which are significantly active against CQ resistant strain of. *P. falciparum* in *in vitro*. On the basis we have designed new compounds by selectively modifying the pendant amino group of 4-aminoquinoline with a view to facilitate, (i) their accumulation in the food vacuole, and (ii) achieve better interaction with hematin leading to improved antimalarial activity. These results will be discussed.

I-15

Parasitic enzymes as chemotherapeutic targets for antiparasitic drug discovery

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The parasitic diseases still continue to be a formidable problem due to lack of definite action on parasites. Recent advances in molecular and computational biology have revolutionized ways to the identification of targets for antiparasitic agents. However the validation and optimization of identified target can be very well conducted by biochemical studies of the interaction between target and candidate inhibitor. Human lymphatic filariasis is an infectious disease caused by lymph dwelling nematode parasites and transmitted by mosquitoes. *Wuchereria bancrofti* is the causal parasite for most of the cases of filariasis. One reason for not having ideal drugs against filariasis is that chemotherapeutic targets in filarial parasites are not well characterized. Therefore it is an utmost need to identify new targets for drug development against this disease. Since parasitic nematodes have an absolute dependency on carbohydrate, glycolysis is an important pathway for their energy metabolism. Hexokinase, the first regulatory enzyme of glycolytic pathway, represents an important putative target for antihelminthic development. The reaction product glucose-6-phosphate also serves as the substrate for pentose phosphate pathway (PPP), yielding NADPH and pentose sugars. While

former maintains the redox potential and detoxification of the cell, the latter molecules are utilized for the biosynthesis of nucleic acids. Hexokinase, the regulatory enzyme of glycolysis, was cloned and characterized from the filarial parasite. The cloning of hexokinase encoding cDNA from filarial parasites has opened avenues to express the open reading frame in a suitable expression system to study the biochemical properties of the enzyme for target validation.

I-16

Development of Novel Dihydropyridines as mdr Reverting Agents- A New Look for Lead Optimization

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Our last few years work was aimed at developing new class of modified multidrug resistance reverting (mdr) agents. Many p-gp inhibitors which are identified so far as first and second generation are of limited clinical use due to their inherent (and parent)pharmacological activity.
In recent years, this laboratory has developed several small libraries of compounds which have shown to possess powerful P-gp inhibiting activity, almost devoid of cardiovascular effects, but capable of inhibiting liver CyP3A. Thus, the current work aims at presenting a review work on DP-7-a lead compound for the development of novel dihydropyridines which do not affect CYP enzyme system, but still retain the activity towards ABC-efflux transporters. An effort towards lead optimization will also be presented.

References:

1. Synthline 2006 data base. Entry no.-318546.
2. F. Fusi, S. Saponara, M. Valoti, S. Dragoni, P. D'Elia, T. Sgaragli, D. Alderighi and S. Sgaragli, *Current Drug Targets* (2006), 7, 949-959.
3. Helaga Engi, Hirohsi Sakagami, Masami Kawase, Alpesh Paracha, Denish Manvar, Himanshu Kothari, Priti Adlakha, Anamik Shah, Noboru Motohashi, Imre Ocsovszki & Joseph Molnar, *in vivo*, (2006), 20, 637-644.
4. Sufi Reza, M.D. Morshed, Ken Hashimoto, Yukie Morotani, Masami Kawase, Anamik Shah, Kazue Satoh, Hirotaka Kikuchi, Hirofumi Nishikawa, Jun Maki & Hiroshi Sakagami, *Anticancer Research*, (2005), 25, 2033-2038.
5. Tulpule Anil, *Current Opinion in Oncology*, (2005), 17(5), 466-468.
6. Cheol-Hee Choi, *Cancer Cell International* (2005), 5, 30.
7. Simona Saponara, Masami Kawase, Anamik Shah, Noboru Motohashi, Joseph Molnar, Katalin Ugocsai, Giampietro Sgaragli & Fabio Fusi, *British Journal of Pharmacology* (2004) 141, 415-422.
8. Masami Kawase, Anamik Shah, Harsukh Geveriya, Noboru Motohashi, Hiroshi Sakagami, Andreas Varga & Joseph Molnar, *Bioorganic & Medicinal Chemistry* (2002), 10, 1051-1055.
9. Gyongyi Gunics, Noboru Motohashi, Joseph Molnar, Sandor Farkas, Masami Kawase, Setsuo Satio & Anamik Shah, *Anticancer Research* (2001), 21, 269-274.

10. Anamik Shah, Harsukh Geveriya, Noboru Motohashi, Masami Kawase, Setsuo Saito, Hiroshi Sakagami, Kazue Satoh, Yukio Tada, Agnes Solymosi, Kriatina Walfard & Joseph Molnar, *Anticancer Research*, (2000), 20, 373-378.

I-17

Biocatalysis at BASF: An Elegant Path to Pharmaceutical Intermediates

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Biocatalysis is of fast growing importance for pharmaceutical, agricultural and the chemical industry. Presently, BASF and others have successfully developed several biocatalytic production processes to an industrial scale.

Biocatalysis offers various advantages:

- Reduction of reaction steps in production through single-step transformations
- High yields because of excellent selectivity
- Energy savings due to mild reaction conditions and minimization of the number of reaction-steps
- Environmentally friendly due to less waste formation
- Opportunity for the development of new products

Biocatalytic processes are not intrinsically superior to chemical synthesis. In each single case a thorough analysis has to be done which process is the best, a skilful optimization being pivotal to fully exploit the enormous potential of biocatalysis. We consider biocatalysis and chemocatalysis as complimentary techniques to provide sophisticated products. The synergies between them have to be exploited.

I-18

Novel strategies for vaccine construct towards enhanced immunogenicity and HIV recognition

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Vaccination strategies remain elusive that are effective against viral disease pathogens yet remain gentle enough for widespread human use. We developed a model system that relies on the recognition of specific T-cell epitopes from immunodominant antigens of HIV to explore single-stranded CpG-oligodeoxynucleotides (ODN) (CpG) as an adjuvant. We improved upon current strategies of utilizing CpG in combination with peptide vaccines by covalently modifying epitope fusion peptides with CpG motifs. Characterization of the immune recognition of DNA–peptide conjugates was carried out in a murine model of human HLA A2. Immunogenicity of DNA–peptide conjugates was superior in sensitivity to non-covalently linked mixtures of the same functional molecules as measured by peptide-mediated

cytotoxicity and IFN-_ release, as well as protection against viral infection. Enhancement of sensitivity of immune recognition by covalent attachment of DNA to epitope peptides should be further evaluated as a novel prophylactic vaccine strategy for HIV infection and other infectious diseases.

I-19

Heterocylces for Pharmaceuticals

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Heterocycles form by far the largest of classical divisions of organic chemistry and are of immense importance biologically, industrially and indeed to the functioning of any developed human society 85% pharmaceutical are heterocycles. Many heterocyclic compounds are biosynthesized by plants and animals and are biologically active. Some heterocycles are fundamental to life, such as haem derivative in blood and chlorophyll essential for photosynthesis. Similarly, the paired bases found in RNA and DNA are heterocycles, as are the sugars that in combination with phosphates provide the backbones and determine the topology of these nucleic acids. The biological properties of heterocycles in general make them one of the prime interests of pharmaceutical industry and biotechnology industry.

Although the formation of by-products resulting from undesirable side reactions can be avoided by improving reaction conditions, formation of co-products i.e. accompanying reactions leading to desired product is inevitable. Unless isolation and conversion of such co-products into useful compounds are very easy, they become waste materials. To be useful on industrial scale, it is particularly important to avoid column chromatography in the isolation procedure. Thus, development of effective and efficient methods for recovery and reuse of co-products is highly desirable from both an environmental and economic perspective. In this context, we have initiated work on the synthesis of heterocycles with an aim to understand their various biological activities.

With increasing environmental concerns and the regulatory constraints faced in chemical and pharmaceutical industries, development of environmentally benign organic reactions has become crucial and demanding research. Therefore, more and more chemists undeavors are devoted toward green chemistry which means the reagents, solvents and catalysts are environmentally friendly.

Over the past few years significant amount of research activities in chemical community have been directed the development of new technologies and novel methodologies for environmentally benign process for pharmaceuticals and their intermediates that have little or no pollution potential or environmental risk and are both economically and technologically feasible. As a part of this program a significant effort was directed towards development of efficient, economical and green technologies and methodologies.

References:

1. B. P. Bandgar, Sampada Bettigeri *Organic Lett.* **2004**, *6*, 2105.
2. B. P. Bandgar, S. S. Pandit *Tetrahedron Lett.*, **2003**, *44*, 2331.
3. B. P. Bandgar, S. S. Pandit, *Tetrahedron Lett*. **2003**, *44*, 3855.
4. B. P. Bandgar, S. S. Pandit *Tetrahedron Lett*. **2002**, *43*, 3413.
5. B. P. Bandgar, K. A. Shaikh, *Tetrahedron Lett.*, **2003**, *44*, 1959.

6. B. P. Bandgar, S. S. Sawant, *Synth. Commun*. **2006**, *36*, 859.
7. B. P. Bandgar et. al. *Synlett*, **2006,** *17*, 2719.
8. B. P. Bandgar, et. al. *J. Mol. Cat. A; Chemical* **2006**, *256*, 99.
9. B. P. Bandgar, A. V. Patil, *Tetrahedron Lett.* **2007**, *48*, 173.
10. B. P. Bandgar et. al. *Tetrahedron Lett.*, **2007**, 48.

I-20

Chemistry of Novel Paclitaxel Analogs

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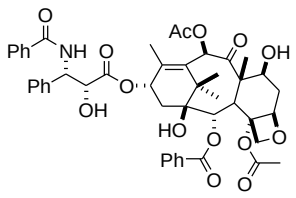
Paclitaxel (Taxol®) and docetaxel (Taxotere®) are anticancer drugs widely used in the treatment of ovarian cancer. Their cytotoxic activity is due to their ability to enhance microtubule assembly and to stabilize microtubules by preventing their depolymerization. Although both paclitaxel and docetaxel posses potent antitumor activity, treatment of these drugs often results in a number of side effects including multidrug resistance (MDR). Recent efforts are aimed at developing new taxoids with a superior antitumor profile against a variety of paclitaxel sensitive and resistant tumor models. Such analogs will have the potential to demonstrate an expanded or improved spectrum of activity in cancer patients without displaying any additional toxicity. Challenges in the development of these novel paclitaxels will be presented.



Paclitaxel

New Analogs

I-21

Studies on glycal derived 2, 3-epoxy alcohols and their application towards syntheses of trisubstituted THF derivatives

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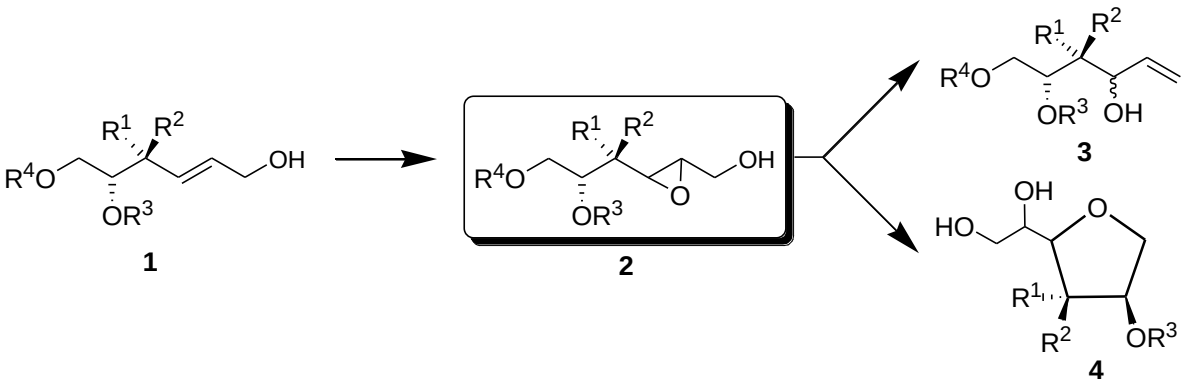
Carbohydrates as precursors in tetrahydrofuran (THF) synthesis have been used extensively. Among the plethora of methods available in literature intramolecular cyclization of epoxyalcohols in S_N2 is one of the useful reactions for the construction of these oxygen heterocycles (oxolanes). Actually, many biologically active compounds have been synthesized according to this strategy. Recently, we carried out a detailed study on the sugar derived 2,3-epoxy alcohols whose synthesis and applications will be discussed in detail.



I-22

Synthesis of several new series of heterocyclo-thiazolidin-arylidine and thiadiazolyl-azetidines: Biological active molecules

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Heterocyclic products has captured our attention for many important reasons among them they are biological importance and drug applications. Heterocycles and their derivatives have attracted the attention of chemists mainly because of broad spectrum biological activities associated with this class of the compounds. Heterocyclic chemistry is a branch which is inseparable from mankind origin or history since it fulfils our basic need. Heterocyclic ring systems containing nitrogen and sulphur hetero atoms exhibited marked chemotherapeutic activities. 4-Oxo – thiazolidines and their 5-arylidines derivatives possess a variety of therapeutic activity as reported in the literature. The N-C-S linkage present in thiadiazoles makes them of versatile biological interest as pesticides and chemotherapeutic agents. A large number of antibiotics contain azetidinones(â-lactam) moiety. The reactivity of azetidinones influences largely on substitution. 2- azetidinones and its derivatives show several biological activity. Therefore methods for the synthesis or elaboration of such systems are of significant interest. A new strategy has been developed for the synthesis of these bioactive compounds using azines and azoles as the potent intermediates. We have selected so many heterocycles and synthesised several 2-arylidenylamino-1,3,4-thiadiazoles; 4-substituted-aryl-3-chloro-2-oxo-azetidines; 2-substituted aryl-4-oxo-thiadiazolidines and 5-arylidine-2-aryl-1,3-thiazolidin-4-ones. The structures of the products were confirmed by spectral and chemical methods. Most of the synthesised products were screened for their antimicrobial, antiinflammaory, anticonvulsant, analgesic, diuretic, anthelmintic, antitubercular, anti-HIV, anticancer etc activities. Some of the compounds displayed acceptable and remarkable biological activity.

I-23

Phosphatidylinsitol kinases/phosphatases as drug targets for Inflammation and Cancer

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The phosphatidylinositols, a unique class of phospholipids, have acquired great importance in cell and membrane biology. A number of key cellular events (signal-transduction, vesicular-traffic, chemotaxis, development, membrane micro domain organization etc) are mediated by these lipids and specific kinase/ phosphatase enzymes involved in their biosynthesis and function. Recent advances in the biology of PI signaling pathway have shown that in a number of disease conditions (inflammation and cancer), the PI signaling pathway is up-regulated providing newer opportunities for drug discovery. The cell biology of PI biosynthesis and new approaches for targeting PI pathway for management of inflammation and cancer will be discussed.

I-24

Joys of Natural Molecules for Drug Discovery and Rationalising Indian Traditional Medicines

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Historically, anti-infective and anti-tumor targets have been the effective area of natural product research worldwide. Today, with the advent of genomic research and newer molecular biological tools for developing bioassays, more specific biological assays are being employed routinely in industrial drug discovery paradigm. However, success has been confined mainly to microbial resources, where pharmaceutical industry took more interest. Consequently, this paradigm shift brought in an emerging perception that chemical diversity, especially amongst low molecular compounds, may no longer be in short supply and the influence of natural product upon drug discovery may start to diminish. Truly, there has been a decline in the discovery processes from the traditional or empirical local medical practices. The higher plants that served mankind for millennia as traditional medicines were cast aside for years. In recent Rediscovering Natural Products popularly known as "Natural Products Redux" natural products drug discovery appears to be reclaiming attention and is on the verge of a comeback. There is betting on Natural Products for Cures. In the natural products drug discovery, traditional, as well as novel approaches are being applied. Moving beyond Natural Products, organic synthetic chemistry amplifies the potential of natural products as drug leads. However, the influence of natural product upon drug discovery shall remain a subject of debate until the newer strategies fulfill their promise. For India, the research on traditional medicines has become even more urgent as fallout of WTO and little interest of multinational pharmaceutical companies in our traditional systems of medicines and use of biodiversity therein.

In order to focus the research in traditional medicines to serve national interests of our Country, the first priority is the need for the objective assessment of the therapeutic quality of herbal medicines. The dividing line between the modern therapies and traditional therapies is imprecise. The assessment of quality can be made easier if distinction is drawn between rational and empirical medication. The main problem in establishing the former is the occurrence of marked psychodynamic effect associated not only with the active substances itself, but also with its typical indications. The future course of natural products development shall hold in pre-clinical stages only till some breakthrough occurs with respect to rationalization of indigenous systems of medicine.

This presentation shall attempt to provide the synopsis of the most important researches that contributes in rationalizing traditional medicines through development and discovery of bioactive molecules. Our group is actively involved in generation of vast known/unknown natural product libraries from traditional medicines and creating innovative formulations from thereof. The author's laboratory has contributed in discovering and identifying new chemical entities (NCEs) for the therapeutic areas of diabetes, inflammation/immunomodulation, gynecology, endocrine dysfunction, CNS, cancer, protozoal, infective diseases, obesity and hyperlipidemia etc. The group also has standardized models in the above mentioned areas for the screening of natural products. In a paradigm shift from discovery of single bioactive molecules, multiconstituent mainstay of bioactive extracts for synergistic and antagonistic studies at cellular and molecular levels is given emphasis for rationalizing traditional medicines.

I-25

Design and Synthesis of Novel Kinase Inhibitors

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Perturbation of protein kinase mediated cell signaling pathways is associated with a number of diseases, including cancer, diabetes, and inflammation. Protein kianses can be targeted at various stages of cell signaling pathway; from the a) receptor tyrosine kinases that initiate intracellular signaling, through b) second-messenger generators and kinases involved in signaling cascades, to the c) kinases that regulate the cell cycle that governs cell fate. Thus, kinase inhibition has become a major area for therapeutic intervention.
As a part of oncology programme at Dr. Reddy's, we have carried out an intense medicinal chemistry efforts in generating a number of structurally diverse kinase inhibitors targeting the 1) Ras-MAPK signaling cascade comprising of Ras / Raf / MEK / MAPK and 2) Aurora kinases. The design, synthesis and the biological results will be presented.

I-26

A versatile strategy for evaluating herbal remedies

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Efforts to understand and properly define therapeutic potentials of traditionally known herbal remedies have led not only to the discovery of numerous currently prescribed drugs, but also to many modern concepts and principles of pharmacology. Since many such herbs have not yet been properly explored, they continue to be of interest of many modern drug discovery projects. Major goals of these more modern efforts are: 1) to obtain structurally novel therapeutic leads and hits, 2) to identify bio-active components suitable for standardising therapeutically used herbal preparation, 3) to experimentally verify a traditionally known medicinal use of a herb, 4) to obtain a patentable herbal extract suitable for a defined therapeutic purpose, or 5) to meet the demands of drug control authorities. Although diverse feasible strategies for achieving each of these goals are now available, none of them are particularly suitable for systematic search of novel modes of actions plausible for traditionally known herbal remedied. Since many laboratories are not adequately equipped, several of them

can not yet be properly explored by many. In addition, validity of some of the more modern approaches has not yet been established.

It can not be overemphasised that traditionally known medicinal uses of many herbs are not identical to those of modern drug and that such uses of most of them are not restricted to one define therapeutic indication only. In general, these and many other traditionally known, or more recently realised facts, are often neglected by most medicinal plant based drug discovery projects. In view of the situation, attempts were made to identify the most prominent, or appropriate, therapeutic potential of some traditionally known medicinal herbs in more modern sense of the term. The strategy and concepts used to achieve the goal will be discussed in this communication. In this approach, existing knowledge on chemical constituents medicinal herbs, and on their reported bio-activities, are given due considerations for selecting extraction, fractionation and pharmacological screening procedures. In addition, structure activity studies with chemical constituents of the herbs are integrated in these studies. Extensive use of existing knowledge, and modified use of well established pharmacological screening models are the salient features of this strategy.

Using this approach not only novel therapeutic potential of a three traditionally known medicinal plants, but also several structurally and functionally novel hits and leads suitable for drug development purposes could be identified. Several bio-active herbal constituents useful for validating and identifying therapeutically relevant pharmacological targets were also the fruits of these efforts. Knowledge and experience gained by the use of the strategy reaffirm the convictions that proper definition of the therapeutic indication of traditionally known medicinal plants in terms of modern medicine is an essential pre-requisite for achieving broader acceptance of herbal remedies. Therefore, it seems reasonable to suggest that, at present, proper evaluation therapeutic alternatives offered by many herbal remedies is possible only when all existing knowledge on them is given due considerations.

Oral-1

Design, Synthesis and SAR of Peptide Analogs of CIYKYY as Src Tyrosine Kinase Inhibitors

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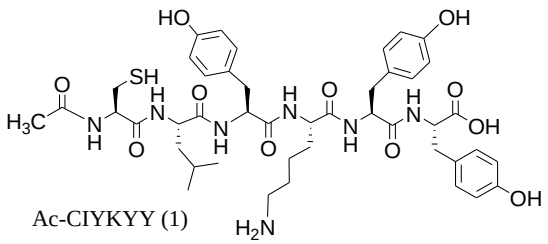
Src tyrosine kinases have been implicated in the development of osteoporosis and inflammation-mediated bone loss and different cancers for which the transformed phenotypes have been correlated with Src mutations and/or overexpression. Therefore, Src has become an intriguing target for drug discovery [1,2]. In contrast to ATP binding site, a few peptides have been identified as substrates for Src tyrosine kinases. Most of these peptide substrates are rather weak inhibitors with K_m in high micromolar or in millimolar range. The best example from these studies is Ac-CIYKYY (**1**), which was reported to be an inhibitor of Src [3]. The mechanism of c-Src inhibition by **1** remains unknown. Our radioactive kinase assay showed that **1** (IC_{50} 400 μM) was a weak inhibitor of polyE_4Y phosphorylation by active c-Src [4].

To understand the structure-activity relationship of peptide inhibitors and develop potent Src tyrosine kinase inhibitors from weak inhibitors we synthesized two classes of peptide analogues of **1**. Class I included linear peptides that were synthesized by replacing tyrosine residues with tyrosine mimics containing other functional groups or by modifying the side chains of tyrosine residues. Class II included conformationally constrained peptides that were synthesized by linking the side chains of amino acids together. Four types of conformational constraints were introduced by linking the amino acids head to tail, *C*-terminal to a side chain, *N*-terminal to a side chain, and a side chain to a side chain. All final compounds were purified (>95%) using preparative HPLC and characterized by a high-resolution time-of-flight mass spectrometer. The inhibitory potencies of the synthesized linear and constrained peptides against active c-Src were examined using a radioactive kinase assay with polyE_4Y as the substrate. Peptide Ac-CIYKF(NO_2)Y, in which the nitrophenylalanine is located at position 5, exhibited a significantly higher inhibitory potency (IC_{50} = 0.53 μM) by approx. 750-fold vs. Ac-CIYKYY. Furthermore, a constrained peptide synthesized by linking side chains Y3 and K4 exhibited an approximate 1400-fold increase in inhibitory potency (IC_{50} = 0.28 μM) when compared to the corresponding linear peptide. The details of synthetic schemes, inhibitory potencies and SAR will be presented.



Ac-CIYKYY (1)

REFERENCES:

1. K. Parang, G. Sun, *Expert Opin. Ther. Patents* **2005**, *15*, 1183.
2. K. Parang, G. Sun, *Curr. Opin. Drug Disco*V*ery De*V. **2004**, *7*, 630.
3. K S. Lam, J. Wu, Q. Lou, *Int. J. Pept. Protein Res.* **1995**, *45*, 587.

4. A. Kumar, G. Ye, Y. Wang, X. Lin, G. Sun, K. Parang, *J. Med. Chem*. **2006**, *49*, 3395

O-2

Synthesis And Biological Potential of A Natural Cyclopeptide – Segetalin D

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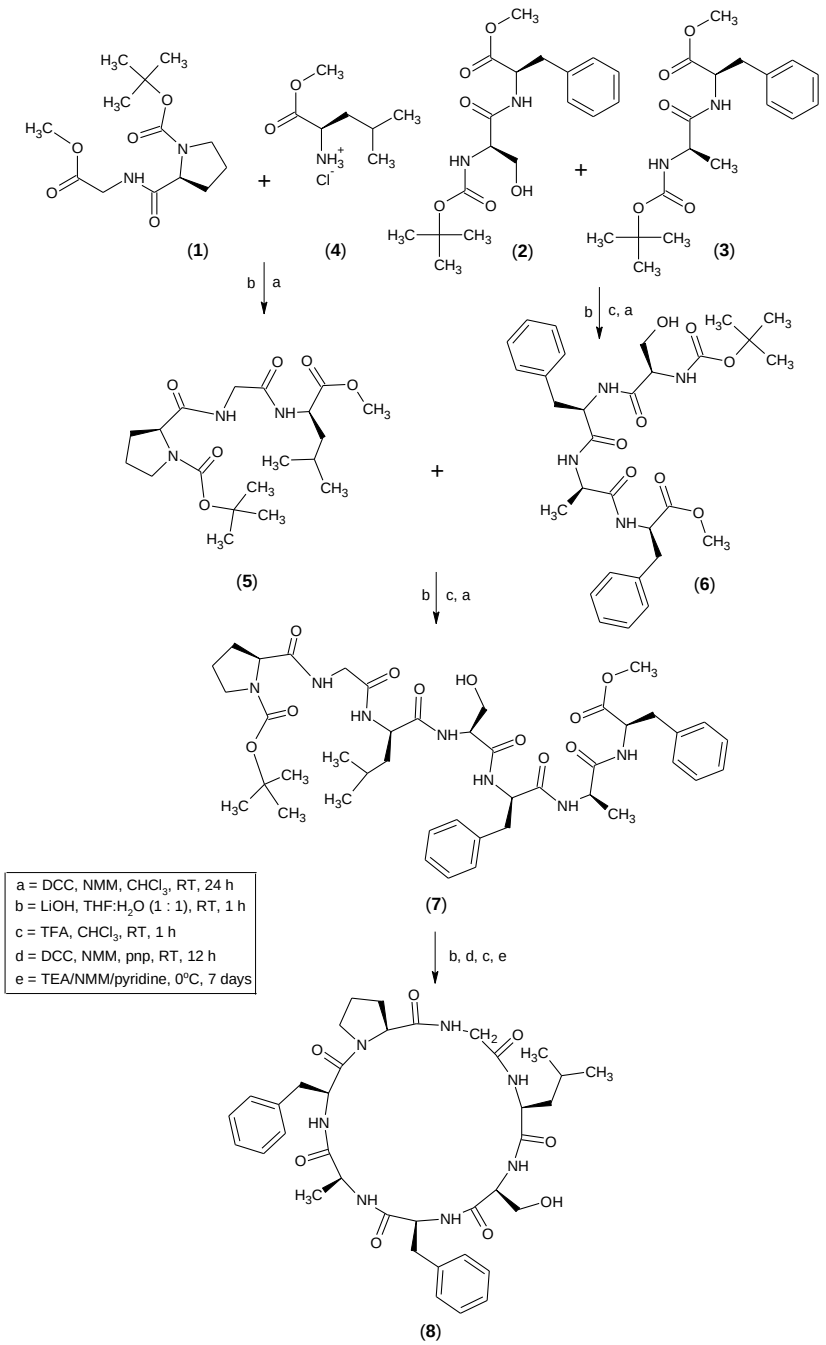
Segetalins are the natural cyclic polypeptides isolated from seeds of higher plant *Vaccaria segetalis* (Caryophyllaceae) and exhibited potent cell growth inhibitory activity against P-388 leukaemia cells and estrogen-like activity. Keeping in view the biological potential of segetalins as well as to obtain a bioactive peptide in good yield, the present work was aimed at synthesis of phenylalanine rich cyclic heptapeptide, Segetalin D by solution phase technique.

In order to synthesize, the molecule was disconnected into three dipeptide units and a single amino acid unit: Boc-Pro-Gly-OMe (**1**), Boc-Ser-Phe-OMe (**2**), Boc-Ala-Phe-OMe (**3**) and Leu-OMe.HCl (**4**). After deprotection at carboxyl terminal, dipeptide unit (**1**) was coupled with amino acid methyl ester hydrochloride (**4**) using DCC to get the tripeptide unit Boc-Pro-Gly-Leu-OMe (**5**). Similarly, dipeptide units (**2**) and (**3**) were coupled with each other to obtain tetrapeptide unit Boc-Ser-Phe-Ala-Phe-OMe (**6**), after appropriate deprotection at carboxyl and amino terminals. The ester group of tripeptide unit (**5**) was removed using LiOH and Boc group of tetrapeptide unit (**6**) was removed using TFA. Both the deprotected units were now coupled using DCC and NMM to get Boc-Pro-Gly-Leu-Ser-Phe-Ala-Phe-OMe (**7**). After introducing p-nitrophenyl ester group and removal of Boc group, linear heptapeptide unit was cyclized by keeping the whole contents at 0 □ C for 7 days in presence of catalytic amount of TEA / NMM / pyridine to get Segetalin D (**8**) (**Scheme I**).

The structure of the synthesized cyclopeptide was confirmed by spectral as well as elemental analysis and found to possess high level of cytotoxic and anthelmintic activity, in addition to good antimicrobial activity against pathogenic fungus *Candida albicans* as compared to standard drugs.



Scheme I

O-3

One Pot Multicomponent Reactions Catalised By Cyanuric Chloried Synthesis Of Benzopyran Derivatives Under Mild Conditions

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The multicomponent reactions strategies offer significant advantages over conventional linear type synthesis to provide products with the diversity needed for the discovery of new compounds. In 1893 the Italian Chemist Pietro Biginelli reported a cyclocondensation

reaction between the active methylene compound, aldehyde & urea under strong acidic conditions.
In the present work we report, one pot multicomponent reaction for the synthesis of benzopyran derivatives by using cyanuric chloride as a catalyst. Cyanuric chloride is safe and highly in expensive reagent. The active methylene aldehyde & substituted phenols reacts with catalytic amount of cyanuric chloride to offered the benzopyran derivatives in good to excellent yield under mild reaction condition.

O-4
Synthesis of Novel Pyrazoles by Microwave and Conventional methods

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Indoles are the well known heterocycles which are present in variety of natural products and medicinal agents.Pyrazole ring systems is associated with diverse biological activities like fungicidal, herbicidal, virucidal and insecticidal. In view of these it was thought of interest to combine these two in order to develop a molecule which is biologically more potent.
α-β-Unsaturated ketones are obtained by the base catalyzed condensation of substituted acetophenones and various 5-substituted-2-phenylindole-3-carboxaldehydes.These on reaction with substituted hydrazide in ethanol yielded substituted pyrazoles. All the compounds were characterized by their physical and spectral data.

O-5

A Journey Towards The Search for New Antidiabetic Agents

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India is now facing a major health care burden due to rising prevalence of type 2 diabetes mellitus (T2DM). Urbanization and the changes in life style are strong risk factors for diabetes and other associated disorders. Though it was thought in the mid of 90's that there will be strong need to evolve targets-oriented approach in evolving R & D strategies to meet the challenge of control of hyperglycaemia and prevent the secondary complications of T2DM. R & D efforts in the last years though have witnessed many of the molecular targets and PPAR-alpha and gamma receptor activators but a successful therapy is still awaited.
Strategies and modalities to control diabetes mellitus exist in the Indian system of medicine "Ayurveda". Medicinal as well as edible plants can play a very significant role in addressing specific targets, to operationalize the aforesaid strategy and leads for the design and synthesis of new antidiabetic agents In the last 10 years nearly 200 medicinal plants and 100 marine flora and fauna have been evaluated for antihyperglycaemic activity by our group, and the active species were further fractionated and the fractions were evaluated towards the search for antidiabetic entities. The success stories lie in the terrestrial plants *Derris indica, Aegle marmelos, Ficus bengaliensis*, and marine mangrove *Ceriops tagal, Rhizophora apiculata* and soft corals *Sinularia firma and Sinularia erecta*, respectively.

O-6

Synthesis and Antidiabetic Evaluation of New Thiazolidinediones.

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Diabetes mellitus is a chronic condition that occurs due to abnormal carbohydrate metabolism characterized by hyperglycemia, which can lead to serious damage to many of the body's systems, especially the heart, eye, kidney, nerves and blood vessels etc. A number of 2,4-thiazolidinediones are endowed with wide range of biological activities. The interest in 2,4-thiazolidinedione derivatives has been heightened markedly because of their development as a new class of oral antidiabetic drugs, improving insulin sensitivity and lowering blood glucose, free fatty acids and triglyceride levels.
Considering the urgent need of new safer antidiabetic molecules, some attempts have been made to obtain new thiazolidinediones. 3-[(5'-Arylidenyl-2',4'- thiazolidinedionyl) - methyl]-1, 3, 4-oxadiazolin-5-thiones **(4)** have been synthesized starting from 5-arylidenyl-2,4-thiazolidinediones **(1).** These 5-arylidenyl-2,4-thiazolidinediones **(1)** on condensation with bromoethyl acetate and then subsequently with hydrazine hydrate gave 5-arylidene-2,4-thiazolidin-3-yl acid hydrazides**(3)**. Thus formed 5-arylidene-2,4-thiazolidin-3-yl acid hydrazides**(3)** on cyclization with CS_2 in presence of KOH yielded the titled, 3- [(5 '-arylidenyl - 2', 4'- thiazolidinedionyl) - methyl]-1, 3, 4-oxadiazolin-5-thiones **(4)**. All the compounds have been evaluated for antidiabetic activity using alloxin induced rat models. The details of the synthetic path and the antidiabetic activity will be presented.

O-7

Synthesis of New Benzopyrano{4,3-d]-2-toluene sulfonamido pyrimidines

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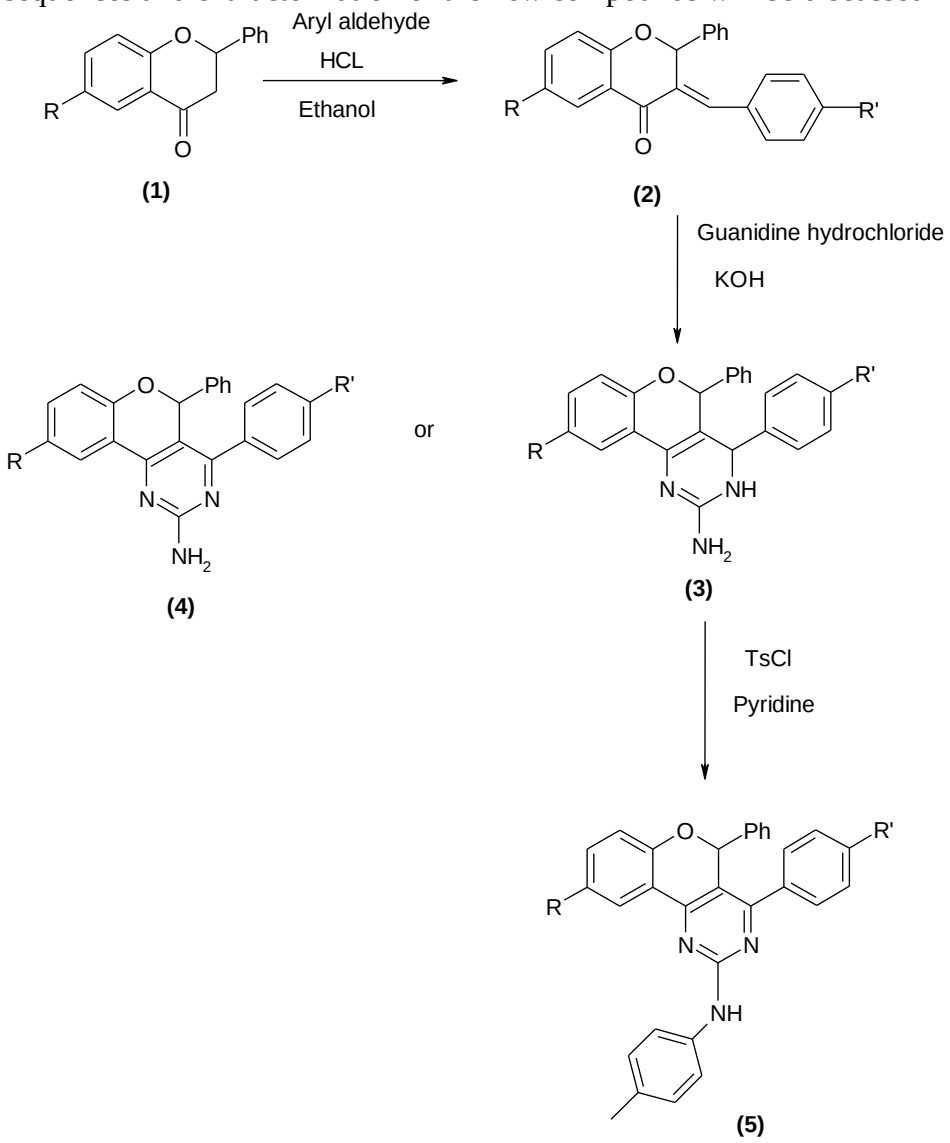
Sulphonamide, chromanone and 2-amino pyrimidine derivatives are widespread in medicinal and natural products chemistry. Sulphonamide is a diverse group of compounds of considerable medical importance and are used as protease inhibitor, analgesic, erectile dysfunction and antimigraine agents etc. 3- Substituted-4-chromanones constituted the basic structure of natural products possessing biological activities such as anti-mutagenic, anti-inflammatory and antiviral activity against HIV. 2-Amino pyrimidines is an interesting structural element that is found in compounds with potential biological functions as diverse as antipsychotic, cardioprotective and antimalerial activities
Inview of the above pharmaceutical significance, hence it was planned to construct new molecules having all the above pharmacophores in a molecular framework with a hope to obtain the new molecules with intensified bioactivities.
Therefore, the synthetic path for the synthesis of 4-aryl-5-phenyl-9-substituted benzopyrano[4,3-d]4,3-dihydro-2-(4'-methyl benzene sulphonamido) pyrimidines **(5)** has

been developed. The required intermediates, 3-arylidene-2-phenyl-6-substituted chromanones (chalcones) **(2)** have been synthesized by condensing 2-phenyl-6-substituted chromanones **(1)** with aryl aldehydes, using Claisen-Schmidth reaction. These chalcones on cyclocondensation with guanidine hydrochloride yielded 4-aryl-5-phenyl-9-substituted benzopyrano [4,3-d] 3,4-dihydro-2-amino pyrimidines **(3)** by reacting in presence of alcoholic potassium hydroxide. Thus obtained 2-amino pyrimidines **(3)** when then refluxed with 4'-methyl benzene sulfonyl chloride in pyridine gave compounds, 4-aryl-5-phenyl-9-substituted benzopyrano [4,3-d] 4,3-dihydro-2-(4'-methyl benzene sulphonamido) pyrimidines **(5).** The details of the synthetic sequences and characterization of the new compounds will be discussed in the presentation



O-8

Bioactive Molecules from the Flora of North East India : Phytochemical Investigations at RRL, Jorhat

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India was identified as one of the twelve megacentre of biological diversity endowed with about 45,000 species of plants and nearly 81,000 of animals species; about 33 % of these are endemic to this country only.[1-2] The North Eastern part of this country is often called a sleeping giant because of its huge natural sources and most of which are not fully explored for benefit of mankind. Although the total area of this region is about 2,55,037 square kilometres, about (8% of that of the country). Because of its unique geographical, geological as well as ecological conditions, this area possesses about 50 % of the total flora of India; out of which about 3000 species have been identified as medicinal plants. This region is inhabited by a large number of isolated ethnic tribal groups, who depend mostly on the local herbs for their primary health care and therby possess a vast knowledge base of traditional medicines. The Regional Research Laboratory (RRL), Jorhat, since its inception has been putting emphasis on the effective utilization of this unique natural resources. A large number of such plants and also few microbes, have been chemically examined at RRL-Jorhat and isolated hundreds of new molecules of diverse structural types.[3-12] Many of these compounds have been evaluated against insects pests and few of them have also been tested for other biological activity. In this presentation we will discuss, results of the investigation done at RRL-Jorhat.

REFERENCES:

1. Anonymous, ***The Hindu Business Line***, 15 May, **1995.**
2. Myers, N., R. A.*et al*. ***Nature* 2000**, **403**, 853-858
3. Bordoloi,M.*et al* ***Phytochemistry*, 1993**, **34**(2) , 583-584.
4. Bordoloi M., *et al* ***Phytochemistry*, 1997, 44**, (5), 939-942.
5. Bordoloi M, *et al*, ***Tetrahedron Letters***, **1985, 26**(4), 509-510.
6. Bordoloi M *et al*; ***Tetrahedron Letters*, 1996, 37**(37), 6791-6792
7. Bordoloi M *et al*; ***Phytochemistry*, 1996, 41**, 557-559
8. (a) Bordoloi G N, Kumari B, Guha A, Bordoloi M, Roy MK and Bora TC; ***Biosci. Biotech. Biochem***. **2001, 65**(8): 1856-1858. (b) Bordoloi G N, Kumari B, Guha A, Bordoloi M, Roy MK and Bora TC; "2-methylheptylisonicotinate and process for production thereof" **USA patent application**, 20020161027 dated 31-10-2002.
9. Bordoloi G N, Kumari B, Guha A, Bordoloi M, Roy MK and Bora TC; ***Pest Manag. Sci.* 2002, 58**, 297-302.
10. Chakroborty v and Bordoloi M**,** 2,3,9,20,21-pentahydroxycholest-7-en-6-one from Eastern Himalayan Yew, ***Ind. J Chem*, 2003, 44B,** 944-945. and references cited therein (b) Chakroborty V and Bordoloi M**,** "A novel phytoecdysteroid" **Indian Patent** No 0165/DEL/2001.
11. Kotoky R, Kanjilal PB, and Bordoloi M, ***Ind. J. Chem***., **2005, 44B** , 434-435 and references cited therein.
12. Bordoloi PK, Bordoloi M and Rao PG, ***Phytochemistry*, 2007** (manuscript under preparation).

O-9

Green chemical alternatives from synthons to biodynamic heterocycles: Selectivity under microwaves

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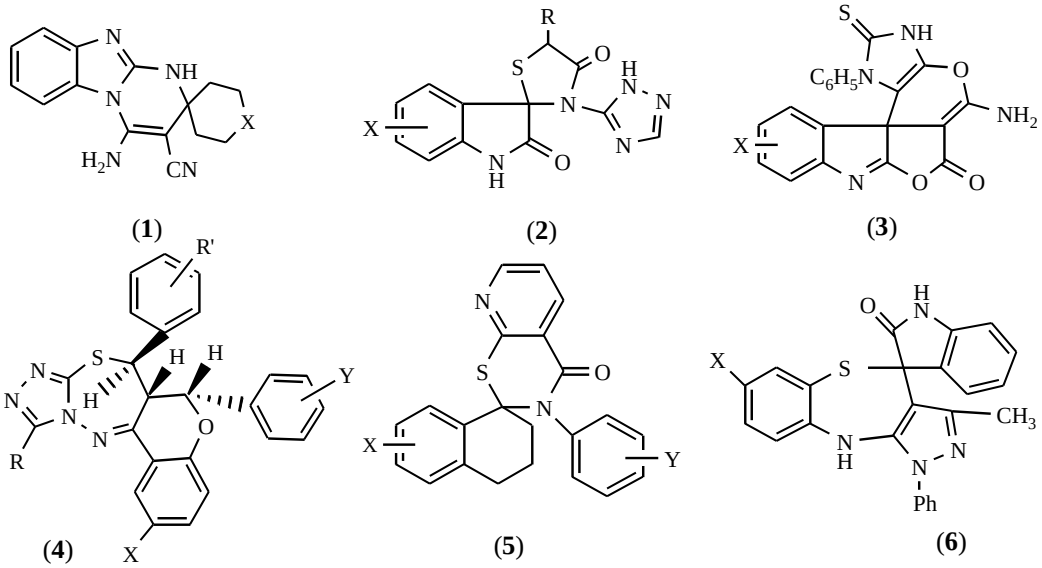
Multi-component reactions (MCRs) involving domino process with at least three different simple substrates have emerged as a powerful strategy for medicinal chemistry and drug discovery applications. Under the framework of 'Green Chemistry', we have developed environmentally benign, solvent-free, multi-component approaches for the synthesis of wide variety of biologically important scaffolds, spiro and annulated heterocylces under non-traditional conditions. Chemo/regio/diastereoselectivity was also observed in the synthesis of novel spiro-pyrimido[1,2-a]benzimidazoles (**1**), spiro-thiazolidinones (**2**), imidazolo[5″,4″; 5′,6′]pyrano[4′,3′;3,4]furo[2,3-b]indoles (**3**) and benzopyrano[4,3-e]triazolo[3,4-b][1,3,4]thiadiazepines (**4**). There is a remarkable improvement over the conventional two component synthesis, favoring atom economy and leads to reduction in time, enhancement in conversions with several advantages of eco-friendly approach. In few cases, e.g., synthesis of spiro[pyrido-thiazines](**5**) and pyrazolo[4,3-c][1,5]benzothiazepines (**6**), even those system that were reluctant to under go any reaction thermally under harsh conditions for many days could be induce to react under microwaves. The structure of some representative compounds has been confirmed by X-ray crystallography.



References:

1. A. Dandia, P. Sarawgi, J. E. Drake and R. Ratnani**, J. Chem. Res.,** 445-448, **2006.**
2. A. Dandia, R. Singh and S. Khaturia, **Bioorg. and Med. Chem.,**14, 1303-1308**, 2006.**
3. A. Dandia, K. Arya and M. Sati, **Tetrahedron**, 60(24), 5253-5258, **2004.**
4. Dandia, R. Singh and P. Sarawgi, **J. Fluorine Chem,** 125(12), 1835-1840**, 2004;** 125(9), 1273-1277, **2004**.
5. Dandia, M. Sati and K.Arya, **Chem. Pharm. Bull.,** 51(10),1137-1141, **2003**.
6. A. Dandia, M. Sati, K. Arya and A. Loupy, **Heterocycles**, 60(3), 563-569, **2003.**
7. A. Dandia, M. Sati and A. Loupy, **Green Chemistry**, 4(6), 599-602, **2002**

O -10

DBU Catalyzed One-Pot Synthesis of 2-amino-4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile Derivatives Under Solvent-Free Conditions

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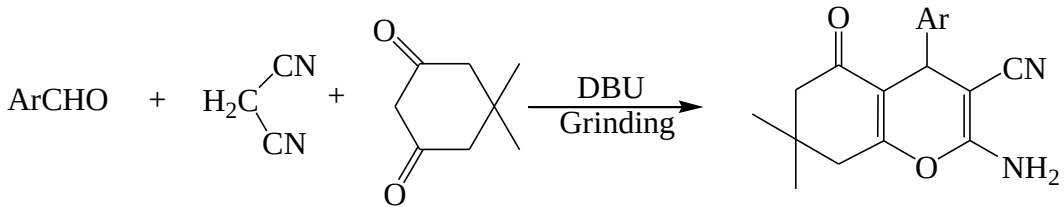
The grinding method has increasingly been used in organic synthesis in recent years. Compared with traditional methods, many organic reactions occur more efficiently in the solid state than in solution and in many cases even more selectively, because molecules in the crystals are arranged tightly and regularly.[1]

In continuation of our ongoing research to develop newer, environmentally benign methods, it has been decided to investigate the use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a catalyst for one-pot synthesis of 2-amino-4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile derivatives under solvent free condition.



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

Reaction Time – (5- 8) min; Yield – (89-95) %.

In conclusion, we have successfully demonstrated the use of DBU as novel and efficient catalyst, for the first time, to the three-component, one-pot synthesis of 4*H*-chromene derivatives at room temperature. This new method is superior to the reported methods with respect to the reaction time and simplicity of the procedure. Moreover conversion is achieved by grinding the reactant in a mortar & pestle under solvent free condition at room temperature. The attractive features of this procedure are the mild reaction conditions, high conversions, cleaner reaction profiles, solvent-free reaction conditions and operational simplicity, all of which make it a useful and attractive strategy for the preparation of 4*H*-chromene derivatives at room temperature.

O-11

Synthesis and DNA Cleavage Studies of Novel Heterocyclic Aza-enediynes

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A class of enediyne antineoplastic antibiotics that are isolated from various Streptomyces bacterial species consist of (*Z*)-1,5-diyne-3-ene core unit embedded within their complex

structures and exert their cytotoxic effects upon suitable activation leading to a highly reactive 1,4-didehydrobenzene diradical via Bergman cycloaromatization.[1] In past, considerable efforts were devoted towards the design and synthesis of simpler analogues of the naturally occurring enediynes and tune their biological activity to meet the requirements of an efficient antitumor drugs being highly active, selective and non-toxic.[2] Incorporation of nitrogen atom into endiyne framework led to the design and synthesis of 3-aza-3-ene-1,5-diyne, which undergoes an aza-Bergman cyclization to afford the fleeting 2,5-didehydropyridine diradicals.[3-5] The protonated 3-aza-3-ene-1,5-diynes anticipated to undergo aza-Bergman cyclization even more readily and can afford products of diradical trapping. However, the hydrolytic instability of the 3-aza-3-ene-1,5-diyne moiety prevents its use in pH dependent DNA cleavage. Recently, we have synthesized more hydrolytically stable systems containing the 4-aza-3-ene-1,6-diyne framework. Synthesis and DNA cleavage studies of [1-methyl-2-(phenylethynyl)-3-(3-phenylprop-2-ynyl)-3*H*-benzimidazolium tetrafluoro borate] and structurally related heterocycles lacking the aza-enediyne functionality, [1,3-dimethyl-2-(phenylethynyl)-3*H*-benzimidazoliumtriflate] and [3-methyl-2 (phenylethynyl)benzothiazoliumtriflate] will be discussed in the presentation.

1. Nicolaou, K. C.; Dai, W.-M.; Tsay, S.-C.; Estevez, V. A.; Wrasidlo, W. Scie***nce*** 1992, 256,1172. (b) Smith, A. L.; Nicolaou, K. C. *J. Med. Chem.*, **1996**, *39*, 2103.
2. Nicolaou, K. C.; Smith, A. L.; Yue, E. W. *Proc. Natl. Acad. Sci.USA* **1993**, *90*, 5881.
3. David, W. M.; Kerwin, S. M. *J. Am. Chem. Soc.* **1997**, *119*, 1464.
    a. Nadipuram, A. K.; David, W. M.; Kumar, D.; Kerwin, S. M. *Org. Lett.* **2002**, *4*, 4543. (b) Kumar, D.; David, W. M.; Kerwin, S. M. *Bioorg. Med. Chem. Lett.*, **2001**, *11*, 2971.
4. Feng, L.; Kumar, D.; Kerwin, S. M. *J. Org. Chem.* **2003**; *68*, 2234.

O-12

Exploring *Leishmania donovani* pteridine reductase 1 as a therapeutic drug target

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Infection with pathogenic *Leishmania* results in a spectrum of human diseases, termed leishmaniasis. The human devastation dealt by these parasites continues, with an annual incidence of 2 million cases in 88 countries. *Leishmania* have a digenetic life cycle, first residing in the gut of phlebotomine sand flies where they replicate as procyclic promastigotes. During a blood meal, the parasites are transmitted and engulfed by vertebrate macrophages, where they will then transform into the amastigote stage and divide within the acidified phagolysosomes. No effective vaccines are available against *Leishmania* infection as yet and treatment relies on chemotherapy. To generate the adequate armory of drugs to treat visceral leishmaniasis, new and effective drug targets are required to combat this dreadful disease. Biochemical pathways present in *Leishmania* but absent from their hosts should, in theory, provide excellent targets for rational drug design. The enzyme pteridine reductase 1 (PTR1, EC 1.5.1.33) of *Leishmania* is one such validated drug target. Biochemical studies indicate that this enzyme is a NADPH dependent pterin reductase and active as a tetramer. This enzyme acts as a metabolic by pass of dihydrofolate reductase (DHFR) so if antifolate chemotherapy is to be developed against *Leishmania*, it must target both DHFR and PTR1 activities. We have characterized *L. donovani* PTR1 at the molecular level, which includes

biochemical studies and structure - modeling approach to generate new insight on this validated drug target in order to identify inhibitors targeting this enzyme specifically. In this regard we have cloned, overexpressed and purified recombinant PTR1 from *L. donovani* clinical isolate, which is chemotherapeutically relevant pathogenic strain. We have also found that regulation of PTR1 is growth phase dependent and it degrades in the stationary phase of growth, when the parasite is undergoing metacyclogenesis. This is mediated by the proteasome and leads to lower levels of H_4-biopterin, which favors metacyclogenesis, and subsequently results in a highly infective stage of the parasite. Therefore, this finding has importance to identify new target molecule like the proteasome for therapeutic intervention.

O-13

Arylated substituted azino/azolo acetylamino-1,3-thiazolidin-4-ones and azetidinones : Novel Chemistry and potential use in medicine.

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Heterocycles and medicines are both inter related because human are totally dependent on the drugs derived from heterocyclic rings. Most of the modern reported life saving drugs contains the heterocyclic unit in their structures and have also fewer side effects. 1,3-thiazolidin-4-ones are the important synthones for various biologically active molecules. A large number of antibiotics contain azetidinones moiety for examples ceftriaxone-a highly effective 3rd generation parenteral cephalosporin and tazobactum-a superior â-lactamase inhibitor are good in activity. In view of wide spectrum of biological activity shown by these molecules incorporating acetylamino-1,3-thiazolidin-4-ones /azetidinones, these molecules have been considered as an important pharmacophore for the introduction in the design of biologically active molecules. I have selected 2-acetylphenothiazine and 2-mercaptobenzothiazole for the present study. The –NH and -SH groups in these heterocyclic moities were used as the target for chemical modifications of important drug products. Several new classes of 5-arylidine-2-substituted-3-acetylamino-1,3-thiazolidin-4-ones and 4-substituted-aryl-acetylamino-3-chloro-2-oxo-azetidines were synthesized. The structures of the products were confirmed by spectral and chemical methods. Most of the synthesised products were screened for their antifungal activity against Trichoderma viride, Botrytis cinerea, Fusarium oxysporium, Aspergillus fumigatus and Rhizopus stolonifer. The ED50 values of active antifungal products were also calculated on a log probit scale from percent inhibition growth data. The antibacterial activity of the products were also determined against Proteus vulgaris, Escherichia coli,Shigella dysenterae and Bacillus pumilis . Some of the products were found to exhibit appreciable activity.

O-14

Experimental and theoretical studies on podophyllotoxin derivatives as effective cytotoxic and anti-fungal agents.

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The anti-fungal and cytotoxic studies of seven C-4 substituted podophyllotoxin derivatives, viz: trans-cinnamyl, cis-cinnamyl, o-methoxy cinnamyl, dimethyl acrylyl, p-methoxy phenyl acetyl, 3,4-dimethoxy phenyl acetyl and 2,5-dimethoxy phenyl acetyl esters of podophyllotoxin on four fungi, viz: *Macrophomina phaseolina*, *Fusarium oxysporum*, *Myrrothecium verrucarria* and *Asperigillus candidus*, and analysis of the results using QSAR studies indicated there is a close linear relation ship between the Log P value of the derivatives and their anti-fungal activity. A linear relationship between the cytotoxic activity and the HOMO-LUMO gap was also observed, indicating that the mode of action of these compounds may be by possible interference in the respiratory cycle of the cells. This study paves the way for the development of lignan based effective anti-fungal agents, while providing an insight into the mode of action of these type of compounds.

O-15

Cobalt Chloride Containing Indicator Grade Silica Gel as a Cheap, Efficient and Reusable Catalyst for Aerobic Oxidation of *p*-Cresol to *p*-Hydroxybenzaldehyde

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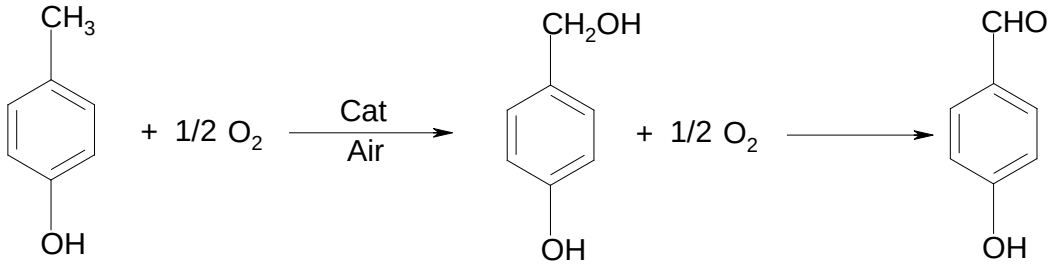
p-Hydroxybenzaldehyde (PHB) is an important intermediate for the manufacture of vanillin, a widely used flavoring agent, trimethoxybenzaldehyde, various agrochemicals, and pharmaceuticals such as semi-synthetic penicillin, amoxycillin, and the antiemetic drug trimethobenzamide.[1-3] The conventional methods for the synthesis of PHB include the oxidation of alkyl benzenes using chromic acid or potassium permangnate,[4] base-catalyzed reaction of formaldehyde with phenol to give *p*-hydroxybenzyl alcohol and its oxidation over platinum or palladium catalysts,[5] and the Reimer-Tiemann process in which phenol reacts with chloroform and aqueous sodium hydroxide to give benzal chlorides, which are rapidly hydrolyzed by the alkaline medium to give salicylaldehyde as a major product and PHB as a byproduct.[6] However, these methods suffer from expensive catalyst systems, generation of environmentally hazardous byproducts or low yields of the desired product, PHB. Therefore, several catalyst systems have been evaluated in the recent past for the liquid phase oxidation of *p*-cresol to PHB, most of which include cobalt in monometallic homogeneous or heterogeneous[7] or bimetallic[8] form. Rode et al have reported liquid phase oxidation of p-cresol to PHB with high conversion and selectivity using insoluble cobalt oxide catalyst (Co_3O_4) and at elevated oxygen pressure.[9]
We report in the present study the application of indicator grade silica gel as an efficient and reusable catalyst for the liquid phase oxidation of *p*-cresol to PHB with high selectivity, in the presence of air as the oxidant. Indicator grade silica gel (ISG) is used as a desiccant for gases in chromatographic analysis, and contains cobalt chloride immobilized on the silica gel surface, which acts as the indicator for moisture content of the gas.

The oxidation of *p*-cresol **1** to PHB **3** is considered to be a sequential reaction, via *p*-hydroxybenzaldehyde **2**, as shown in the scheme below.



1 **2** **3**

Good yields of PHB were obtained using this catalyst. The product was isolated form the reaction mixture by solvent extraction and recrystallization and characterized by ^{1}H and ^{13}C NMR, IR and elemental analysis.

The conversion of the substrates was monitored on a HP 6890 series Gas Chromatograph, using a HP FFAP capillary column, while the product, PHB was monitored on a series 1100 Agilent HPLC, using an RP-8 column using an acidic buffer mobile phase.

The catalyst was recovered after the reaction by filtration and activated in oven at 80˚C for 8 hours, and used as recycled catalyst for the next reaction. It was found that there was negligible loss of catalytic activity upon recycle. The liquid filtrates of the reaction mixture were analyzed for cobalt content by Inductively Coupled Plasma analysis, and it was confirmed that there was almost no leaching of the heterogeneous catalyst. The recycle activity was checked for five successive recycle experiments, and consistent yields of PHB were obtained in all the reactions.

References:

1. Sigeru, T.; Hideo, T.; Takasi, S.; Mitstio, A. *J. Org. Chem.* **1979**, *44*, 3305
2. Rao, D. V.; Stuber, F. A. *Synthesis* **1983**, 4308.
3. Mitchell, S. *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed.; Willy-Interscience: New York, 1998; Vol. 13, pp 1030-1042.
4. Hudlicky, M. Oxidations in Organic Chemistry, American Chemical Society National Meeting, Washington, DC, 1990.
5. J. Oyamada, C. Jia, Y. Fujiwara, T. Kitamura, Chem. Lett. (2002) 380.
6. E.C. Horning, in: Organic Synthesis, Vol. III, Wiley, New York, 1955, p. 281.
7. (a) Nishizawa, K.; Hamada, K.; Aratani, T. EP 0012939, 1979.
   (b) Sharma, S. N.; Chandalia, S. B. *J. Chem. Technol. Biotechnol.* **1990**, *49*, 141.
   (c) Lin, P.; Alper, H. *J. Mol. Catal.* 1992**, *72*, 143**
8. (a) Peeters, M. P. J.; Busio, M.; Leijten, P. *Appl. Catal., A* **1994**, *118*, 51.
   (b) Yumin, L.; Shetian, L.; Kaizheng Xingkai, Y., Yue, W. *Appl. Catal., A* **1998**, *169*, 127.
   (c) Wang, F.; Yang, G.; Zhang, W.; Wu, W.; Xu, J. *Chem. Commun*. **2003**, 1172.
9. Rode, C. V.; Sonar, M. V.; Nadgeri, J. M.; Chaudhari, R. V. Org. Proc. Res. Dev., 8(6), 873-878, 2004

O-16

Biodiversity Hotspot of Northeast India: Urgent Need for Conservation Using Triple Helix Approach

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Plants provide us a number of drugs starting from morphine to taxol and a great future lies ahead in plants from marine sources. There are around 2,65,000 flowering plants in the world but we have knowledge in detail only about 0.5% of them. Modern scientists/experts know about 5-10% of the medicinal plants found in the rain forest area whereas a tribal person knows about medicinal use of 48-80% of the plants around him. Out of the 25 hotspot of biodiversity in the world, India has the two hot spot of biodiversity namely in Western ghats and Northeast region, but the north east has a unique location. On one side it has Himalayan impact and on the other hand there is a coastal impact. This unique climatic combination makes the region of Northeast a very important goldmine of biodiversity. Unfortunately this vast area of rich and unique biodiversity is still not explored. To accomplish this major task of biodiversity conservation we need a triple helix approach which involves the active role of academia, industry and government.
The paper will focus on the effective use of novel concept of scientoons developed by the author for the first time in the world, in planning strategy using the triple helix approach for biodiversity conservation especially for Northeast region of our country.

O-17

A double blind placebo controlled study of BacoMind™ on cognition enhancement in elderly volunteers

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Memory loss in elderly people is an important health problem worldwide and its unpredictable response with available therapies has paved the way to evaluate the use of complementary and alternative system of medicine. Traditionally *Bacopa monnieri* (*B. monnieri*), is used as a brain tonic to enhance cognitive performance. BacoMind™ is an enriched phytochemical composition of *B. monnieri* extract standardized to specific bioactive constituents. The objective of this study was to evaluate the efficacy of BacoMind™ on cognitive improvement compared with placebo on chronic administration in elderly volunteers. The study employed a randomized double blind placebo controlled parallel design. In the present study, sixty-five volunteers with mini mental state examination score of twenty-four and above were enrolled with mean age of 65.59 years in BacoMind™ group while in placebo it was 64.40 years. The study schedule included administration of 450 mg of BacoMind™ or placebo as a single daily dose for the initial duration of 12 weeks and thereafter no medication was given for the next 12 weeks following withdrawal of treatment. Combination of well established battery of neuropsychological tests was chosen to evaluate attention, memory and speed of information processing. BacoMind™ decreased baseline value of cancellation test from 190.70 ± 9.09 sec to 171.20 ± 10.56 sec ($p \leq 0.05$) in 12th week. In memory tests, list learning delayed recall test showed 1.93 ± 0.34 (26.97%) improvement at the end of 12 weeks which further increased to 2.72 ± 0.31 (78.95%; $p \leq 0.01$) at 24 weeks. Similarly the delayed recall of passage showed improvement in BacoMind™ group as the

score increased from the baseline value of 10.14 ± 1.03 to 11.66 ± 0.80 (14.99%) at 12 weeks which further increased to 12.97 □ 0.86 (27.91%; p≤0.01) at 24 weeks. In information processing test no remarkable change with BacoMind™ treatment was noticed. There were no adverse events reported throughout the study period. The findings of the current study revealed that BacoMind™ given at the dose of 450 mg once daily for 12 weeks improved the attention span and delayed component of verbal memory in elderly individuals.

***Keywords*:** *Bacopa monnieri*, BacoMind□, Efficacy, Tolerability, Elderly volunteers, Memory loss.

O-18

***In vivo* safety evaluation of Zigbir, a hepatoprotective polyherbal formulation, in rats**

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Zigbir, a polyherbal formulation used as a hepatoprotective, was evaluated for its safety in acute and repeated dose oral toxicity studies. In acute oral toxicity study, Zigbir at the dose of 2000 mg/kg in Sprague Dawley rats did not cause mortality and did not exhibit any signs of intoxication immediately following dosing and during the 14 day observation period, post treatment. Zigbir did not reveal any adverse effect on the body weight gain during the 14 day observation period. No major gross pathological alterations were observed in any of the treated rats. Based on the findings of this study, the median lethal dose (LD_{50}) of Zigbir after oral administration as a single dose to female Sprague Dawley rats was found to be more than 2000 mg/kg body weight. In 14 day repeated dose oral toxicity study, male and female rats were administered with Zigbir daily for 14 days at the doses of 0, 100, 250, 500 and 1000 mg/kg. No abnormal changes were observed both in male and female rats up to 1000 mg/kg. The 90 day oral toxicity study at the dose levels of 0, 250, 500 and 1000 mg/kg did not cause any mortality or treatment related clinical abnormalities. Male rats from the treated groups exhibited comparable body weight gain with that of control whereas mild reduction in body weight gain was observed in female rats from 500 and 1000 mg/kg treatment groups. The female rats from 1000 mg/kg reversal dose group exhibited normal body weight gain during the 28 day recovery period. Food consumption of control and treated rats was found to be comparable throughout the dosing period. Ophthalmoscopic examination did not reveal any abnormality. Haematological and biochemical analysis revealed no major abnormalities attributable to the treatment except for elevation in alkaline phosphatase level in male and female rats from 1000 mg/kg treated group. The absolute and relative organ weights of vital organs from treated groups did not differ significantly from that of the control. The gross and histopathological examination did not show any remarkable treatment related changes. Based on these findings, the no observed effect level (NOEL) of Zigbir in Sprague Dawley rats when administered through oral route, over a period of 90 days was found to be 500 mg/kg body weight for male rats and 250 mg/kg body weight for female rats.

Keywords: Zigbir, Polyherbal formulation, Acute oral, Repeated dose toxicity studies, NOEL.

P-1

Polymer supported facile synthesis of some bioactive 2-(6-bromochroman-2-yl) N-alkyl and acyl benzimidazole.

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Benzimidazole is one of the important group of heterocyclic compounds and number of its derivatives have found to possess different biological activities such as antiulcer, antitumor, antimicrobial etc. In benzimidazole, especially C-2 substituted compounds found to possess potent bioactivities.
In continuation of our work on the synthesis of biologically active compounds and considering the pharmaceutical and pesticidal properties of benzimidazole, we report here the facile synthesis of alkyl and acyl derivatives of 2-(6-bromochroman-2-yl) -1-H benzimidazole. The 2-(6-bromochroman-2-yl) -1-H benzimidazole firstly supported on a polymer [Amberlite IRA 400, (Cl^- form)] and then reacted with different alkyl halides and acyl halides to afford N-alkyl and acyl benzinimadoles, respectively. The dimerisation of 2-(6-bromochroman-2-yl) -1-H benzimidazole, using dihaloalkanes and diacid chlorides has also been achieved successfully. All the synthesized compounds have been characterized by their physical constants, ^{1}H-NMR and IR spectroscopy. A comparative study on the basis of yield and purity of the products with different polymer support and solvents is in progress.

P-2

A Novel Bioadhesive Material From The Fruit Pulp Of *Cordia dichotoma*

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Cordia dichotoma, fruits pulp enriched with amino acids, flavonoids, saponins and mucilages. The current aim of our work is to isolate a biomaterial from the fruits pulp of *Cordia dichotoma* by a simple and economical process and the isolated material was subjected to various physicochemical studies and IR, NMR, Mass and SEM analysis. The isolated material is further subjected for the assessment of mucoadhesivity property by shear stress method and modified flow channel method.
The isolated biomaterial exhibited the presence of carbonyl, primary amine and secondary alcohol groups. From this study, it reveals that the biomaterial is polymeric in nature and also it exhibited a promising mucoadhesive property. From the above studies the conclusion was drawn that the isolated natural biomaterial possesses a novel mucoadhesive property and the same biomaterial can be used in various mucoadhesive formulations as a natural bio-mucoadhesive agent.

P-3

A Novel Biomaterial From *Mangifera indica* And Its Pharmaceutical Applications

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Mangifera indica, fruit pulp is composed of polysacharrides like glucan and 1-4 linked galactourinol. The aim of our research work is to separate and characterize a biomaterial from the fruits pulp and to evaluate its pharmaceutical applications. The novel biomaterial from the fruit pulp of *Mangifera indica* was isolated by a simplified process and the isolated material was subjected for various preliminary studies, chemical test, solubility studies, IR, NMR and Mass studies. The isolated material is further assessed for its mucoadhesive character by comparing with the existing standard polymers like sodium CMC and Carbopol.
From our studies, it revealed that the isolated biomaterial possessed carbonyl, amine and alcohol groups. The mucoadhesive studies also showed promising mucoadhesive property. From the above study, the conclusion was drawn that the isolated material could serve as a good mucoadhesive material and the same can be used in the various mucoadhesive formulations.

P -4

Isolation and Characterization Of A Novel Biomaterial From *Lotus corniculatus*

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*Lotus corniculatus*I seeds composed of polysaccharides, proteins and fixed oils .
The present aim of our work is to separate a biomaterial from the seeds of lotus and to characterize by performing various physicochemical tests. The seeds were soaked in water for 12hrs and mechanically stirred for 4hrs at 4000 rpm and strained. The mucoadhesive material was separated by adding a specified quantity of acetone and purified. The isolated material is subjected for drying in vacuum desiccators for 12 hrs. The isolated material was subjected for various physicochemical tests like color, texture, solubility, chemical tests, charring point, viscosity, IR, NMR, Mass and SEM analysis. The material is also further assessed for its bioadhesive character by shear stress method and modified flow channel method.
The results of our studies revealed that the isolated material possesses carbonyl and Primary hydroxyl groups and melting point showed a color change at 210^{o}C. From this study, it revealed that it is polymeric in nature. From the mucoadhesive studies, it revealed that the polymer is possessing inbuilt mucoadhesive character. Finally, the conclusion was drawn that polymer can serve as a mucoadhesive platform and it can be used in various mucoadhesive formulations.

Poster -5

Synthesis and antitubercular activity of substituted benzyl- and heteroaryl amines[#]

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Since the beginning of medical history and chemotherapeutic principles of various amine derivatives have been known either as therapeutic agents or as biological tools. A number of aromatic and heteroaromatic amines were synthesized and evaluated for their antitubercular efficacy and some of them possess very good antitubercular activities. Benzyl-and pyridylmethyl amines were synthesized either by reductive amination of aromatic/heteroaromatic aldehydes with amines or by conjugate addition of amines to the

cinnamates followed by reduction of the ester group with lithium aluminium hydride to the propanolamines. The structures of all the compounds were established on the basis of spectroscopic data and analysis. All the synthesized compounds were evaluated against both avirulent and virulent strains M. tuberculosis. Many of the compounds exhibited MIC as low as 1.56µg/ml. The selected potent compounds were also evaluated against clinical isolates of MDR TB and found to be active at one or other concentrations with MIC as low as 1.56µg /ml. Detailed results will be presented.

References:
1. Ruckdeschel, G.; Stransky, D.; Schoneberger, H. *Pharmazie*, **1976**, *31*, 374.
2. Ruckdeschel, G.; Stransky, D.; Schoneberger, H. *Pharmazie*, **1976**, *32*, 119.
3. Meindl, W. R.; Angerer, E. V.; Schonenberger, H.; Ruchdeschel, G. *J. Med. Chem*. **1984**, *27*, 1111-1118.
4. Grange, J. M.; Snell, N. J. C. *J. Ethnopharmacology*. 1**996,** *50*, 49-53.
5. Vestal, R.E.; Kornhauser, D. M.; Shand, D. G. *J. Pharmacol. Exp. Ther.* **1980**, *214,* 106-11.
6. Arai, K.; Yasuda, N.; Isohashi, F.; Okamoto, K.; Ohkuma, S. *J. Biochem*. **2002**, *132*, 529-534.
7. Selected references from RP Tripathi Katiyar, D.; Tiwari, V. K.; Tewari, N.; Verma, S. S.; Sinha, S.; Gaikwad, A.; Srivastava, A.; Chaturvedi, V.; Srivastava, B. S.; Tripathi, R. P. *Euro. J. M. C*. **2005**, *40*, 351-360.

P -6

An efficient synthesis of tetramic acid derivatives with extended conjugation from L-Ascorbic Acid.

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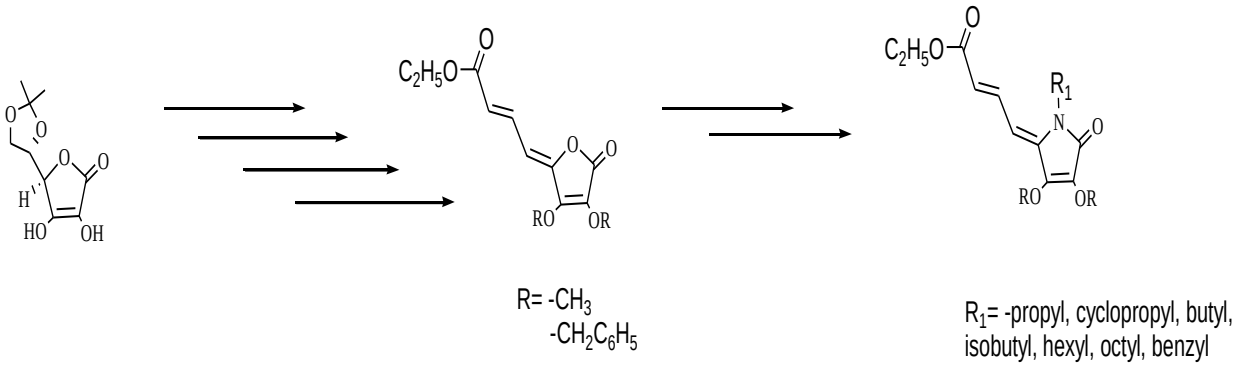
Tetramic acid derivatives are the key structural core found in a variety of natural products including many antibiotics such as melophilin B, reutericyclin, tirandamycin, blasticidin A and vancoresmycin. The wide spectrum of biological activities in this class of molecule include potent antiviral, antibiotic, and antifungal properties as well as cytotoxicities and antitumor action. Very recently many antibiotics with 3-acetyl tetramic acid moiety were reported as anti HSV and anti HIV agents with potent tyrosine inhibitory activities. Most of the biologically active tetramic acid antibiotics with dienyl and polyenyl units such as erythroskyrine, streptolydigin, cylindramide etc. has recently attracted the attention of many chemists as a challenging field of synthetic organic chemistry. There fore in our ongoing programs of developing new antitubercular agents, we thought to synthesize tetramic acid analogues having an extended alkenyl unit at C-5 as new antitubercular agents. The reason behind this synthesis is thiolactomycins, a class of thiotetronic acid with alkenyl chain at C-5 posses very good antitubercular activity.

The synthesis start from L-Ascorbic acid via protection, followed by dialkylation, formation of allyl alcohol, PCC oxidation of allyl alcohol followed by olefination and subsequent reaction with different amines to give 5-hydroxy lactams, which underwent pTSA catalysed dehydration to give the required tetramic acid derivatives.



References:

1. Kulkarni, B.A.; Ganesan, A. *Tetrahedron Lett.* **1998**, *39*, 4369-4372.
2. Singh, B.K.; Dwivedi, N.; Verma, S. S.; Tripathi, R. P. *Tetrahedron Lett.* **2006**, *47*, 2219-2222.
3. Khan, M. A.; Boyes, S. A. *Molecules* **1996**, *1*, 27-36.

P-7

Isolation And Characterization Of Novel Biomaterial From *Cajanus indicus*

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Cajanus indicus (Arhar daal), Family: Leguminosae enriched with proteineous matters. The aim of our study is to isolate a novel biomaterial from Arhar daal by innovative process which is economic, reliable and reproducible. The isolated biomaterial is subjected for physicochemical investigation like solubility, color change temperature, viscosity, IR, NMR, and Mass spectral studies. The biomaterial is also evaluated for the mucoadhesivity property by *in vitro*, shear stress method and modified *in vivo* flow channel method and compared with the standard synthetic polymers like carbopol and NaCMC. From the study, the isolated biomaterial revealed that it is protein polymeric in nature and also having a novel mucoadhesivity with promising potential. Finally, the conclusion was drawn that the isolated material can serve as a suitable mucoadhesive candidate for formulating mucoadhesive dosage forms.

P-8

A Novel Bioadhesive Material From *Logelaria siceraria*

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The current aim of our research work is to isolate and characterize a bioadhesive material from the fruit pulp of *Logelaria siceraria* (Lauki) Family: Cucurbitaceae The biomaterial is isolated by a simplified process and it is subjected for physicochemical evaluation like texture, particle shape, particle size, solubility, SEM analysis, IR, UV, NMR, color change point and TLC. The isolated biomaterial was further screened for its bioadhesivity by shear stress method, modified Park & Robinson method and modified flow channel method. From these studies, the material exhibited the presence of protein polymeric nature. It showed an excellent mucoadhesive property and promising mucoretentivity. This study directs that the

material can serve as a good mucoadhesive agent and it can be used in formulating different mucoadhesive formulations.

P-9

Synthesis of quinoline substituted oxazolo[5, 4-b]pyridine compounds and study their antimicrobial activities

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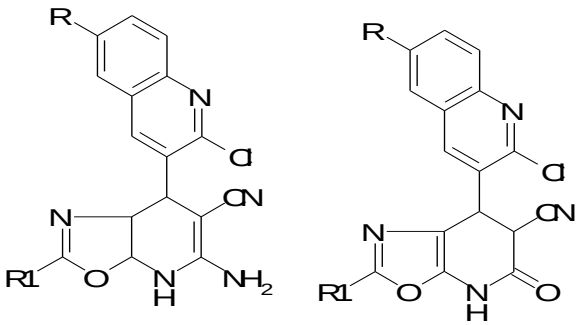
A series of 5-amino-7-(2-chloro-6-substituted quinoline-3-yl)-2-substituted 4,7-dihydro-oxazolo[5,4-b]pyridine-6-carbonitrile and 7-(2-chloro-6-substituted quinoline-3-yl)-5-oxo-2-substituted 4,5,6,7-tetrahydro-5H-oxazolo[5,4-b] pyridine-6-carbonitrile have been synthesized by condensation between 4-(2-chloro-6-substituted quinoline-3-yl methylene)-2-phenyl-4H-oxazole-5-one and active methylene compounds like malononitrile and ethylcyanoacetate respectively. All the compounds were characterized by their elemental analysis, melting point, ^{1}H-NMR and FT-IR spectroscopy. These compounds were screened for their antibacterial activity against some gram positive bacteria and gram negative bacteria and antifungal activity against *A. Niger* and *T. Viride.*



P-10

Synthesis Of Some New Quinoxaline-2,3-Dione Derivatives As Potential Antibacterial And Antitubercular Agents.

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Quinoxalines, which belong to an important group of nitrogen containing heterocyclic compounds, have been extensively explored for their biological applications. It is well documented in the literature that quinoxalines and their derivatives exhibits antibacterial, antifungal, antitubercular, antiviral, anticancer, antidiabetic, antiinflammatory, AMPA and NMDA receptor antagonist, antiallergic and anticonvulsant activity. Moreover significant biological properties associated with azomethines and thiazolidin-4-ones have aroused considerable interest to design quinoxalines in which thiazolidine ring system is incorporated.
The titled compounds 6,7-bis[2-(substitutedphenyl)-4-oxo-thiazolidin-3yl] quinoxaline-2,3 (1*H*,4*H*)-dione (IIa-f) have been synthesized by the condensation of 6,7-bis(substitutedbenzylideneamino)quinoxaline-2,3(1*H*,4*H*)-dione (Ia-f) with thiogl- ycolic acid in presence of anhydrous zinc chloride, whereas the intermediate 6,7-bis(substitutedbenzylideneamino)quinoxaline-2,3(1*H*,4*H*)-dione (Ia-f) have been prepared by the action of substituted aromatic aldehydes on 6,7-diaminoquinoxaline-2,3(1*H*,4*H*)-dione in methanol in presence of catalyic amount of anhydrous zinc chloride.
The constitution of newly synthesized products have been characterized by elemental analyses, IR, ^{1}HNMR and Mass spectral study and purity of all the compounds have been checked by thin layer chromatography. All the compounds have been screened for their *in-vitro* biological activities, like antitubercular activity towards a strain of *Mycobacterium tuberculosis* $H_{37}RV$ at a concentration of 6.25 □ g using Rifampicin and Isoniazid as a standard drugs, antibacterial activities towards Gram+ve and Gram-ve bacterial strains like *Staphyllococus aureus*, *Bacillus cereus* and *Pseudomonas aeuroginosa* respectively. The biological activities of the synthesized compounds were compared with standard drugs.

P-11

Synthesis and Antiviral Screening of Thiosemicarbazones

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Thio-semicarbazides and thio-semicarbazones are associated with broad spectrum of biological activities. The present work is undertaken with a view to synthesize compounds having better biological properties. Some 2-(4'-substituted-phenyl)-3-methyl-5-thiazole acetyl-3'-substituted thio-semicarbazones (IV) were synthesized by reaction of 2-(4'-substituted aryl semi-carbazides (III). The compound (II) was prepared by reaction of 3-chloro acetyl acetone (Ia) with 4-substituted phenyl -thiocarbamides (Ib). The thiocarbamides used were prepared following the method of Frank and Smith. The substituted phenyl thiocarbazides (III) were synthesized from substituted aniline, hydrazine and DMF when refluxed with alcohol. Elemental analysis, IR, ^{1}HNMR and Mass spectral studies have confirmed the constitution of synthesized compound. All the compounds were tested for their antiviral activity.

Poster -12

A Comparative QSAR study of [4,6-(4-subtituted aryl-yl)-2-thioxo/oxo/amino 1, 2,3,4,tetrahydropyrimidine-5yl] acetic acid derivative as Nonsteroidal Anti Inflammatory agent

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Inflammation is a normal and essential response to any noxious stimulus, which threatens the host and may vary from a localized response to a more generalized one. In view of the complexity and multitude of biochemical factors involved in inflammatory events, few general correlations of chemical structures and physicochemical properties with biological activities would be expected. Never the less some general features seem to be commonly associated with a large number of active drugs. However, these main features are not sufficient, but they could reflect certain physicochemical requirements for in vivo efficacy.
Aryl alkanoic acid is the most studied class of non-steroidal anti-inflammatory drug, which cover the major NSAIDs. But now intensive research focused on anti-inflammatory activity of pyrimidine nucleus**.** The multifunctionalized pyrimidine represents a heterocyclic system of remarkable pharmacological efficiency. In view of this three series of [4,6-(4-subtituted aryl)-2-thioxo/oxo/amino1,2,3,4, tetrahydropyrimidine -5yl] acetic acid derivative were selected for comparative quantitative structural activity relationship (QSAR), as no QSAR analysis has been reported for this series. Such studies may help for designing and synthesis of more potent anti-inflammatory drugs. As QSAR is a useful means for maximizing the potency of a new lead compound. In the lead optimization phase various QSAR procedures with the aid of computer technology have been proposed. Among them, the classical Hansch approach has been widely used leading to quite a few successful examples. In the QSAR approaches, the prescription to optimize the lead structure is inferred from mathematical equations correlating variations in the potency of a certain biological activity with physicochemical and structural descriptors among congeneric molecules.
A series of 54compounds, which was synthesized and evaluated for their biological activity, was converted into trainee and test set .By correlating biological activity (Log CPE %) with selected descriptor, the multiple linear regressions analysis was carried out to generate various equations that further used to predict the biological activity. It is suggested that traditional SAR and QSAR helpful in synthesis, design and minimization of synthetic work leading to drug discovery.

P-13

Polymer supported facile synthesis of some bioactive 2-(6-bromochroman-2-yl) N-alkyl and acyl benzimidazole.

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Benzimidazole is one of the important group of heterocyclic compounds and number of its derivatives have found to possess different biological activities such as antiulcer, antitumor, antimicrobial etc. In benzimidazole, especially C-2 substituted compounds found to possess potent bioactivities.

In continuation of our work on the synthesis of biologically active compounds and considering the pharmaceutical and pesticidal properties of benzimidazole, we report here the facile synthesis of alkyl and acyl derivatives of 2-(6-bromochroman-2-yl) -1-H benzimidazole. The 2-(6-bromochroman-2-yl) -1-H benzimidazole firstly supported on a polymer [Amberlite IRA 400, (Cl^- form)] and then reacted with different alkyl halides and acyl halides to afford N-alkyl and acyl benzinimadoles, respectively. The dimerisation of 2-(6-bromochroman-2-yl) -1-H benzimidazole, using dihaloalkanes and diacid chlorides has also been achieved successfully. All the synthesized compounds have been characterized by their physical constants, ^{1}H-NMR and IR spectroscopy. A comparative study on the the basis of yield and purity of the products with different polymer support and solvents is in progress.

P-14

Process Development For Preparing Ph Sensitive Film Coating Material - Methacrylic Acid Co-Polymer

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Methacrylic acid co-polymer–A is a co-polymer of Methacrylic acid and Methyl methacrylate in 1:1 molar ratio, which is soluble above pH 6. The present work was undertaken as an attempt to develop a cost effective process to prepare Methacrylic acid copolymer-A with high quality standards. The new emulsion polymerization process was developed to prepare Methacrylic acid copolymer-A. Monomer addition method of emulsion polymerization was employed for present study. The process was optimized with respect to the emulsifier and its concentration, concentration of initiator, concentration of chain transferring agent and process variables.
The prepared polymer was evaluated by properties like I.R. spectra, Film forming properties, Viscosity, loss on drying, residual monomer content, residue on ignition, solubility, acid value, density, refractive index, molecular weight and disintegration time of tablet coated with the polymer.
I.R. Spectra of the co-polymer formed matches with standard and shows good film forming properties. The acid value, refractive index, molecular weight, of the polymer formed are with in the acceptable limits.

P-15

Synthesis of quinoline substituted oxazolo[5, 4-b]pyridine compounds and study their antimicrobial activities

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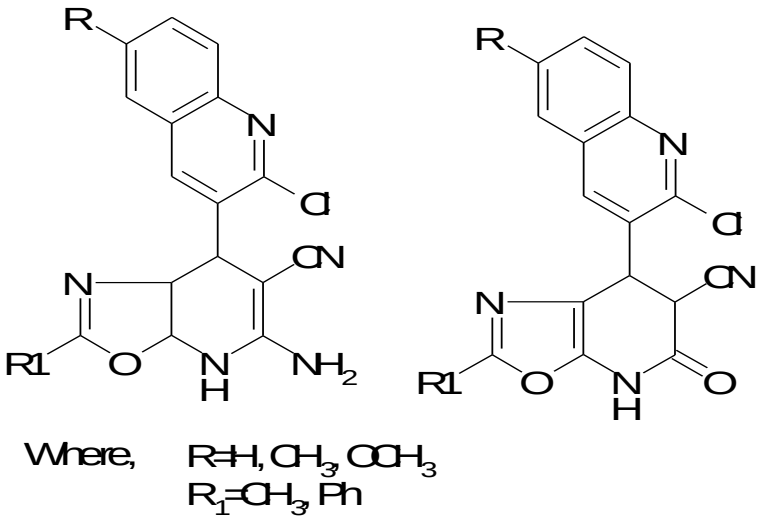
A series of 5-amino-7-(2-chloro-6-substituted quinoline-3-yl)-2-substituted 4,7-dihydro-oxazolo[5,4-b]pyridine-6-carbonitrile and 7-(2-chloro-6-substituted quinoline-3-yl)-5-oxo-2-substituted 4,5,6,7-tetrahydro-5H-oxazolo[5,4-b] pyridine-6-carbonitrile have been

synthesized by condensation between 4-(2-chloro-6-substituted quinoline-3-yl methylene)-2-phenyl-4H-oxazole-5-one and active methylene compounds like malononitrile and ethylcyanoacetate respectively. All the compounds were characterized by their elemental analysis, melting point, ^{1}H-NMR and FT-IR spectroscopy. These compounds were screened for their antibacterial activity against some gram positive bacteria and gram negative bacteria and antifungal activity against *A. Niger* and *T. Viride.*



P-16

Synthesis of New 1, 5-Benzothiazepines As Potential CNS And CVS Agents

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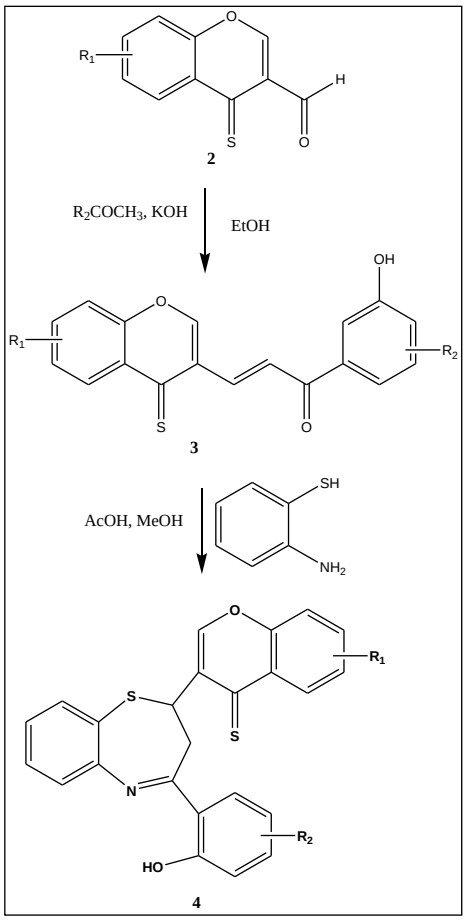
Effective cardiovascular drugs like diltiazem, clentiazem and siratiazem are found to contain 1, 5-benzothiazepine nucleus. Recently 1, 5-benzothiazepines having psychopharmacological and cardiovascular activities are reported. Benzothiazepines are structurally similar to dizepam, an established drug showing CNS depressant activity . Thionation of oxygen heterocycles has shown enhanced biological activity. These observations and our earlier interest in these heterocycles led us to take up the synthesis of new thio chromonyl 1, 5-benzothiazepines.

In the present work the starting 3-formyl chromones **1** were synthesized by using Vilsmeir –Haack reaction from o-hydroxy acetophenones .The compounds **1** thionated to respective 3-formyl thio chromones **2** by refluxing with stoichiometric amont of P_2S_5 in pyridine.Condensation of 3- formyl thio chromones **2** with o-hydroxy acetophenones in presence of piperidine resulted in the formation of α, β- unsaturated ketones **3** .The cyclo condensation of **3** and 2-aminobenzene thiol when carried out, yielded the 2-[substituted thiochromon-3'-yl]-4-[2'-hydroxy-3'/5'- substituted phenyl]-2, 3-dihydro-1, 5-

benzothiazepines **4** (Scheme I).The newly synthesized compounds were evaluated for CVS activities. Due to the CNS action of diazepam, it was thought that the benzothiazepines will also have some degree of activity on CNS especially CNS depression. With this view, the test compounds were also evaluated for the CNS and CVS activity and have shown promising results.



P-17

Diaryl amines from Fischer carbenes

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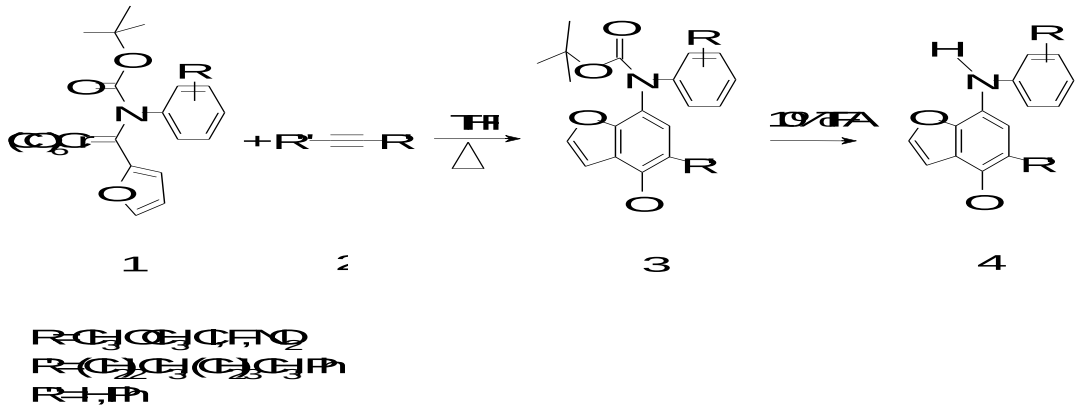
Our research involves novel synthesis of diaryl amines from Fischer arylamino carbenes via Dötz Benzannulation strategy. Diarylamines are biologically active molecules, viz. Flu (acts as inhibitor of amyloid fibrils), Aceclofenac and Niflumic Acid (natural products containing anti-inflammatory and analgesic properties). They are also applied as brightly colored synthetic dyes.
Our methodology involves reaction of Fischer carbene **1** with substituted and terminal acetylenes **2** in THF at around 50-60^{o}C. To enhance the activity of arylamino carbenes towards benzannulation we substitute the nitrogen of the carbenes with *tert*-Boc group enabling the diarylamine formation under mild conditions (50-60^{o}C).



P-18

α-Methylene oxygen heterocycles from alkyl fischer carbenes

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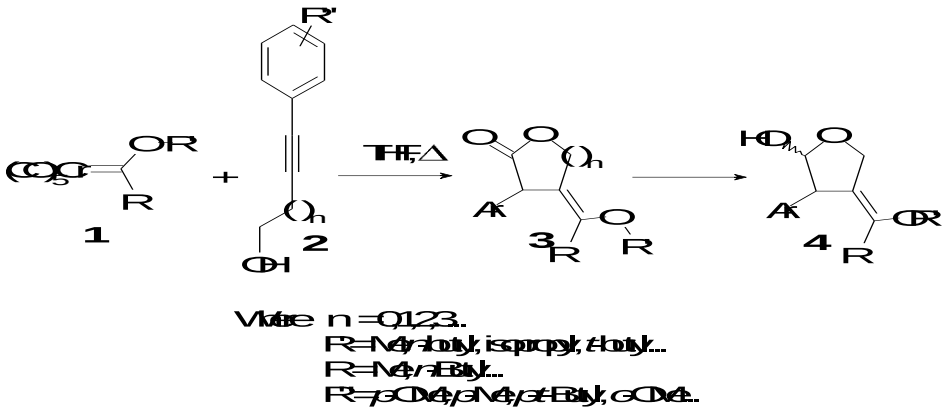
Our research involves novel synthesis of α-methylene oxygen heterocycles from fischer carbenes under mild neutral conditions. These oxygen heterocylces are pharmacophore in a variety of natural products *viz*. cytotoxic Mycalamides, antitumor Theopederins and antiviral Onnamide A.



The methodology involves reaction of fischer carbenes **1** with substituted alkynols **2** in THF, under mild neutral conditions. The reaction proceeds via ketene intermediate. The terminal hydroxy group of the alkyne then attacks the ketene carbon, to generate the heterocycles **3**. We have shown a novel synthetic route for these aryl substituted lactones.

P-19

Rapid and solvent free Intramolecular Benzannulation of Fischer carbenes to produce dibenzofurans.

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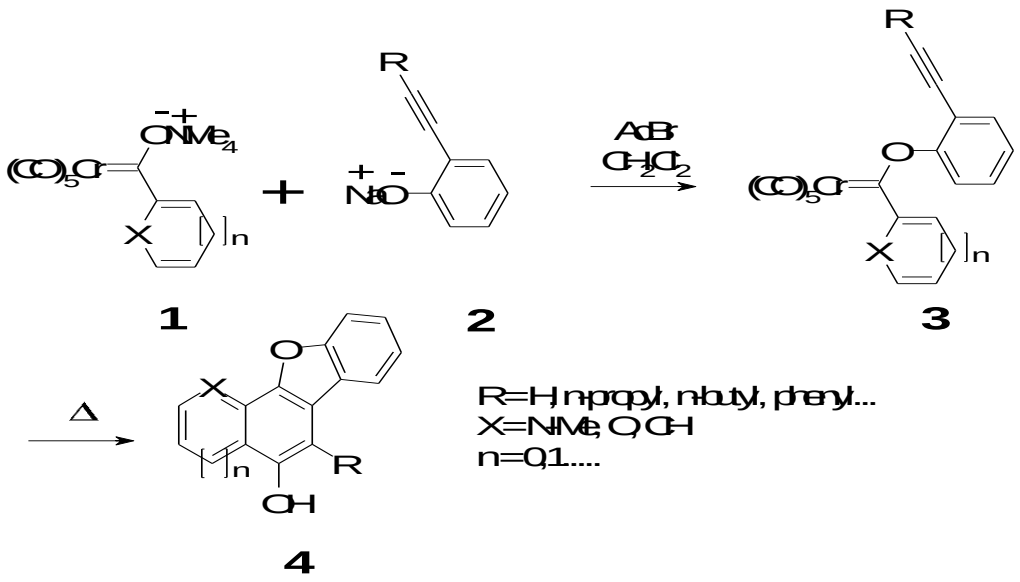
Our research involves synthesis of dibenzofurans **4** via Dötz benzannulation of aryloxy Fischer carbenes. These biologically active molecules are pharmacophore in a variety of natural products *viz*. antimicrobial strepsilin, antihyperglycemic achyrofuran and antibacterial usnic acid
Initially, o-iodophenols are reacted with various substituted alkynes to get alkynyl phenols. These in turn are further reacted with sodium hydride to form sodium phenolate **2**. **2** then reacts with fischer carbene salt **1** to give aryloxy fischer carbenes **3**. The final step involves an intramolecular benzannulation strategy; where the alkyne is tethered to the aryl group. We have focused on solvent-free neutral conditions, which expedite reactivity by about 80 folds.



P-20

Microwave Assisted One Pot Synthesis Of Novel 2-Amino-3-Cyano Pyridines

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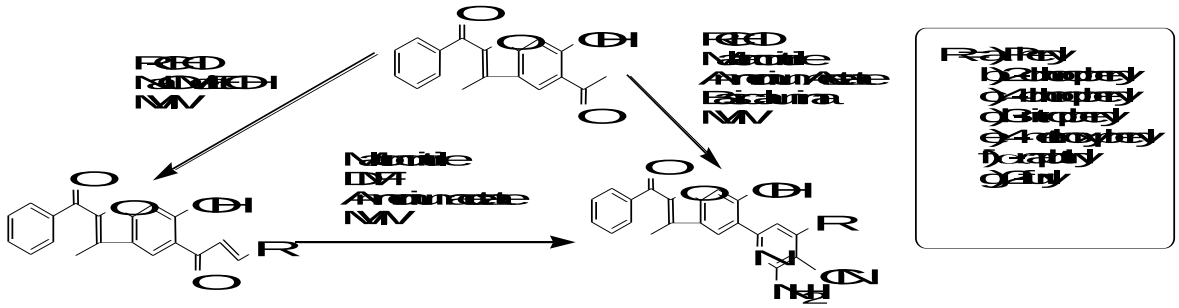
Pyridine moiety has been a useful functionality for the development of biological interesting molecules. Among them, 2-Amino-3-cyano pyridines have been identified as IKK-□ inhibitors. Benzofuran derivatives have been reported to possess a variety of biological activities. In order to know the combined effect of both benzofuran and pyridine moieties, we have taken up the synthesis of some new pyridine derivatives. Microwave induced organic reaction enhancement chemistry (MORE) offers a simple, non-conventional technique for the synthesis of a wide variety of compounds having medicinal, pharmaceutical and commercial importance.

An eco-friendly method is an important salient feature of this technique, since it requires no solvent (dry media synthesis in which reactions are carried out in solid state) or very little solvent as energy transfer medium.

In continuation of our studies on microwave assisted reactions, we wish to report a one pot microwave assisted synthesis of novel 2-Amino-3-cyano pyridines from 5-Acetyl-2-benzoyl-6-hydroxy-3-methyl benzo[b]furan using malanonitrile, ammonium acetate and various aromatic aldehydes.

The synthesized 2-Amino-3-cyano pyridines were characterized by their analytical and spectral data such as UV, IR, ^{1}H-NMR & Mass.



P-21

Studies on Synthesis and bioactivity of Novel Schiff bases derived from Dapsone and halo Dapsone

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Schiff bases are important intermediates for the synthesis of some bioactive compounds such as B-lactams. Furthermore, they are reported to show variety of interesting biological actions, including antibacterial, antifungal, antimouse hepatitis virus, inhibition of mosquito larvae and herbicidal activity. It is also known that the presence of chloro in different types of componds can lead them to exhibit pesticidal activity. Dapsone is used as anti-leprosy agent.
In light of the interesting variety of biological activities seen in compound containing azomethine and Dapsone moiety, it was thought of interest to synthesized Schiff bases having all above functionalities present simultaneously in one structure. Based on this notation we decided to synthesize some new schiff bases from Dapsone and halo Dapsone with excellent yield via the condensation of different aromatic aldehydes. The Structures of synthesized compounds were confirmed by IR, NMR, & Mass. All new compounds were screened for their antibacterial activity. Interestingly compounds have shown very good antibacterial activity.

P-22

Spectrophotometric Method For Simultaneous Estimation Of Nimesulide And Diclofenac Sodium In Pharmaceutical Dosage Forms

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A simple accurate spectrophotometric method has been developed for simultaneous estimation of nimesulide and diclofenac sodium. The method involves solving of simultaneous equation based on measurement of absorbances at two wavelengths i.e., at 276 nm and 395 nm.
Key words: Nimesulide, Diclofenac sodium, simultaneous equation, and UV

P-23

Microwave Assisted Synthesis Of Novel Coumarins

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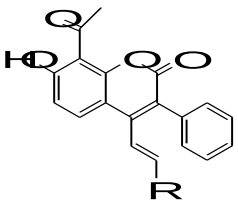
Coumarins have been popular substrates for the generation of heterocyclic compounds, in addition to this the chemistry of coumarins has assumed significant because these compounds are used as bactericides, fungicides, anti-inflammatory,anti-coagulant, anti-tumour agents. These pharmacological properties of coumarins aroused our interest in synthesizing several novel coumarins with the aim of obtaining more potent pharmacologically active compounds.The wide applicability of microwave assisted synthesis is due to cleaner products, higher yields, shorter reaction time, operational simplicity and minimization of side reactions. In recent years the microwave irradiation under solvent free reaction conditions on an inorganic solid support is a promising alternative to conventional methods as these reactions represent a clean, efficient, safe, economical and eco-friendly procedure. In view of these advantages and use of microwave assisted organic synthesis, we have synthesized novel coumarins using environmentally benign solvent free procedure in the presence of inorganic solid support under microwave irradiation.
Condensation of 2,4-diacetyl resorcinol and aromatic aldehydes using basic alumina under solvent free microwave irradiation in a modified Claisen-Schmidt condensation reaction gave selectively mono chalcones in high yields, whereas the conventional method require longer periods and with low yields. Microwave irradiation of monochalcones with arylacetylchlorides over basic alumina under solvent free conditions resulted in a Green Chemistry procedure for the preparation of coumarins in very good yields. This method has several advantages as compare to conventional methods in terms of shorter reaction times; increase yields and purity of the products, environmentally benign and safe protocol.
All the compounds synthesized were characterized on the basis of their analytical and spectral data such as IR, UV, ^{1}H-NMR and Mass.



R = a = 4-Chlorophenyl
b = 2-Chlorophenyl
c = 3-Nitrophenyl
d = 2-furyl
e = 3,5-Dimethylaminophenyl

P-24

Efficient Oxidation of Dichalchones With Mercury (Ii) Acetate Under Microwave Irradiation

D. Ashok***** and **D. Shravani**
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The environmental protection has become a global concern and the synthetic organic chemists are searching the ways of developing and applying more efficiently and environmentally benign strategies for future sustainable growth. One of the thrust areas for achieving this target is the environmentally friendly, solvent free approach that involves the exposure of neat reactants to microwave irradiation to give high yield of pure products thus eliminating the use of solvent, catalyst and solid support from the reaction. The salient features of this high yield protocol are, enhanced reaction rate, easy workup, enhanced yields, operational simplicity, greater selectivity and experimental ease of manipulation, low cost and economical.

Aurones are useful in alleviating allergic manifestations such as allergic astama, allergic rhinitis and a topic dermatitis. Aurones are also found to exhibit anti-fungal, anti-bacterial, anti-plasmodial, anti-leishmanicidal and anti-viral activities.

As a part of our ongoing research programme towards the non-conventional approach to the experimental set ups of organic reactions, the concept of Microwave assisted Organic Reaction Enhancement (*MORE*) chemistry has been adopted for the rapid and efficient synthesis of some novel aurones of biological interest.

The required dichalcones were synthesized by condensing 4,6-diacetyl resorcinol with aromatic aldehydes in the presence of alkali under microwave irradiation. Which on oxidation with mercury (II) acetate in DMF under microwave irradiation gave diaurones. All the compounds synthesized in the present investigation were characterized by their analytical and spectral data such as IR, UV, ^{1}H-NMR,^{13}C-NMR and Mass.

P-25

Synthesis of 3 □, 26-Dihydroxy- □^{13}-17,17-Dialkyl-22-Oxo-18-Norsteroids using Ceric Ammonium Nitrate induced Wagner-Meerwein Rearrangement of Furostenols

Archana Moni Das and **Pritish Chowdhury***
Natural Products Chemistry Division Regional Research Laboratory: Jorhat

Synthesis of 18-Norsteroids is a useful area is steroid transformation as many of them possess diverse biological properties. Wagner-Meerwein rearrangement is generally observed to get 18-norsteroids from 17-methyl-17-hydroxy steroid derivatives during their acid catalyzed dehydration that prevail in the stomach. Several mwethods are reported on the synthesis of 18-norsteroids using different synthetic methodologies.

Acid catalyzed cleavage of tetrshydrofuran is a good technique towards the preparation of 4-halobutylcarboxylates. Such type of reaction is also reported in steroid field and in some cases migration of adjacent group leading to the formation of rearranged product. We would like to report here a simple but high yield production of 18-norsteroids from Sapogenin of natural

origin. The laboratory has developed a number of process for the production of important steroid drug intermediates including 16-dehydropregnenolone acetate (16-DPA) which persuaded us to work on the present synthesis. Besides ,applications of Ceric Ammonium Nitrate (CAN) have also been explored in the steroid field. In the present work diosgenin was converted to pseudodiosgenin diacetate using catalytic or under pressure to produce in yield of 80-92%. When pseudo diosgenin diacetate was subjected to reaction with CAN in Acetic acid it directly furnished the desired 18-norsteroid viz., 3 □ , 26-Dihydroxy- □^{13}-17,17-Dialkyl-22-Oxo-18-Norsteroids in an yield of 50-60%.

P-26

Synthesis And Microbial Activity Of Novel 6-Hydroxy-4-Oxo-Pyrido[2,3-H]Quinoline-3-Carboxamides

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A number of amides with substituted piperazine at C-3 position of pyrido quinolone have been synthesized and evaluated their potency against gram positive and gram-negative bacteria, ciprofloxacin and gatifloxacin is used as standard drug. Compound **5** to **21** showed moderate activity against ciprofloxacin and gatifloxacin. Compound **22** to **31** showed good activity against ciprofloxacin and gatifloxacin. Thus substituted piperazine attached at C-3 as amide, enhanced activity of pyrido quinolone.

P-27

Synthesis And Microbail Studies Of New (2-Oxo-Azetidinyl)Quinazolin-4(3*h*)Ones

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Synthesis of 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[4□-(4-substitutedphenyl-3-chloro-2-oxo-azetidinyl)aryl]-6-bromo quinazolin-4(3*H*)ones **VI$_{a-k}$** have been achieved from the starting material 2-[(2□,6□-dichlorophenyl)amino]phenylacetic acid **I** to benzoxazine **III,** further reaction with *p*-phenylindiamine and substituted aromatic aldehyde gave 2-[2□-(2□ □,6□ □-dichlorophenyl)amino]phenylmethyl-3-(4□-amino)aryl-6-bromo quinazolin-4(3*H*) ones **IV** to form Schiff base **V$_{a-k}$**, which on cyclization with chloroacetylchloride gave the desire compounds **VI$_{a-k}$**. Final compounds have been screened for antibacterial and antifungal activity at two concentrations and compared with standard drugs. All the compounds have been characterized on the basis of elemental analysis, IR and ^{1}*H*-NMR spectral data.

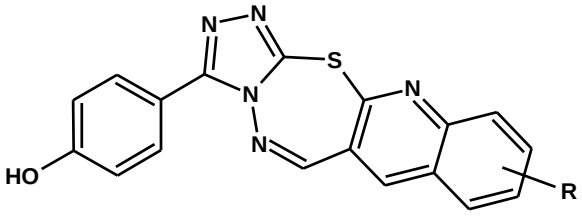
P-28

Methoxyquinolino [3',2'-f]-1,3,4-Thiadiazepine As An antiMicrobial Agents.

Vishal Sankharava and **Ranjan Khunt***
Department of Chemistry, Saurashtra University,Rajkot-360005(Gujarat).

Pharmaceutical development in the 21st century will be shaped by the recent targets in antimalarial technologies which can speed up the drug discovery process. Our efforts are focused on the introduction of chemical diversity in the molecular frame work in order to synthesize pharmacologically interesting compounds of widely different composition. Random screening is by far the most promising method used today in the search for new active substances of medicinal interest. Moreover, research on new substances possessing an antimicrobial activity is still of considerable interest owing to the continuous increase in bacterial resistance.

Thiadiazepine have been extensively explored in the field of medicine because of the use of chloroquine as an antimalarial agent. Recently, incorporation of these compounds has witnessed a great upsurge in the treatment of tuberculosis and other diseases.



Type (I)

Keeping this in view, we have investigated thiadiazepine, bearing Triazole moiety. Thiadiazepine derivatives of type (I) have been synthesised by one pot reaction of 3-mercapto-4-N-amino-5-p-hydroxyphenyl-1,2,4-triazole with substituted 2-chloro-3-formyl-quinolines in the presence of K_2CO_3. Elemental analyses, IR, ^{1}H NMR and mass spectral study accomplished proof of the newly synthesized compounds.

The titled compounds are evaluated for antimicrobial activity at a concentration of 40 μg/mL.

P-29

Sulfonamido]- 2-methoxy-n^3-[2-{(3, 4, 5- tri methoxy) phenyl}-4-oxo-thiazolidino]carboxamide

N. B. Patel[*] & R. D. Rathod

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5-N^2-[{6-fluoro-7-(substitutedanilino) benzothiazolyl} sulfonamido] 2-methoxy-N^3-[2-{(4-hydroxy) phenyl}-4-oxo-thiazolidino] carboxamide 4 $_{a-l}$ have been synthesized by cyclization with thioglycolic acid of Schiff bases $\mathbf{3}_{a-l}$ from corresponding 5-N^2-[{6-fluoro-7-(substitutedanilino) benzothiazolyl}sulfonamido] 2-methoxy benzoyl hydrazine $\mathbf{2}_{a-l}$. Compounds $\mathbf{2}_{a-l}$ in turn is prepared by dehydroxyhalogenation followed by condensation with hydrazine hydrates of acids $\mathbf{1}_{a-l}$. Compounds $\mathbf{1}_{a-l}$ in turn is prepared by chlorosulfonation followed by condensation with 6-fluoro-7-(substitutedanilino)-2-amino benzothiazoles of acid (1). Final compounds have been characterized by their element analysis, IR, ^{1}*H*-NMR. All the synthesized compounds have been screened for their antimicrobial activity. Some of them show good activity.

P-30

Evaluation Of Hepatoprotective Activity Of The Chloroform Extract Of A*cacia nilotica* Linn.

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In this study, the hepatoprotective effect of the chloroform extract of *Acacia nilotica* flowers was investigated against CCl_4-induced liver damage in rats. The extract was tested in albino rats weighing about 120gms. The doses were fixed (15 and 30mg/kg/b.w) and initially the liver of all the animals in all the groups were damaged with carbon tetrachloride administration for the first 6 days, then the drug was administered for the next 6 days up to 12^{th} day Serum samples were taken to determine the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) The histopathological and histochemical effects on the liver tissue were also investigated to support the above parameters. The results of the present study indicated that the levels of serum AST, ALT were significantly (P <0.05) elevated by CCl_4 administration as compared with the control group and significantly reduced at P<0.05 by the treatment with the plant in the CCl_4-intoxicated rats. Microscopic examination of liver of CCl_4 treated animals revealed focal necrosis and lymphocytic infiltration in the periportal areas with massive fatty infiltration. The histopathological examination also showed clearly that the extract of *Acacia nilotica* flowers reduced the alterations that were induced in liver by CCl_4. The maximum protection against CCl_4-induced hepatic aberrations was achieved with the optimum dose of the extract and the effect of *Acacia nilotica* seems dose- and time-dependant. In conclusion, the results suggest that *Acacia nilotica* exerts hepatoprotective effects against CCl_4-induced liver injury.

P-31

Formulation of Site Specific Drug Delivery System

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Over the past three decades, the pursuit and exploration of devices designed to be retained in the upper part of the gastrointestinal (GI) tract has advanced consistently in terms of technology and diversity, encompassing a variety of systems and devices such as floating systems, raft systems, expanding systems, swelling systems, Bioadhesive systems and low-density systems. Gastric retention will provide advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region. Also, longer residence time in the stomach could be advantageous for local action in the upper part of the small intestine, for example treatment of peptic ulcer disease. Furthermore, improved bioavailability is expected for drugs that are absorbed readily upon release in the GI tract. These drugs can be delivered ideally by slow release from the stomach.
Controlled release drug delivery systems that can be retained in stomach for a long time are important for drug that are degraded in intestine or for drugs like antacids or certain enzymes that should act locally in the stomach. If the drugs are poorly soluble in intestine due to alkaline pH, gastric retention may increase solubility before they are emptied, resulting in improved gastrointestinal absorption of drugs with narrow absorption window as well as for controlling release of drugs having site-specific absorption limitation.

Keywords:- Controlled release;GRT;Narrow absorption window drug

P-32

Comparative Bioavailability of Rifampicin, Isoniazid From a Fixed Dose Combination At The Same Dose Levels

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Fixed dose combination (FDC) formulations became popular in the treatment of tuberculosis (TB) because of the better patient compliance, reduced risk of monotherapy and emergence of drug resistance in contrast to treatment with separate formulations of two to four first-line drugs. However, its successful implementation in national programs is limited by probable bioinequivalency of rifampicin if present in FDC form. In this regard, World Health Organization (WHO) and International Union Against Tuberculosis and Lung Disease (IUATLD) recommend FDCs only of proven bioavailability.
Thus a pharmaceutical manufacturer needs to sincerely stuy the bioavailability of anti-tuberculosis formulations,if for no other reason,to ascertain the efficacy of that formulation. The data is of use not only for the satisfaction of formulation department. A bioavailability study conducted under the prview of Good Laboratory Practices (GLP) can speak volumes on the true value of a product.
To determine the true efficacy of a formulation, the bioavailability needs to be studied.In this study, the method of analysis for bioavailability of three antituberculosis drugs,Rifampcin,Isoniazid and Pyrazinamide were developed and the bioavailability of one formulation,Rifa I-6 was compared with that of a comparable market preparation. The result showed that Rifa I-6 has greater Rifampicin bioavailability as compared to the market product.

Keywords: Fixed dose combination; Tuberculosis; Bioavailability;Bioequivalence; Isoniazid; Rifampicin;

P-33

Studies On Lecithin Microemulsion Based Organogels For Topical Delivery Of Clotrimazole

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Lecithin organogels are readily obtained by adding a minimal amount of water to a solution of lecithin in organic solvents. Surprisingly high viscosities can be achieved in various organic solvents on addition of water. Such systems have currently generated great interest as topical and transdermal drug delivery carriers.
Clotrimazole an antifungal agent is a synthetic imidazole derivative it is practically insoluble in water. In the present study, lecithin based microemulsions were formulated as topical

carriers to enhance the release and to provide more sustained topical antifungal effect of clotrimazole.
The formulations were prepared using lecithin as a gelator moiety, Isopropyl myristate (IPM) as the organic solvent and water employed as the polar agent, clotrimazole was incorporated and these gels were then evaluated for various parameters which included physical appearance, pH, spreadability, viscosity, drug content, in vitro release, in vitro antifungal activity and gel life (stability). It was observed that the pH of the organogels studies was between 6-7.17, an increase in the proportion of lecithin resulted in a decrease in pH. The viscosity of the organogels were found to increase as the amount of lecithin increased thus resulting in decrease spreadability, FM5 formulation showed maximum viscosity38300 cps. *In vitro* release of clotrimazole from organogel showed that organogel formulation FM5 gave highest release 63.75% in 8 hrs. *In vitro* antifungal activity of clotrimazole organogels against *Candida albicans, Penicillium notatum, Aspergillus niger* was in the order FM5>FM3>FM4>Reference >FM6>FM7> FM2>FM1.
The results suggest that formulations containing very low and very high concentrations of lecithin FM7, FM6 and FM2, FM1 respectively show low release of the drug and thus less antifungal activity, whereas FM5, FM3, and FM4 formulations have comparatively greater drug release and better antifungal activity. FM5 (4:6 Lecithin: IPM) showed highest antifungal activity with a zone of inhibition corresponding to 09±0.2, 11±0.1, 15±0.1 for *Candida albicans, Penicillium notatum, Aspergillus niger* respectively
Accelerated stability studies of FM5 formulation determined after 180 days indicated that the FM5 formulation were stable.
Thus, finally it may be concluded that lecithin-microemulsion based organogel formulation FM5 FM5 (17.69%w/w lecithin, 26.54% IPM, 53.97%w/w water and 2% w/w of clotrimazole) have a good potential as carrier for topical delivery of antifungal agent such as clotrimazole.

P-34

Synthesis And Bioassay Of Mono And Bis Five Membered Heterocycles

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Compounds incorporating heterocyclic ring systems continue to attract considerable interest due to the wide range of biological activities they possess. Amongst them five membered heterocyclic compounds occupy a unique place in the realm of natural and synthetic organic chemistry. 1,3,4-Thiadiazoles find wide application in the design of compounds possessing useful properties. The triazole nucleus has a broad spectrum of antimicrobial activity. Molecules having both triazole and thiadiazine units possess antiparasitic activity. Moreover, 1,3,4-oxadiazoles exhibit broad spectrum of biological activities such as HIV, antibacterial and antifungal. In addition, pyrazolines have gained importance due to their various chemotherapeutic properties. In fact, celecoxib, a pyrazole derivative is now widely used in the market as an anti-inflammatory drug.
Our continued interest in this field prompted to synthesize a new class of mono and bis five membered heterocycles from suitable substrates adopting simple, versatile and elegant synthetic methodologies. The work related to the synthesis of oxadiazoles, thiadiazoles, triazoles and bis heterocycles viz., pyrazolines in combination with oxadiazoles, thiadiazoles and triazoles and their bioassay would be presented.

P-35

Synthesis and Bioassay of Five and Six Membered Heterocycles

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Heterocyclic compounds particularly five and six membered heterocycles have attracted the attention of pharmaceutical community over the years due to their therapeutic value. A number of barbiturate and thiobarbiturate derivatives exhibit anticonvulsant, anaesthetic, sedative and hypnotic properties. in fact, Phenobarbital and mephobarbital are used for clinical treatment of epilepsy. Barbiturates still are used worldwide in hospitals as injection narcotics. Besides this pyrazole and isoxazole derivatives possess bacteriostatic, antidiabetic, analgesic, antiarrhythmic, anti-inflammatory, antifungal and antiviral properties. Celecoxib, a pyrazole derivative, valdecoxib, an isoxazole derivative are now being used as anti-inflammatory drugs. In fact, a continues effort is maintained in our laboratories for the development of biologically potent heterocycles. In this direction we wish to report our recent findings in the synthesis and bioassay of five and six membered heterocycles.

The Michael addition of active methylene compounds *viz*., dimethyl malonate, ethyl cyanoacetate to activated sulfones has been carried out in the presence of different bases. The *gem* cyano ester functionality in Michael adducts has been explored to develop five and six membered heterocycles, amino-pyrazolones, amino-isoxazolones, amino-hydroxypyrimidinones, imino-pyrimidinediones and amino-mercapto-pyrimidinones by cyclocondensation with different nucleophiles. Work related to these aspects and bioassay of the lead molecules would be presented.

P-36

Synthesis of a New Class of Sulfone Linked Bisheterocycles.

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The development of simple, facile and efficient synthetic methods for the construction of five membered heterocycles is one of the major challenges in organic synthesis. Amongst these five membered heterocycles pyrroles, oxazoles and thiazoles have gained importance because of their varied physiological activities. Hence, it is thought that a worthwhile programme would be to prepare molecules having both pyrrole and oxazole / thiazole rings. Earlier we have reported the synthesis of oxazolines by the traditional four step three intermediate route from sulfonylacetic acid methyl ester *via* hydroxyethylacetamide followed by treatment with thionyl chloride and cyclocondensation in the presence of base. However, the use of lanthanide (III) compounds as catalyst or promoters in organic synthesis is of recent origin. Although lanthanide triflates, alkoxides and amides have been extensively used, lanthanide amino alkoxide complexes as reagents for similar purpose are sparsely reported. Hence we

wish to report the synthesis of hitherto unknown sulfone linked bisheterocycles having a pyrrole in combination with an oxazole or a thiazole unit adopting Michael mechanism and reaction with samarium 2-amino alkoxide complexes that are prepared *in situ* using an aminoalcohol / aminothiol and samarium chloride. Results in this direction would be presented.

P-37

Organotin(IV) Carboxylates: Composition Tailored Architectures Versus Cytotoxic Potential

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Organotin(IV) compounds are involved in cancer treatment via different mechanism at the molecular level. The binding ability of organotin(IV) compounds towards DNA depends on the coordination number and nature of groups bonded to the central tin atom. The phosphate group of DNA sugar backbones usually acts as an anchoring site and nitrogen of DNA base binding is extremely effective, this often resulting in the stabilization of the tin center as an octahedral stable species. Recent studies have shown that low doses of organotins can exhibit anti-tumoural activity and have suggested an action mode via gene-mediated pathway in the cancer cells, opening a new research sub-area on organotin(IV) compounds.
In view of the therapeutic potentials of organotin(IV) compounds, we have prepared and characterized some organotin(IV) carboxylates which allow for easy fine-tuning of structural and functional features. Some of these organotin(IV) carboxylates were screened in vitro against WIDR, M19 MEL, A498, IGROV, H226, MCF7 and EVSA-T human tumor cell lines. The in vitro cytotoxic activity of some di- and tri-organotin(IV) carboxylates (in conjunction with the standard drugs that are in current clinical use as antitumour agents) will be presented along with their molecular structures derived from single crystal X-ray crystallography.

P-38

Studies On Hydrotrope-Starch Gel As Topical Carrier For Rofecoxib

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Starches form an important class of gel forming material of natural origin, hydrotropic salts not only induce swelling and gelatinisation of starch at reduced temperatures but at fairly high concentrations increase the solubility of poorly soluble drugs in water.
The present investigation explores the potential of hydrotrope-gelled starch as a carrier for Rofecoxib a practically water insoluble anti-inflammatory drug.
Various batches of hydrotrope-gelled starches were prepared using 3^2 factorial designs. Potato starch, cornstarch along with hydrotropic salts sodium salicylate and sodium benzoate were

used. The formulations were evaluated for various parameters such as physical appearance, homogencity, pH, drug content uniformity, and rheological properties. *In- vitro* drug release of rofecoxib from the formulations was studied using Keshary-Chein type diffusion cell.
It was observed that hydrotropic salt sodium salicylate induced better gelling than sodium benzoate. The viscosity increased with an increase in the concentration of polymer, gels prepared using potato starch were more viscous than gels prepared with cornstarch. Higher concentration of salts yielded more viscous gels. The gels prepared using sodium benzoate showed higher viscosity.
In-vitro release data indicated that hydrotrope-gelled starch containing 1% rofecoxib in 10%w/w corn starch and 15%w/w sodium salicylate (W_{8SCD}) showed highest percent drug release 23.53% in 6hrs followed by formulation containing 15%w/w sodium salicylate and 5%w/w potato starch (W_{7SPD}) with a percent release of 16.65 in 6 hrs while formulation containing 15%w/w sodium salicylate and 10%w/w potato starch (W_{8SPD}) showed a release of 16.39% in 6hrs. These formulations showed much higher release when compared to some marketed formulations whose percent release were between the ranges of 15.81% to 4.77% in 6hrs.
The release of rofecoxib from hydrotrope-starch gel formulations was influenced by initial drug concentration in the vehicle, starch concentration and to a lesser extent the hydrotrope concentration. Thus different release rates may be achieved by controlling these factors.

P-39

An Efficient Synthesis Of 2-Benzylidene, 5, 5-Dimethyl-γ-Lactones

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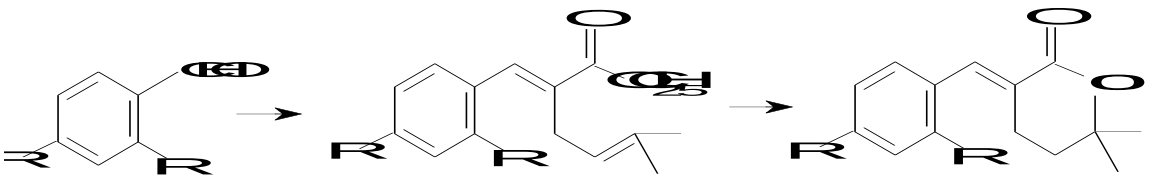
Gamma - lactones and *delta* - lactones are important flavour and aroma substituents in many natural products. *Gamma* - lactones are also known to possess wide range of biological activities due to which these are target of several synthesis. In comparison, *delta* - lactones are less studied.
Herein, we describe a convenient and efficient synthesis of 2-benzylidene-5, 5 -dimethyl-γ-lactones. The two step protocol involves Wittig reaction followed by PPA cyclisation.



P-40

Intramolecular Wittig Reaction: A Simple Entry Towards Pyrrolam A

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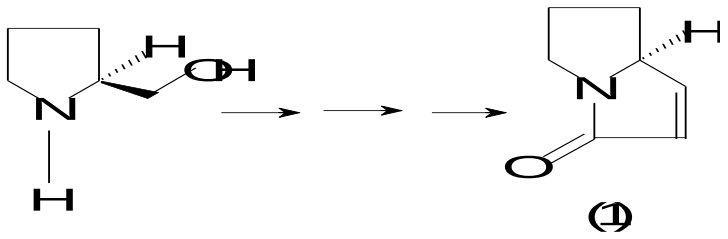
Pyrrolam A **(1)** a pyrrolizidine alkaloid was isolated[1] from bacterial strain *streptomyces olivaceous* and it shows low herbicidal activity against wheat and rice seedling. In this paper we described a new three step approach towards the synthesis of **(1)** from readily available (S)-Prolinol. The key step in the synthesis involves intramolecular Wittig reaction.



(1)

References:
Grote, R.; Zeeck,A.; Stumpfel J.; Zahner,H. *Liebigs Ann. Chem*. **1990**, 525.

P-41

Improved Intestinal Transit And Some Biochemical Parameters Of N^g-Nitro-L-Arginine Supplementation In Metformin Treated Hyperglycemic Rats

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Objective: To study the effect of N^G-nitro-l-arginine supplementation on intestinal transit and some biochemical parameters in metformin treated hyperglycemic rats.

Materials and methods: The study was carried out on 18 albino rats of either sex divided into three groups of six each. Hyperglycemia was induced by injecting alloxan (60mg/kg) through the tail vein, and the rats with blood glucose in the range of 200-300mg/dl were included for the study. Rats were administered N^G-nitro-l-arginine daily orally for 24weeks, with intermittent evaluation of blood glucose, cholesterol, bilirubin and SGPT level at every four weeks and after 24 weeks rats were administered charcoal meal, killed under ether anesthesia to observe the intestinal motility. The protocol of the study was approved by the local Institutional Animal Ethics Committee.

Results: Our findings suggest that the intestinal motility increases in chronic hyperglycemic rats as against normal rats. Treatment with N^G-nitro-l-arginine and metformin reversed the increased intestinal motility in hyperglycemic rats while preventing the increase in glucose, cholesterol, bilirubin and SGPT levels in hyperglycemic rats.

Conclusion: N^G-nitro-L-arginine supplementation with metformin can be useful in impaired intestinal transit in chronic hyperglycemic rats without increasing cholesterol, bilirubin and SGPT levels.

Key words: Metformin, N^G-nitro-l-arginine, Cholesterol, GI motility

P-42

Domino Wittig Diels-Alder Reaction: A Short entry to BC ring system of furanosesquiterpenes

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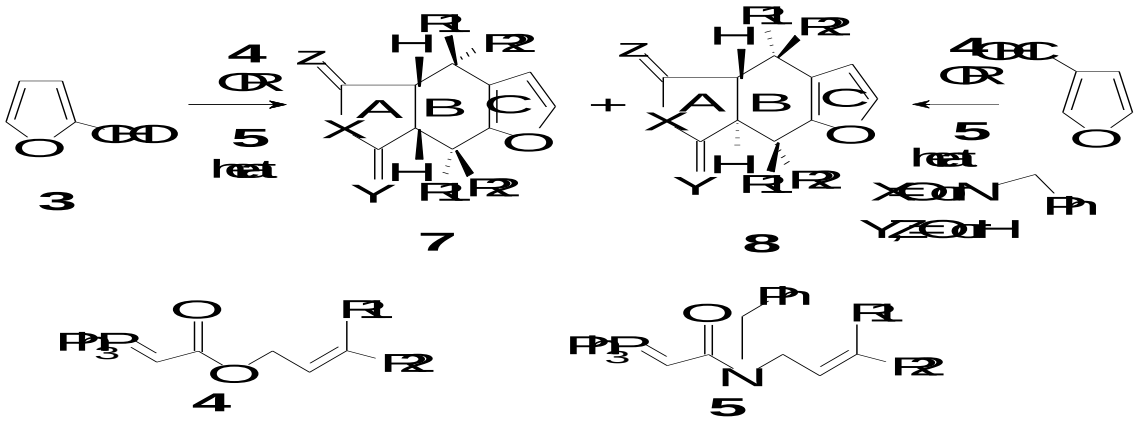
A short entry into BC ring system of furanosesquiterpenes having functionalised ring B ready to elaborate to ring C using domino Wittig reaction is described
A number of furanosesquiterpenes are reported from marine invertebrates. Among them Furodysin and Furodysinin are chthytoxic ,
Towards our programme to make synthetic analogues of bioactive marine natural products we needed to develop a general method for the synthesis of furansesquiterpenes having different substituents in AB ring. We reasoned that if we can make a BC ring system with functionalized ring B, we can easily manipulate to build the A ring.
Intramolecular Diels-Alder (IMDA) reaction is a good tool to construct complex molecules. There is great surge of interest in Domino reactions[1] as it helps to reduce the number of steps in organic synthesis thereby helping in reducing environmental damage. Our continuing interest in such reactions[2] prompted us to explore the tandem Wittig Diels-Alder reaction to build the BC ring system of furansesquiterpenes.



4,5a) $R_1=R_2=H$, **b**) $R_1=H$, $R_2=CH_3$, **c)** $R_1=R_2=CH_3$.

Ref: 1)Tieze, L. F. *Chem Rev*. **1996**, 96, 195
2) Shet, J. B.; Desai, V. G.; Tilve, S.G. *Synthesis*, **2004**, 11, 1859

P-43

Anti-Inflammatory And Anti-Nociceptive Activities Of Some Novel 8-(R)-3-Amino-4-Oxo-1,2-Isoxazolo[4,5-D] Pyrimido [2,1-B] Benzothiazoles In Rats And Mice.

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Heterocycles like benzothiazoles, pyrimidines and isoxazoles, alone are known to act as effective pharmacophores. We thought it worthwhile to synthesize these heterocycles fused with one another and to study its pharmacological behaviour. Hence, our study aimed at determining the possible anti-inflammatory and anti-nociceptive effects of the newly synthesized 8-(R)-3-amino-4-oxo-1,2-isoxazolo[4,5-*d*] pyrimido [2,1-*b*] benzothiazoles. The anti-inflammatory effect of these (25 mg / kg) was investigated and compared with diclofenac sodium (100 mg / kg) using the technique of egg white –induced hind paw method in wistar rats. The anti-nociceptive effect of these compounds each in different doses (10, 25 and 50 mg / kg) was investigated and compared with codeine (30 mg / kg) by employing acetic acid-induced writhing test in mice. The present results demonstrated that the compounds significantly diminished the nociceptive response showing at the same time considerable anti-inflammatory activity in the experimental animals. These novel heterocycles can thus serve as promising future drug candidates acting against pain and inflammation.

P-44

One Pot Synthesis Of 2,2'-Biindole And Its Derivatives

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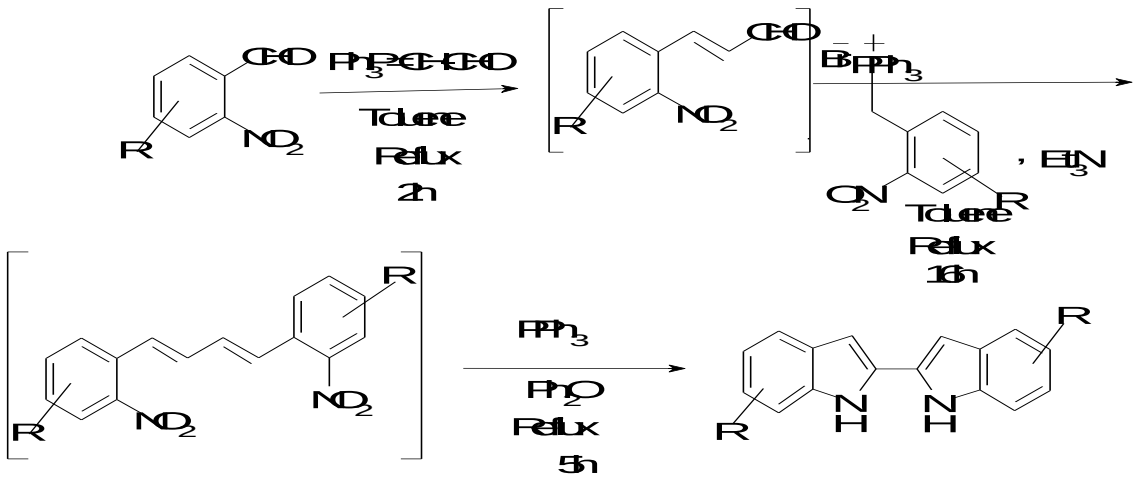
A number of natural products containing the 2,2'-Biindolyl unit have been isolated and are extremely interesting due to wide range of biological activities that they possess.Specific biological activities includes cytotoxicity, antitumor, hypotensitive and other pharmacological activities. 2,2'-Biindolyl as a structural element is present in the dyes Indigo & Tyrian purple. The two nitrogens in the 2,2'-Biindolyles has also been exploited in the construction of various ligand system.
One pot synthesis of 2,2'-Biindoles and its derivatives with different substituents in the benzene portion of the molecule is achieved via double Wittig and double reductive cyclization reactions in three steps.



P-45

The implementation of Process Analytical Technology (PAT) in Indian Pharmaceutical industry: Tools, Benefits, and Challenges

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Process analytical technologies (PATS) are systems for analysis and control of manufacturing process that on a timely basis measures critical parameters and performance attributes of raw and in-process materials to assure and acceptable end drug product quality. To achieve both understanding and control of process variables that are link to drug product critical quality attribute. The role and application of chemometrices and multivariate statistical methods in implementation of PAT. Pharmaceutical industry objectives and needs when using PATs. The advent of PAT has given a new impetus to the introduction of RMMs. Various PAT tools can provide in necessary specificity to analyze pharmaceutical drug products (e.g., Raman spectroscopy etc.). Multiple benefits associated PAT implementation but these benefit not without associated barriers (Limited technical knowledge). The FDA anticipates three main benefits, which follow from the implementation of PAT in Pharmaceutical industry. Limited knowledge with respect to PAT process analyzers appears to be the primary factors limiting PAT implementation.

Keywords: Pharmaceutical operations, Pharmaceutical manufacturing, Pharmaceutical analysis, Multivariate tools, Process analyzers, PAT, Quality, PAT benefits, PAT challenges.

P-46

Synthesis And Antimicrobial Evolution Of 2-(P-Amino Phenyl) Substituted Benzimidazole Containing Thiazolidinones.

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Email: dhmore@rediffmail.com

Among various heterocycles, benzimidazole is important nitrogen heterocycle that exhibits excellent pharmacological properties such as antiulcer, antiarthitis, anti-inflammatory, antisecretory, antitumor, etc. It is also a key feature in cardiotonic agent such as pimobenden, adibenden. Moreover, azetidinone, thiazolidinones shows versatile pharmacological properties such as antifungal agent, antibacterial, anthelmentic etc and it is industrially important.
In the present work Furyl thiazolidinones 2-Substituted Benzimidazole containing Furon thiazolidinone were synthesized by condensation of (p-Amino Phenyl) substituted benzimidazole with Furaldehyde to afford Schiff Bases which on cyclized with thioglycolic acid to obtain 2-Substituted Benzimidazole containing thiazolidinones .
The newly synthesized compounds were characterized by modern spectroscopic techniques and antimicrobial testing is in progress.

P-47

Synthesis and Characterization Of Some Novel Hetro Aryl Benzimidazole

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Heterocyclic compounds occupy important place among both natural and non-natural bioactive compounds. The benzimidazole nucleus is an important heterocyclic ring since several of its derivatives have pharmacological properties and have been marketed as commercial products. Most significantly, the benzimidazole ring system has been found to be an integral part of Vitamin-B_{12} in the form of 5, 6-dimethyl-1-(□-D-ribofuranosyl) benzimidazole.The literature precedence revealed that the substitutions at 1, 2 and 5 positions of the benzimiazole moiety is crucial for the compounds to exhibit wide range of pharmacological activities.

Owing to the mentioned biological activities of benzimidazole we have done condensation of 1*H*-benzimidazole-2-thiol with 5-(4-chlorobutyl)-1-cyclohexyl-1*H*-tetrazole,followed by oxidation ,that resulted in the formation of novel 2-{[4-(1-cyclohexyl-1*H*-tetrazol-5-yl)butyl]sulfinyl}-1*H*-benzimidazole and 2-{[4-(1-cyclohexyl-1*H*-tetrazol-5-yl)butyl]sulfonyl}-1*H*-benzimidazole .This compounds will be tested for the its potential biological activity. Similarly various 1-substituted benzimidazoles will be synthesized from this and they will also be tested for pharmacological activities.

P-48
Diastereoselective Synthesis Of Tetra Substituted Tetrahydrofuran Template From Methyl-A-D-Glucopyranoside

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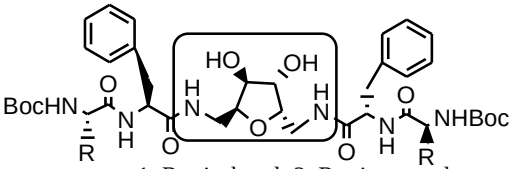
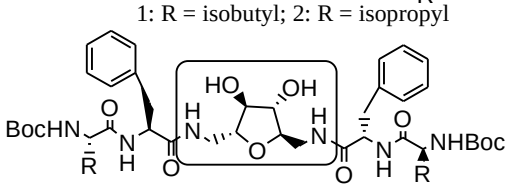
[*]

Tetrasubstituted tetrahydrofurans are key parts of various natural products and biologically active compounds. Compounds **1-4** act as potential HIV-1 protease inhibitors that are based on carbohydrate-peptide hybrid structure[1].

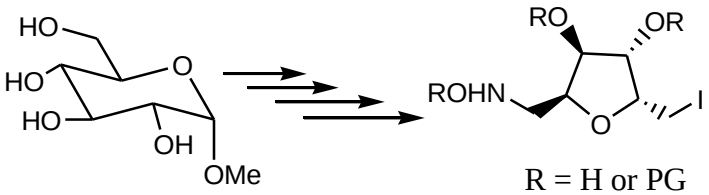


1: R = isobutyl; 2: R = isopropyl



3: R = isobutyl; 4: R = isopropyl

An efficient method for the synthesis of tetrasubstituted tetrahydrofurans starting from glucopyranoside is described.



R = H or PG

References:

1. Ward, R. S.; *Nat. Prod. Rep*., **1999**, 16, 75-96
2. Chakraborty, T. K.; Ghosh, S.; Rao, M. H. V. R.; Kunwar, A. C.; Chob, H.; and Ghosh, A. K.; Tetrahedron Letters **2000,** 41 10121–10125.
3. Marco-Contelles, J.; Gallego, P.; Rodriguez-Fernadez, M.; Khair, N.; Destabel, C.; Bernabe, M.; Martinez-Grau, A.; Chiara, J. L.; *J. Org. Chem* **1997**, 62, 7397-7412

P-49

Synthesis, molecular docking and PTP1B inhibitory activity of functionalized naphthofurans and dibenzofurans

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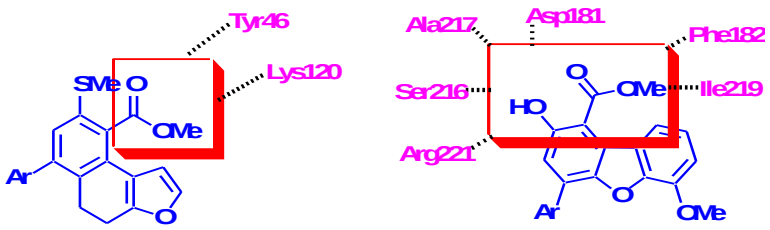
Over the last few years, a tremendous amount of efforts have been devoted on developing orally active PTP1B inhibitors for the treatment of diabetes. Majority of known inhibitors possess tyrosine mimetic structures functionalized with negatively charged moieties such as phosphonates,[1] malonates,[2] carboxylates,[3] or cinnamates.[4] Although highly potent PTP1B inhibitors have been identified, most of these are either too large, too negatively charged or too lipophilic leading to lack of the necessary physicochemical properties that are required for bioavailability and high efficacy. The development of small molecule PTP1B inhibitors has emerged only recently as a rapidly growing area of investigation in medicinal chemistry.[5]

Based on the ligand-receptor binding interactions of known PTP1B inhibitors, it was envisaged that simulation of both hydrophilic and hydrophobic moieties such as carboxylates, hydroxy and methylsulfanyl onto a naphthofuran and dibenzofuran scaffold might lead to potential PTP1B inhibitors. In this presentation, we describe synthesis, molecular modeling studies, and PTP1B inhibitory activity of functionalized naphthofurans and dibenzofurans, which formed several non-covalent interactions with the crucial residues of PTP1B and demonstrated good inhibitory activity.



Pharmacophores showing interactions with catalytic residues of PTP1B

(a) Burke, T. R., Jr.; Kole, H. K.;Roller, P. P. *Biochem. Biophys. Res. Commun*. **1994**, *204*, 129. (b) Taylor, W. P.; Zhang, Z.-Y.; Widlanski, T. S. *Bioorg. Med. Chem*. **1996**, *4*, 1515.

(b) Ye, B.; Akamatsu, M.; Shoelson, S. E.; Wolf, G.; Giogetti-Peraldi, S.; Yan, X.; Roller, P. P.; Burke, T. R., Jr. *J. Med. Chem*. **1995**, *38*, 4270. (b) Burke, T. R., Jr.; Ye, B.; Akamatsu, M.; Ford, H.; Yan, X. J.; Kole, H. K.; Wolf, G.; Shoelson, S. E.; Roller, P. P. *J. Med. Chem*. **1996**, *39*, 1021.

(c) Sarmiento, M.; Wu, L.; Keng, Y.-Y.; Song, L.; Luo, Z.; Huang, Z.; Wu, G.-Z.; Yuan, A. K.; Zhang, Z.-Y. *J. Med. Chem*. **2000**, *43*, 146. (b) Iversen, L. F.; Andersen, H. S.; Branner, S.; Mortensen, S. B.; Peters, G. H.; Norris, K.; Olsen, O. H.; Jeppesen, C. B.; Lundt, B. F.; Ripka, W.; Møller, K. B.; Møller, N. P. H. *J. Biol. Chem.* **2000**, *275*, 10300.

(d) Moran, E. J.; Sarshr, S.; Cargill, J. E.; Shahbaz, M. M.; Lio, A.; Mjalli, A. M. M.; Armstrong, R. W. *J. Am. Chem. Soc*. **1995**, *117*, 10787. (b) Cao, X.; Moran, E. J.; Siev, D.; Lio, A.; Ohashi, C.; Mjalli, A. M. M. *Bioorg. Med. Chem. Lett*. **1995**, *5*, 2953.

(e) Ockey, D. A.; Gadek, T. R. Bioorg. Med. Chem. Lett. 2004, 14, 389-391. (b) Umezawa, K.; Kawakami, M.; Watanabe, T. *Pharmaco. Therapeutics*, 2003, *99*, 15-24.

P-50

An Elegant Approach to Biologically Active Oxygen Heterocycles through Ring Transformation Strategy

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Oxygen heterocycles such as coumarins, isocoumarins, dibenzopyranones are an important class of naturally occurring and biologically active lactones[1] which possess diverse pharmacological activities. These scaffolds are known as privilege skeletons and are considered as useful building blocks for the construction of complex natural products of therapeutic importance.
During the course of our recent study[2] on the chemistry of □-pyrones, we identified acetyltrimethylsilane as a novel reagent for the transformation of □-pyrones to unsymmetrical biaryls. The promising structural feature of □-pyrone as versatile intermediate is due to the presence of 2,4,6-trielectrophilic positions in which positions 2 and 4 are highly susceptible to various *C*-, *N*- and *S*-nucleophiles generating molecular diversity.[3] Recently we have developed an efficient and concise route for the synthesis of various oxygen heterocyclic compounds by a carbanion-induced ring transformation of suitable functionalized □-pyrones in excellent yield. The beauty of the reaction lies in the formation of an aromatic ring from □-pyrones utilizing methylenecarbonyl unit of the ketone substrate in a single step through easily accessible precursors.

1. Review: Darbarwar, M.; Sundaramurthy, V. *Synthesis* **1982**, 337-388. (b) Murray, R.; Mendez, J.; Brown, S. *The Natural coumarins: Occurrence, Chemistry and Biochemistry*; John Wiley & Sons: New York, 1982; pp 97-111.

2. Goel. A.; Verma, D.; Dixit, M.; Raghunandan, R.; Maulik, P. R. *J. Org. Chem.* **2006**, *71*, 804-807.

3. (a) Goel, A.; Dixit, M. *Tetrahedron Lett.* 2004, *45*, 8819-8821. (b) Goel, A.; Singh, F. V.; Sharon, A.; Maulik, P. R. *Synlett* 2005, 623-626. (c) Goel, A.; Singh, F. V.; Verma, D. *Synlett* 2005, 2027-2030. (d) Ram, V. J.; Srivastava, P. *Curr. Org. Chem*. 2001, *5*, 571.

P-51

Orally Active Amino Functionalized 1, 2, 4-trioxanes: Synthesis and Antimalarial Assessment

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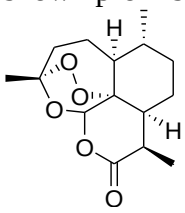
Malaria is a major parasitic disease affecting over 100 countries of the tropical and subtropical regions of the world including India. Around 300-500 million clinical cases of malaria are reported every year of which around 2-3 million die due to complicated cases of malaria[1].Situation is getting worse with the emergence of multi-drug resistant parasites. Against this background, isolation of artemisinin**1** by the Chinese as the antimalarial principle of *Artemisia annua* has been a major breakthrough in malaria chemotherapy. Artemisinin is active against both chloroquine-sensitive and chloroquine-resistant malaria[2].The peroxide

group present in the form of 1,2,4-trioxane in the artemisinin is essential for antimalarial activity. However due to several disadvantages associated with artemisinin such as limited availability from natural sources, high cost and poor bioavailability, there have been concerted effort from several research groups to prepare structurally simple 1,2,4-trioxanes[3].
As part of our endeavour to develop orally active simple substituted 1,2,4-trioxanes from easily accessible starting material, we have synthesized a new series of amino functionalized 1,2,4-trioxanes (prototype**2**) and assessed them for their antimalarial activity against multi-drug resistant strain *P.yoelii* in Swiss mice by oral route. Several of these trioxanes have shown promising antimalarial activity[4].



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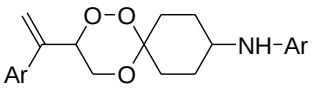

2

References:

1. W. H. O. *Drug Inf. Bull.* 1999, *13*, 9.
2. L. Qinghaosu. *Science*1985, *228*, 1049-1055. (b) Luo, X. D; Med. *Res. Re*v. 1987, *7*, 29-52. (c) Posner, G. H. *Ad*v. *Pharmacol.* 1997, *37*, 253-297. (d) Bhattacharya, *Heterocycles;* 1999, *51*, 1681-1745. (e) Shapiro, T. A.; Posner, G. H. *Int.J. Parasitol.* 2002, *32*, 1661-1667. (f) Ploypradith. *Acta Trop.* 2004, *89*, 329-342. (g) O'Neill, P.M.; Posner. *J. Med. Chem.* 2004, *47*, 2945-2964.
3. For recent reviews on antimalarial peroxides see: (a) Jefford, C. W. Curr. Med. Chem. 2001, 8, 1803–1826;(b)McCullough, K.J.;Nojima, M. Curr. Org. Chem. 2001, 5,601–636;(c) Bez, G.; Kalita, B.;Sarmah, P.;Barua, N.;Dutta, D. K. Curr. Org. Chem. 2003, 7, 1231–1255;(d)Tang, Y.;Dong, Y.;Vennerstrom, J. L. Med. Res. Rev.2004, 24, 425–448.
4. (a) Singh,C. *Tetrahedron Lett*. 1990, *31*, 6901-6902. (b) Singh, C. *Bioorg. Med. Chem. Lett.* 1992, *2*, 497-500. (c) Singh, C. *Bioorg. Med.Chem. Lett.* 1995, *5*, 1913-1916. (d) Singh, C.*Bioorg.Med. Chem.* 2004, *12*, 5553-5562.

P-52

Synthesis and Evaluation of Novel Benzocycloheptapyridines as Anticancer Agents.

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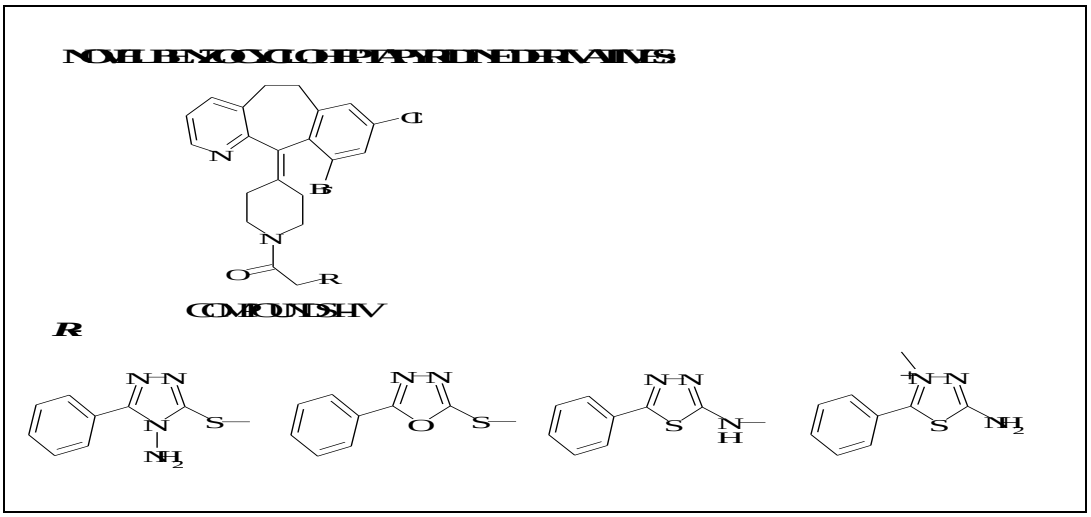
A novel class of benzocycloheptapyridine derivatives was synthesized as potential anticancer agents, as compounds belonging to this class have shown potent anticancer activity and specifically Farnesyl protein Transferase (FPT) inhibitory activity.
In the present work, we report the synthesis of four novel benzocycloheptapyridine analogs. They were also evaluated in MCF7 Human Breast, Hop62 Human Lung, and Colo205 and HT29 Human Colon Cancer Cell lines. Sulforhodamine-B (SRB) semi automated assay protocol was followed using adriamycin as a standard. The test compounds were evaluated at 10, 20, 40, and 80 µg/ml concentrations.
Activity was expressed as % inhibition as compared to control. Of the four compounds tested, two compounds exhibited % inhibition in the range of 20.8 to 86.0. Compound I was found to

have % inhibition greater than that of adriamycin at the doses tested in HT29 human colon cancer cell line indicating superior activity compared to adriamycin.



P-53

Synthesis of a Tetra and a Trisaccharide Related to the Antitumor Triterpenoid Saponin julibroside J_{28} Isolated from *Albizia julibrissin*

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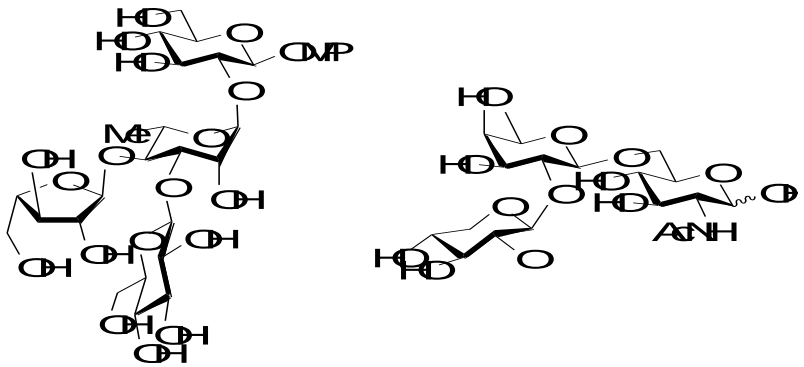
Chemical synthesis of bioactive natural products has become an important area of current research owing to the difficulties associated with the isolation of natural products in quantity. The current poster illustrates the total synthesis of a tetra- and a trisaccharide related to the triterpenoid saponin julibroside J_{28} isolated from *Albrizia julibrissin*.[1] The target compound is important due to its significant antitumor activity against PC-3M-1E8, Bel-7402, and HeLa cancer cell lines *in vitro*. Target compounds have been synthesized from commercially available D-glucose, L-rhamnose, L-arabinose, D-xylose, *N*-acetyl-D-glucosamine and D-fucose through rational protecting group manipulation.



Reference: [1]Liang, H.; Tong, W-y.; Zhao, Y-y.; Cui, J-r.; and Tu, G-z. *Bioorg. Med. Chem. Lett.* **2005**, 4493-4495.

P-54

R&D, Innovation And Patents

M. A. Shookur, M. M. Shahroz* S. Nayeem[*]. **M. A. Degan**[#].
**Dr. Rafiz Zakaria Centre for higher education, Rauza Baag, Aurangabad, Maharashtra, INDIA. # Y.B.Chavan College of Pharmacy Rauza Baag, Aurangabad, Maharashtra, INDIA.*

An intellectual property is any product or invention of human intellect that is unique, novel and non-obvious and has some commercial value. The commercial, Strategic and Financial importance of Intellectual property and particularly patents has increased dramatically in the past several years on a global basis. There is increase in patent fillings in countries such as Brazil, China, India, Korea and Mexico. The impact of differences in patent systems. Patent statistics are increasingly recognized as useful indicators of invention activity and of technology flows. Three indicators are presented that weight patent fillings by measures of country size and economic activity, namely population, GDP and research and development expenditure. Growth in PCT international applications. Various issues relating to the international aspect of the patent systems. R&D, Innovation and Patents.

Keyword: Intellectual Property, Patent, Patent Co-operative treaty.

P-55

Novel Gram Scale Synthesis of Clonidine

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Agents stimulating δ_2-adrenoceptors have shown to mediate a variety of physiological functions including reduction of blood pressure, sedation and inhibition of intestinal fluid secretion.[1,2] Designing and synthesis of δ_2-adrenoceptor agonists is of current interest in order to reduce elevated intraocular pressure (IOP).[3] Reduction in IOP is the only currently accepted outcome for a glaucoma medication. It is demonstrated that agents acting at δ_2-adrenoceptors are potent ocular antihypertensive agents.[4] The $\square_2$-adrenoceptor therefore representes an attractive therapeutic target for the treatment of glaucoma. The ideal agent would reduce elevated intraocular pressure without other biological action. In this paper we are going to report novel synthesis of $\square_2$-adrenoceptor, clonidine. Excellent yield of the product with high purity is an important feature of this synthetic route.

References:

1. Maze, M.; Tranquilli, W. *Anesthesiology* **1991**, *74*, 581-605.
2. Hieble, J. P.; Ruffolo, R. R. Jr. *Basic and Clinical Pharmacology*; Ruffolo, R. R., Jr. Ed.; S. Karger A. G. Basel, 1991; Vol. 8, pp 180-220.
3. Shields M. B. *Textbook of Glaucoma*, 3rd ed. Williams and Wilkins: Baltimore, **1992**.

4. Makab, R. *Dtsch. Med. Wochenschr*. **1966**, *91*, 1686-1688.

P-56

Design, synthesis, ^{1}H NMR and X-ray crystallographic study on pyrazolo[3,4-*d*]pyrimidine core based dissymmetrical "Leonard/propylene linker" compounds for studying arene-arene interactions in flexible compounds

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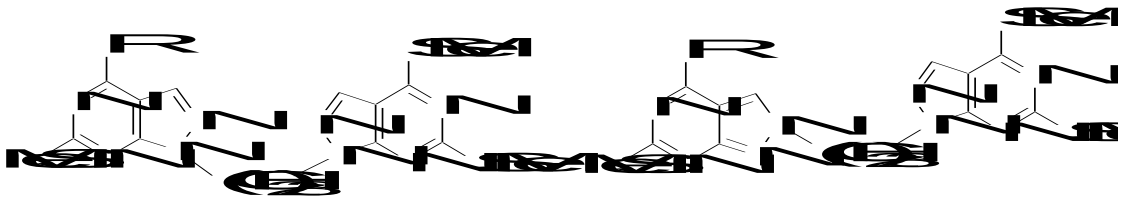
Arene interactions are known to play an important role in chemistry, biology, particularly in molecular recognition and stabilization of DNA/RNA and protein structure, crystal engineering, molecular tweezers/clips, foldamers and drug development.
A thorough understanding of the nature of the arene interaction is essential for their proper utilization.
In 1995 group at CDRI started, for the first time, started use of pyrazolo[3,4-*d*]pyrimidine core, which is isomeric with biologically significant purine system for studying arene interactions in flexible compounds. Thus, they reported first synthesis of 1,3-bis(4,6-dimethylsulfanyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)propane, **1** (N1-N1'- isomer) which showed intra-molecular stacking by proton NMR and both inter- and intramolecular stacking by X-ray crystallographic studies as new flexible model for studying intramolecular arene-arene interaction. Interestingly, positional isomer, **2** (N1-N2'- isomer) of **1** does not show intramolecular stacking by proton NMR or X-ray crystallography.
Now, we report synthesis, proton NMR and X-ray crystallographic study on two new pyrazolo[3,4-*d*]pyrimidine core based dissymmetrical "Leonard/propylene linker" compounds (**3** & **4**) in which one methylsulfanyl group has been replaced by bulky isopropoxy group.



1. R = SMe; **3**. R = O-iso-P **2**. R = SMe; **4**. R = O-iso-P

P-57
Synthesis and Screening of Some Gallic Acid Derivatives

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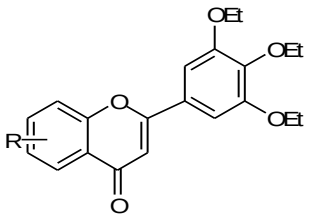
Aurangabad - 431 004.

Gallic acid (3,4,5 trihydroxy benzoic acid) seems to have anti fungal and anti viral properties[1]. It acts as anti oxidant and helps to protect human cells against oxidative damage [2]. Gallic acid is found to show cytotoxicity against the cancer cells without harming healthy cells, particularly against the primarily cultured rat hepatocytes and microphages. Cell death in dRLH-84 cells occurred within 6hrs after gallic acid treatment at a concentration of more than 20micrograms/ml[(3-7)].

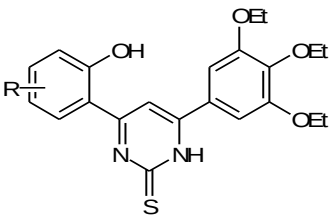
The Heterocyclic compounds like chromones, flavones, pyrimidines, imidazoles, benzothiazines etc. are also found to be associated with various biological activities.

It was thought worthwhile to incorporate gallic acid as a constituent in these heterocycles and screen them for potential biological activity.

Following new derivatives are synthesized and their structures are characterized.



(I)



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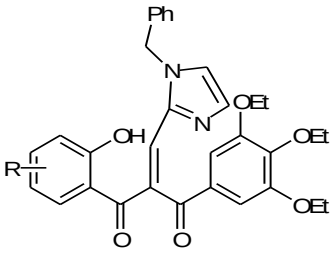

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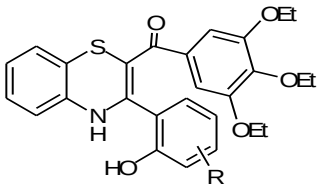

(IV)

References:

1. Current Drug Metabolism, Vol.4, No.3, June 2003, pp.241-248(8)
2. Free Radic Biol Med. 2004, Aug 1;37(3):287-303.
3. Biol Pharm Bull. 1995, Nov; 18(11): 1526-30.
4. Anticancer Drugs. 1999 Oct; 10(9): 845-51.
5. J. Ethnopharamacol. 1996, Aug; 53(2): 57-63.
6. Oncol. Rep. 2000 Nov-Dec;7 (6):1221-23.
7. Biol Pharm Bull. 1999 May; 22(5):471-5.

P-58

Concise Synthesis Of A Trisaccharide Repeating Unit Of The Exopolysaccharide Produced By *Lactobacillus* Spp. G-77

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An wide variety of exopolysaccharides (EPS's) produced by Lactic acid bacteria (LAB) present in the body provide an important contribution to human health by acting as prebiotic substrates, nutraceuticals, cholesterol lowering agents or immunomodulants.[1] Recently it has been observed that EPS produced by lactic acid bacteria have suitable rheological properties for the dairy industry.[2] In wine industry, the polysaccharides produced by LAB can cause the alteration known as oiliness or ropiness by increasing the consistency of the beverage. The structure of a ropy strain of *Lactobacillus* spp. G-77 has been characterized recently,[3] which contains a unique 1,2-*cis* linked branched trisaccharide (Figure 1). In order to analyze and assess the role of EPS produced by *Lactobacillus* spp. G-77, a reasonable quantity of the trisaccharide is required. Recently, we are engaged in synthesizing some oligosaccharides for their evaluation in several biological studies. As a part of our ongoing program, we herein report a concise synthesis of this unique trisaccharide as its methyl glycoside (Figure 1).

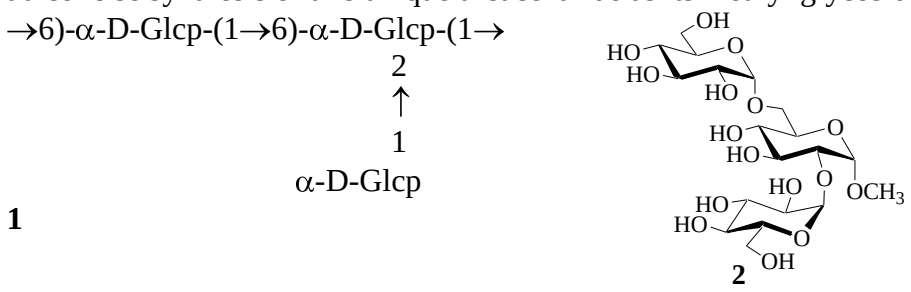

Figure 1: Trisaccharide repeating unit of the exopolysaccharide produced by *Lactobacillus* spp. G-77 (**1**) and synthesized trisaccharide as its methyl glycoside (**2**).

References

1. van Hijum, S. A. F. T.; van Geel-Schutten, G. H.; Dijkhuizen; L.; Rahaoui; H. US Patent US 6,730,502, 2004.
2. Cerning, J. *FEMS Microbiol. Rev*. **1990**, *87*, 113-130.
3. Duenas-Chasco, M. T.; Rodriguez-Carvajal, M. A.; Tejero-Mateo, P.; Espartero, J. L.; Irastorza-Iribas, A.; Gil-Serrano, A. M. *Carbohydr. Res.* **1998**, *307*,125-133.

P-59

Charge Transfer Complexes Of Paraquat With Phenolate And Catecholate Drugs

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Molecular Complexes of Paraquat (PQ) with a few drugs containing phenol and catechol rings were studied spectrophotometrically. Substituted phenolate anions of drugs produced characteristic colours with paraquat indicating the formation of CT complexes and

wavelengths of CT bands are found in the order: Pholedrine > p-Cresol > Tyrosine > Nylidrin > Isoxsuprine > Phenol > Salbutamol. Catecholates exhibited CT bands at wavelengths slightly higher than those of phenolate complexes and are found in the order: L-Dopa > Carbidopa > Dopamine > Epinephrine > Catechol.

The energies of the intermolecular CT bands (E_{CT}) of the complexes in solution were calculated from the frequencies of absorption and significant changes were observed upon substitution. The order of E_{CT} values: L-Dopa < Carbidopa < Dopamine < Epinephrine < Pholedrine < Catechol < p-Cresol < Tyrosine < Nylidrin < Isoxsuprine < Phenol < Salbutamol. The Ionization Potentials of donors were evaluated using appropriate equations. Rose-Drago plots and Job's variation method indicated that the formation of 1:1 complex in each case. The stability constants of the complexes determined by Rose-Drago method increased with electron releasing ability of the donors and were in the order: L-Dopa > Carbidopa > Dopamine > Epinephrine > Pholedrine > Catechol > p-Cresol > Tyrosine > Nylidrin > Isoxsuprine > Phenol > Salbutamol, and are useful in the estimation of the concentration of drugs either in pure form or in formulations and give a guide to the estimation of the drugs in industry and pharmacy.

The thermodynamic parameters (-ve values of ΔH) suggest that the formation of complex is exothermic. The $-\Delta S$ values indicate a decrease in the degree of freedom of the components upon complexation while $-\Delta G$ values indicate that the complex formation is spontaneous and the values give a relative estimation of interaction between donors and acceptors. The linear relationship between ΔH and ΔS indicates that the complexation is unhindered by the substituents present on phenol or catechol.

P-60

Design And Synthesis Of N-Substituted Benzamides

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Epilepsy affects nearly 50 million people worldwide. Existing anticonvulsant agents produce adverse effects such as ataxia, hepatotoxicity, gingival hyperplasia and megaloblastic anemia. Thus there is a need for more effective anticonvulsant agents.
N-substituted benzamides are found to possess potent anticonvulsant activity which on further development can be promising agents to treat various epileptic conditions.
The work was aimed at developing novel N-substituted benzamides. The series of N-substituted benzamides was designed by taking into consideration of a quantitative structure activity relationship and the pharmacophoric distances of reported anticonvulsant molecules. Two point pharmacophore of the reported compounds was generated using Molecular Operating Environment (**MOE**) software *version 2005.06* **(Chemical Computing Group. Inc., CCG, Canada)** running on Pentium IV 1.6 GHz workstation under Windows OS. The pharmacophoric points were mapped on the designed series in order to predict the anticonvulsant activity. The distances between hydrogen bond donor/acceptor to aromatic region for reported compounds were in the range of 3.46 – 6.84 Å. while that for designed series was 3.47 – 4.62 Å.
The designed series of N-substituted benzamides were synthesized by oxidative chlorination of p-amino benzoic acid which gave 4-amino-3,5-dichorobenzoic acid. The acid halide was

obtained using phosphorus pentachloride which was further condensed with various substituted amines yielding the desired series of N-substituted benzamides. The amidation carried out using the six station parallel synthesizer (**MINIBLOCK ™ XT**) which offered advantage in percentage yield in minimum time as compared to the conventional synthesis method. All compounds were characterized by using IR and NMR spectroscopy.

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P-61

Inhibitors Of DPP-IV And Protein Tyrosine Phosphatase 1 B In The Management Of Type 2 Diabetes Mellitus

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Dipeptidyl peptidase (DPP-IV; E.C: 3.4.14.5) is a ubiquitous, yet highly specific serine protease that cleaves N-terminal dipeptides from polypeptides with L-Proline or L-alanine at the penultimate position. It alters or abolishes the biological activity of many regulatory peptides *in vitro*. Glucagon like peptide 1 (GLP-1) is the well known incretin hormone in the body having insulinotropic effect. DPP-IV inactivates native GLP-1 by cleaving the N-terminal two amino acids after proline, thus reducing the half-life of GLP-1 by 1-2 min that leads to decrease insulin stimulated glucose disposal. Compounds capable of specifically inhibiting DPP IV may be candidate drugs for type 2 diabetes mellitus.
Protein Tyrosine Phosphatases (PTP-1B) constitute a diverse family of enzyme and are responsible for the selective dephosphorylation of tyrosine residues. Tyrosine phosphorylation of cellular proteins by protein kinases seems to play a profound but complicated role in β-cell growth, development and secretion. In normal circumstances there is synchronization between these two enzymes i.e. protein tyrosine kinase and protein tyrosine phosphatase. Protein tyrosine phosphorylation is controlled not only by tyrosine kinases but also by the activity of protein tyrosine phosphatases that dephosphorylate phosphotyrosine residues, an important signal transduction pathway in the insulin secretion/ action, which get disturbed in diabetes mellitus and insulin resistance. In the case of insulin resistance the activity of protein tyrosine phosphatase-1B was found to be increased because of the high expression of PTP gene. Therefore, for the treatment of insulin resistance and non-insulin dependent diabetes mellitus, the use of PTPase inhibitors represents a novel strategy.
Of the total compounds screened for PTPase and DPP-IV inhibition activity, the following compounds showed significant inhibition on PTPase 1B i.e. S-005-210, S-005- 197, S-005-461, S-005- 462 CDR-181-K012, CDR- 181-K013, CDR- 181-K 014, CDR- 181-K015, CDR- 181-K-016, CDR-181-K-017, CDR181-K-018, CDR-181-K-019, where as, none of the compound showed inhibition on DPP-IV.

P-62

Antihyperglycemic Activity In Chemical Constituents Of *Derris indica* Fruits

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The use of herbs in the control of blood sugar level is known since Vedic age and plants still today present a large source of structurally novel compounds that might serve as leads for the development of novel drugs. In present study the antihyperglycemic activity of 11 major chemical constituents isolated from the chloroform soluble fraction of the ethanolic extract of *Derris indica* (*Pongamia pinnata)* fruits were examined in streptozotocin-induced diabetic rats and of the active ones in hyperglycemic, hyperlipidemic and hyperinsulinemic db/db mice (Type 2 diabetes model). Results revealed that two among them showed significant antihyperglycemic activity in these models and have been observed to exert their action possibly through inhibition of the enzyme protein tyrosine phosphatase 1B (EC 3.1.3.48). Three other compounds showed mild to moderate antihyperglycemic activity in streptozotocin-induced diabetic rats whereas the remaining six showed no demonstrable antihyperglycemic effect. The, compounds showing significant glucose lowering activity might be useful source of new hypoglycemic agent for development of pharmaceutical entities or as a dietary adjunct to existing therapies of diabetes mellitus.

P-63

Development And Evaluation Of Transdermal Therapeutic System Of Enalpril Maleate Using Piperidine Hydrochloride As Penetration Enhancer

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The aim of this work is to formulate a transdermal therapeutic system (TTS) of enalapril maleate (EM) containing a new penetration enhancer, piperidine hydrochloride. Piperidine Hydrochloride (PH), belonging to the class of Dihydropyridines was previously investigated for its capacity to enhance the percutaneous transport of a model antihypertensive drug enalapril maleate (EM). TTS of EM was prepared using polymers Eudragit E100 and polyvinyl pyrrolidone K-30 in varying ratios, 5% w/w dibutylphthalate as plasticizer and 10% w/w PH as penetration enhancer by solvent evaporation technique. The TTS was evaluated for *in-vitro* release characteristics using paddle-over-disc method and *ex-vivo* skin permeation using Keshary and Chein diffusion cell. The interaction studies were carried out by comparing the results of UV, IR and TLC analysis for pure drug, medicated and placebo formulations. Skin irritation potential of TTS was assessed by visual examination of treated rat skin. Stability studies were conducted according to ICH guidelines at a temperature of 40± 0.5° C and 75 ± 5% RH. The final optimized preparation was evaluated for *in-vivo* pharmacokinetics by HPLC and antihypertensive efficacy on hypertonic saline (2%) induced hypertensive albino rats. The optimized formulation showed (87.36 %) *in-vitro* release of EM over a period of 48 hours with a permeability coefficient (3.86×10^{-2} cm/hr). No chemical interaction was found between the drug and excipients and there were no signs of skin irritation on application of patch. The optimized formulation was assigned a tentative shelf life of two years. There was a significant fall in BP ($p < 0.001$) in experimental hypertensive rats which maintained for 2 days. In vivo pharmacokinetic study showed that the plasma concentration of EM promptly increased and reached the peak level within 1.0-1.5 hours of application of the experimental patch. Area under the curve (AUC_0 approximately 1253.9 ng.h/ml) and C_{max} also linearly increased in a dose-dependent manner up to 62.44 ng/ml of EM. These results demonstrate the feasibility of developing matrix-type TTS of EM for 48 hours for 2 day management of hypertension.

P-64

HPTLC method for quantification of Emodin in *Cassia occidentalis*.

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Cassia occidentalis (Syn. *Senna occidentalis*) is a member of Family Fabaceae Leguminosae i.e. Pea family. It is commonly known as Kasondi. It is found throughout India. Medicinally, seeds, leaves and roots are used in Traditional system and Modern system of medicine. The plant is reported to possess hepatoprotective, antimicrobial, anti- inflammatory, purgative and diuretic etc. like actions. The main chemical constituents reported in plant are anthraquinone glycosides (chrysophanol, emodin, aloe-emodin etc.), quercetin, β- sitosterol, niacin, ascorbic acid etc.
The quantitative estimation of total anthraquinone content and emodin content was successfully carried out in three parts viz, leaf, stem and root of *C. occidentalis* by UV spectrophotometer and HPTLC methods.

P-65

Role Of Adapalene On In Vitro Skin Penetration Of Clindamycin Phosphate

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Adapalene and Clindamycin phosphate have demonstrated clinical efficacy in the treatment of acne vulgaris. When used in tandem they promise enhanced efficacy then either individual agent. The objective of the present study was to investigate the role of topical application of adapalene on penetration of clindamycin phosphate.
For this study, radiolabeled clindamycin phosphate gel at a target dose of 5 mg /dose/cm^2 was applied concomitantly and after pre-treatment of skin sections for 3, 5 and 10 minutes with 10 mg of 0.1% adapalene per cm^2 . At the end of the application period (12 hours), the entire dosing area of skin collected and clindamycin was quantified by liquid scintillation. Data clearly demonstrate that adapalene act as a penetration enhancer and increases the penetration of clindamycin phosphate through rat skin. When clindamycin phosphate gel was applied alone, only 5.13% of radioactive clindamycin phosphate was penetrated into the skin. Concomitant application of adapalene increases the penetration of clindamycin phosphate to 8.7%. Pretreatment of skin with adapalene for 3 and 5 minutes prior to application of clindamycin gel, significantly increases the penetration to 12.75% and 15.5% respectively. Furthermore, no significant influence was observed with further increase in pretreatment time to 10 minutes. The modest amount of radioactive clindamycin phosphate were permeated to the receptor phase indicating enhanced localized drug accumulation and minimized unwanted systemic side effects.
The characteristic property of adapalene, to enhance the penetration of clindamycin phosphate into skin makes it a good choice as therapy in combination with clindamycin phosphate for the treatment of acne.

P-66

Preparation and characterization of bioadhesive microspheres for subgingival delivery of gatifloxacin.

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Periodontitis is a polymicrobial infection characterized with a complex etiology and host microbial responses. Initiated as gingival swelling and hemorrhage it subsequently aggravates into loss of attachment, alveolar destruction and eventually results in tooth loss. Conventionally control and management of such infections warrant systemic antibiotherapy but recently a paradigm shift towards development of local drug delivery systems has emerged as a novel option. Drug loaded natural, biodegradable, bioadhesive chitosan microspheres designated to be placed subgingivally can deliver high concentration locally while circumventing the adverse effects of systemic antibiotics.
Microspheres were prepared by emulsion crosslinking method using chitosan as a biodegradable polymeric carrier and glutaraldehyde as a chemical denaturant.
Formulation parameters such as concentration of cross-linking agent, polymer concentration, cross-linking and stirring time were studied. The optimized formulation was further characterized for surface morphology (SEM), payload, and ex-vivo bioadhesion using everted rat intestine model, in vitro drug release and particle size analysis.
Prepared microspheres exhibited high payload, (79.8%), spherecity and small particle size range (average -50µm) with low poly-dispersity index. Chitosan owing to its strong electrostatic binding exhibited a high bioadhesion percentage of 70- 80%. In vitro release profile indicated controlled release of drug for over 48 hours with initial 30% burst release. Clinical efficacy of the prepared formulation is being undertaken.

P-67

Transformations Of Naturally Occurring Lignans Into Bio-Active Compounds

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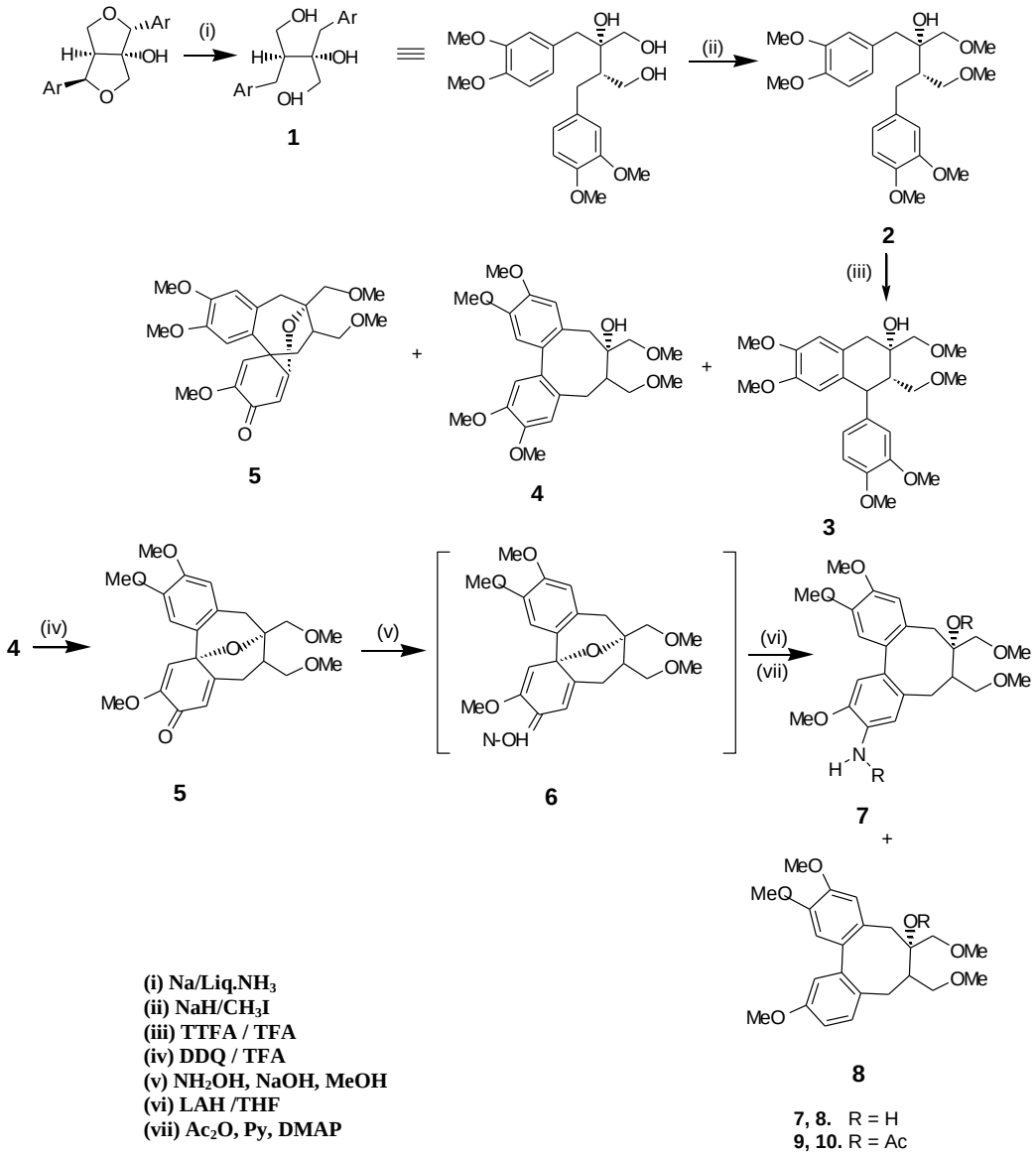
The chemotherapeutic and anti-tumor activity of Podophyllotoxin isolated from Indian species *Podophyllum emodii* and its derivatives etoposide, teniposide and etophos, the platelet activating factor (PAF) antagonistic activity of neo-lignan-futenone and also heptaprotectant activity of dibenzocyclooctadienes, gomisin-A etc., have generated considerable interest in the study of lignans.
In continuation of our studies on the transformations of naturally occurring lignans[1] with a view to produce possibly bio-active lignans, we could develop a methodology to oxidise 1-aryl naphthalene lignan, diphyllin (*Cleistanthus collinus*) with hypervalent iodine reagents, viz. PIDA/PIFA to 1-methoxy-1-aryl-4-oxonaphthalene lactone, which on reductive reactions to a number of lignan derivatives including 3,4-dihydrodiphylin. These results were published in *Tetrahedron, 2006, p. 4463-4473.*
In another experiment with a view to producing amino-substituted dibenzocyclooctadiene, the 2,3-dibenzylbutane-2-hydroxy-1,4-dimethoxy-di-O-methylether (2), prepared from gmelinol hydrogenolysis product (1) was treated with 2-equivalents of TTFA in TFA and a mixture of three products (3, 4, 5) was obtained. 3, 4 and 5 were identified as 1-aryl tetralin dimethyl

ether, dibenzocyclo-octadiene dimethyl ether and spirodienone respectively by spectral characteristics and comparison with authentic samples.

With a view to synthesize amino-substituted dibenzocyclo-octadiene, spirodienone (5) was reacted with hydroxylamine hydrochloride and oxime (6) was obtained, which showed a molecular formula $C_{23}H_{29}O_7N$ (M^+ 431). Based upon its spectral characteristics, compound 6 was identified as spirodienone oxime. Treatment of (6) with LAH/THF gave a mixture of two products, aminoderivative (7) and de-aminoderivative (8). Compounds 7 and 8 on treatment with acetic anhydride and DMAP in pyridine, yielded acetamidodibenzocyclooctadiene (9) and amino dibenzocyclooctadiene diacetate (10). The results will be discussed along with the spectral data.



Scheme-1

Reference:

[1]. Transformations of Lignans: Part 11: Oxidation of diphyllin with hypervalent iodine reagents and reductive reactions of a resulting 11-methoxy-1-aryl-4-oxonaphthalene

lactone R.Venkateswarlu*, C. Kamakshi, P.V. Subash, S.G.A. Moinuddin, D. Rama Sekhara Reddy, R.S. Ward*, A. Pelter, T. Gelbrich, M.B. Hursthouse, S.J. Coles and M.E. Light; *Tetrahedron* 62 (2006) 4463-4473.

P-68

Folding stability of trypanothione reductase from *Leishmania donovani*

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The protozoan parasite *Leishmania* is responsible for several pathologies ranging from self-healing cutaneous lesions to visceral infections that can be fatal if untreated. Leishmaniasis is endemic in 88 countries of the world and is a major public health problem worldwide. Control of the disease relies mainly on chemotherapy despite the complexities of adverse side effects and high costs of current drugs and rapidly emerging clinical resistance to pentavalent antimonials, the first line drug of choice. Hence, there is an urgent requirement for new, effective and safer drugs. The focus is now on exploring the potentials in knowledge based drug development. This calls for the identification and structural characterization of drug targets. One such validated drug target in case of trypanosomatids is trypanothione reductase [TR]. It is vital for intracellular parasite survival and infectivity and is absent in mammalian host. TR is an NADPH-dependent flavoprotein disulfide oxidoreductase central to the thiol redox metabolism of the parasite and catalyzes the reduction of trypanothione to its dithiol form. We have reported the cloning and recombinant expression of TR from *L. donovani*, causative agent of Indian kala-azar. In the present report we have carried out systematic study on the guanidinium chloride- and urea- induced unfolding of trypanothione reductase using optical spectroscopic techniques and enzyme activity measurements.

P-69

Synthesis of 3-(-2-(4-nitrophenyl)-2-(1H-tetrazol-5-yl) vinyl)-4H-chromen-4-ones.

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Tetrazole is a class of heterocycles with wide range of applications that is receiving considerable attention. This functionality has been frequently used as metabolically stable surrogates for carboxylic acid group as well as metabolically stable lipophillic spacers[1].

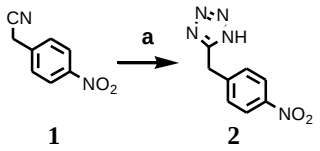
Chromone moieties are associated with interesting physiological activities[2]. Chromones having heterocyclic substituents at 2 & 3 position have been reported to posses' coronary-bilatory activity, muscular relaxation effect and antimicrobial activity.

Condensation reactions of 3-formyl chromones with compounds containing active methylene group were extensively studied[3-5]. Such types of condensations are achieved by using either acids or base catalyst. The condensation reactions of 3-formyl chromones with hydrazine, monosubstituted hydrazine, hydroxylamines and guanidine have been extensively studied.

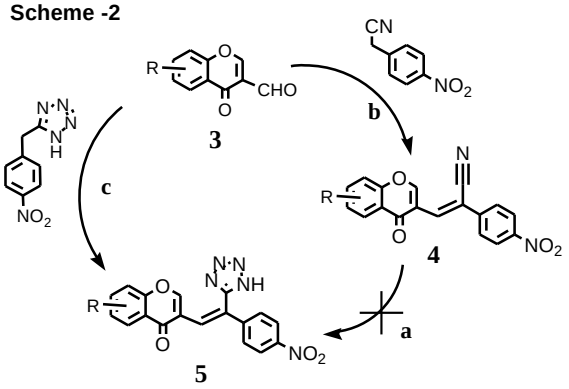
In the present work the condensation of *p*-nitro benzyl cyanide was carried out with 3-formyl chromones and cyano group of [**4**] was tried for conversion into tetrazole moiety under different conditions, but surprisingly the reaction failed in all tested conditions.

However when *p*-nitro benzyl cyanide is converted into corresponding tetrazole derivative [**2**] scheme-1, was found to get swiftly condensed with 3- formyl chromones in pyridine under reflux and yielded title compounds [**5**] in good yields. The compounds synthesized are characterized by spectral data.

Scheme -1



Scheme -2



Reagents : **a**-NaN_3, $ZnBr_2$, water reflux; **b**- acetic anhydride,NaOAc,80^oC;**c**-Pyridine reflux

References:

1. Singh H., Chawla A.S., Prog.Med.Chem; 1980, 17,151-183.
2. C.H.Gill et al.; Ind.J.Chem. 44B, 2005, 422-425.
3. Sarma Rama G V S & Reddy V. M.; Ind.J.Het.Chem. 3,1993, 111.
4. Shingare M.S., Karale B.K., Gill C.H., Ganage K.N., Bachute M.T.; Ind.J.Het.Chem. 9,1999, 153.
5. Hass J., Stanton J.L., J. Het. Chem; 18, 1981,607.

P-70

Synthesis and Biological Screening Of Some Novel Benzimidazoles.

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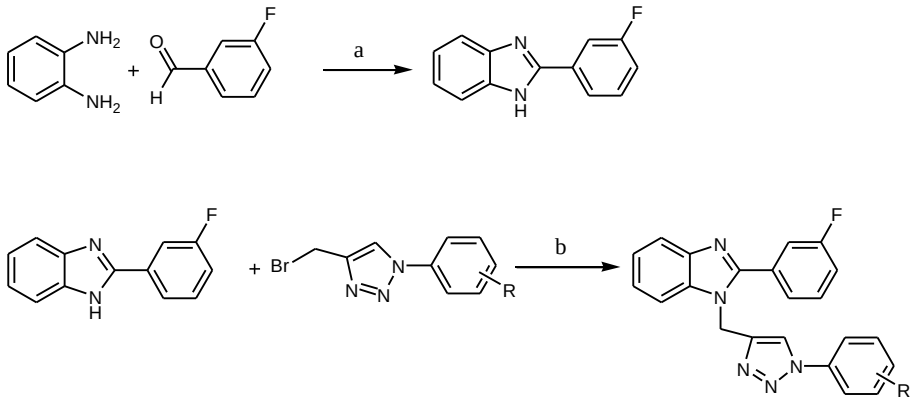
Benzimidazole is one of the important groups of the heterocyclic species because of its synthetic utility and broad spectrum of pharmacological activity. Some benzimidazole derivatives with different pharmacological properties such as human and veterinary anathelmentic, anti-ulcer, cardiotonic, anti-hypertensive etc. have been reported[1-4].

As we know that fluorine in life sciences molecules brings desirable benefits. As many as 30-40% agrochemicals and 20% pharmaceuticals on the market are estimated to contain the fluorine, including half of the top ten drugs sold in 2005.[5]

The pharmacological activities associated with fluorine containing benzimidazoles prompted us to synthesise new benzimidazoles containing fluorine and traizole as substituents and evaluate them for various biological activities.

Scheme 1



R = H, 3-OMe, 3-F, 4-CF_3, 2-OMe
Reaction Conditions; **a** = Toluene, reflux, 4 hrs; **b** = NaH, DMF RT, 15 min.

References:

1. Sheehan D.J., Hitchcock C.A. and Sibley C.M., Clinical Microbiology Rev; 12, 40-79, (1999).
2. Kazimerizeuk Z, Andrrejewska M., Klimesova V., European J. of Med. Chem.; 40, 203-208, 2005.
3. Mariana B., Merchedes G., Mini.Rev. in Medicinal Chemistry; 5, 409-424, 2005.
4. Bins S., Jincheng H., Qun S., Valenzano K.J., Lori S., Scott N., Bio-org. and Med. Chem. Lett.; 15, 719-723, 2005.
5. Ann.M.Thayer,Journal of Fluorine Chemistry,84,15 – 24 (2006)

P-71

Advanced Materials for Organic Electronics

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In the last few decades, conducting polymers (CP) have been very actively pursued. Several discoveries brought CPs to full commercialization with applications in polymer light emitting diodes, solar cells, sensors, and electrochromic devices. Polymer light emitting diodes (PLED) are an emerging and exciting new technology. In the future, these PLEDs have the prospect of competing with or replacing current LCD technology. Also, they have the potential to revolutionize data transmission between computers. (i.e. the internet). They are easier to manufacture, cheaper to produce, and more efficient than normal inorganic LEDs. Organic materials, especially polymers, can be applied over a large area and patterned by lithography. The development of new conjugated polymers with improved performance is a major challenge for material chemists. This seminar will outline design and synthesis of new derivatives of conjugated polymers and copolymers for PLED, memory devices and photovoltaic applications.

References:

1. H. S. Nalwa, Handbook *of Organic conductive molecules and polymers*, John Wiley & Sons, Vol. 1-4, 1997

2. J. H. Burroughes *et al.*, *Nature,* 1990**, 347,** 539-541
3. Horowitz G., *Adv. Mater.*, **1998,** *10,* 365
4. D. Witker *et al.*, *Macromolecules,* **2005,** *38,* 7636

P-72

Antidyslipidaemic Activity Of Terrestrial Plants

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Dyslipidemia, characterized by elevated levels of triglycerides (TG), Cholesterol, LDL-C and low level of HDL-C, is a major risk factor in both type 2 diabetes mellitus (T2DM) and cardiovascular disorders (CVD). High carbohydrate/fat diets have been used in animal models to induce the metabolic changes designated as syndrome X, a disorder in which insulin resistance, hypertension, dyslipidemia and high incidence of cardiovascular diseases (CVD) were described. There exists in Ayurveda, the ancient system of medicine that ceratin plants are being used in the ayurvedic formulations for the management of both T2DM and CVD without much scientific evidence. The high carbohydrate/fat fed hamsters have been potentially found useful in the evaluation of antihyperglycaemic and antidyslipidemic activity of natural and synthetic products. Fenofibrate, a PPAR-alpha selective agonist has been reported to decrease serum cholesterol and triglycerides levels in this model like humans. A number of plant extracts were tested for their antidyslipidemic activity in high carbohydrate/fat diet fed hamsters and out of which the ethanolic extracts of *Glycerrhiza glabra* and *Curcuma* longa showed promising antidyslipidemic activity (i.e. decrease in TG, Chol levels and increase in HDL-C level and HDL-cholesterol/ Cholesterol ratio). Whereas, both the plant extracts had no significant effect on blood glucose levels of these dyslipidaemic hamsters.

P-73

Antihyperglycaemic Activity Of Swertia Chirayita In Validated Animal Models Of Diabetes

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An effort was made to establish and confirm the antihyperglycaemic potential of *Swertia chirayita* (Roxb. ex Fleming) H. Karst. (Gentianaceae) in validated animal models of diabetes. The aqueous extract of *S. chirayita* (CT-1) decreased blood glucose level in the well studied glucose loaded rats (primary screening *in vivo* model), streptozotocin-induced diabetic rats as well as animal models of type 2 diabetes and insulin resistance i.e. db/db mice and high fructose enriched diet fed rats. The extract of *S. chirayita* (CT-1) significantly decreased blood glucose level in both glucose loaded rats and streptozotocin induced diabetic rats. CT-1 also improved glucose tolerance of the hyperglycaemic db/db mice as well as it also improved

the insulin resistance in the fructose enriched diet fed rats after subchronic treatment at dose level of 100 mg/kg body weight. In normal rats CT-1 did not cause lowering of the blood glucose below normal level when fed for 30 consecutive days at 100 mg/kg dose. CT-1 was also found to inhibit α-glucosidase enzyme activity *in vitro*. Present studies thus confirm antihyperglycemic potential in the aqueous extract of *Swertia chirayita*.

P-74

Formulation And Evaluation Of A New Series Of Chalcones And Their Derivatives As Antibacterial Agents.

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Heterocyclic chemistry is a branch which is inseparable from mankind origin or history because it provides our most of the basic need. The efficiency of heterocyclic compounds and its derivatives as pharmaceutical and agrochemicals industries are well established.

Synthesis of 2-(4'-chlorophenylamino)-4-(4'-fluorophenylamino)-6-[4'-{3"-(substituted phenyl/2- furanyl / 2- thienly)-2"-propenon -1"-yl}phenylamino]-*s*-tiazines have been achieved by the reaction between 2-(4'-Chlorophenylamino)-4-(4'-fluorophenylamino)-6-(4'-acetylphenylamino)-*s*-triazine with different substituted aromatic aldehydes and heterocyclic aldehydes, which on cyclisation with hydrazine hydrate in presence of glacial acetic acid give acetyl pyrazolines and also on cyclisation with guanidine hydrochloride in presence of alkali give aminopyrimidines. All the synthesized compounds have been screened for their antibacterial activity against *E.coli* (MTCC 443), *S. paratyphi* (MTCC 733), *S. aureus* (MTCC 96) and *B. subtillis* (MTCC 441). The constitution of newly synthesized compounds have been established on the basis of their elemental analysis IR and H^1 NMR spectral data.

P-75
Friedel Craft Heteroarylation Of Arenes And Heteroarenes: A Facile Entry To 4–(Hetero)-Aryl Substituted Quinazolines And Quinolines

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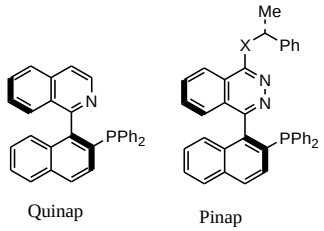
Abstract: The synthesis of 4-aryl/heteroaryl substituted quinazoline and quinoline derivatives via arylation through $AlCl_3$ mediated C-C bond forming reaction is herein reported for the first time. 2,4-Dichloroquinazoline was reacted with a number of (hetero) arenes to give 4-aryl/heteroaryl substituted quinazoline in good to excellent yield. Under similar conditions 4-chloroquinoline derivatives were reacted with (hetero)arenes to furnish 4-(hetero)aryl substituted quinolines.
Atropisomeric biaryls with axial chirality such as Quinap and Pinap containing nitrogen in one of aryl ring are versatile ligands employed in asymmetric catalyzed reactions[1]. These important classes of ligands were synthesized through Suzuki reaction, which requires large

numbers of steps. Alternatively arylation of appropriate hetroaryls through $AlCl_3$ mediated reactions[2] can be elegant short synthetic protocol for the synthesis of these of chiral ligand.



Quinap Pinap

The 4-aryl quinazolines and quinolines have also attracted considerable interest for their antibacterial and other biological activities[3]. 2,4-dichloroquinazoline were reacted with (hetero)arene such as substituted indoles, phenolics in presence of anhydrous $AlCl_3$ in dichloroethane to furnish 4-(hetero)arene substituted 2-chloroquinazoline in 44-86% yield. Under similar conditions electronically deficient 4-chloroquinolines yielded 4-(hetero)aryl substituted quinoline in good yield, the details of which would be presented.

References:

1. a) Chelucci, G.; Orru, G.; Pinna, G.A., *Tetrahedron,* 2003,59,9471. (b) Knopfel, T.F.; Aschwanden, P.; Ichikawa, T.; Watanabe, T.; Carreira, E.M., *Angew.Chem.Int.ed.* 2004,43,5971 and references mentioned therein.
2. Pal M.; Batchu V. R.; Parasuraman K.; Yeleswarapu K.; *J. Org.Chem.* 2003,68,6806.
3. Bedi, P. M. S.; Kumar, V.; Mahajan, M. P., *Bioorg. Med. Chem. Lett.* 2004,14, 5211.

P-76

Synthesis Of Potential Fibrinolytic & Cardiovascular Analeptic Tetrazolo [1,5-A] Quinoxaline Derivatives.

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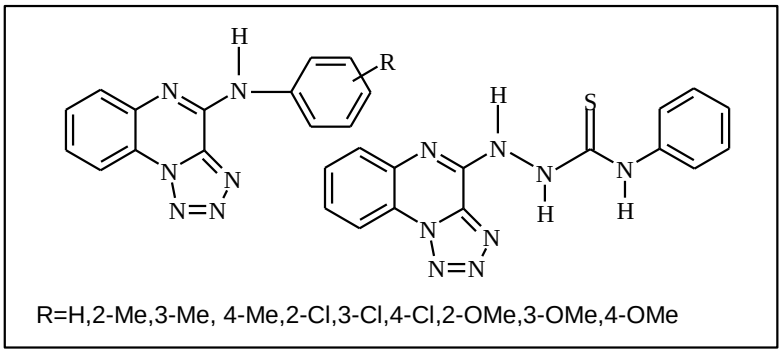
Quinazoline derivatives are of special importance because of their versatile biological and pharmacological activities especially Anti-inflammatory, Anticonvulsant, Hypnotic, Anthelmentic, Hypotensive, Antibacterial agents etc. Similarly, Tetrazoles possess diverse biological activities like antimicrobial, antibacterial, antifungal, anti-inflammatory, anticancer, antiallergic etc. Here we describe an easy and an efficient method to synthesize 2-Hydrazino-3-phenyl-3H-quinazolin-4-ones, which are predicted to be excellent Anorexic, Antiobesity, Anxiolytic and Psychotropic agents. Thus, due to the commendable biological importance of above heterocycles, we report the synthesis new tetrazolo [1,5-a] quinoxalines.
The strategy employed for the synthesis of desired tetrazoles involved synthesis of 4- chloro tetrazolo[1,5-a] quinoxaline which was transformed into 4-arylamino tetrazolo [1,5-a] quinoxalines by interacting with aromatic amines. Further, the compound with hydrazine hydrate yielded 4-hydrazinotetrazolo [1,5-a] quinoxaline, subsequently transformed to 4-

substituted thiocarbamoyl hydrazinotetrazolo [1,5-a] quinoxaline on reaction with phenyl thiocynate. .The structures of the synthesized compounds have been established on the basis of IR, PMR, Mass Spectral and elemental analyses. These compounds were further subjected to computer programme PASS for prediction of biological activities. Thus, tetrazolo [1,5-a] quinoxalines are expected to be potential fibrinolytic and cardiovascular analeptic agents.



R=H,2-Me,3-Me, 4-Me,2-Cl,3-Cl,4-Cl,2-OMe,3-OMe,4-OMe

P-77

Aldose Reductse Inhibitory Activity Studies of Halo-Flavones

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Aldose reductase (AR), a member of aldo- keto reductse super family (AKRIBI) is the first and rate limiting enzyme of the D-sorbitol pathway. AR is frequently formed in highest concentration in lens epithelial tissue. AR activity is responsible for development of secondary diabetic complications such as neuropathy, nephropathy and retinopathy6. Hence, aldose reductase inhibitors are of therapeutic significance in delaying the development of late diabetic complications.

Ten substituted flavones were synthesized and studied for Aldose Reductase Inhibitory (ARI) activity. The inhibitory response of halo-substituted flavones such as 2,4,-dichloroflavones and its derivatives, 3'-iodo-5'-chloroflavone, 3'-iodo-5'-chloro-4'-methyl flavone, 3-iodo-5'chloroflavone and 3'-iodo-4'-methyl-5'-chloro flavone, were studied on bovine lens Aldose Reductase Inhibitory activity. A wide variation in inhibitory pattern was observed with 2,4-dichloroflavone and its derivatives. The level of inhibition was found to be concentration dependent and the compounds showing more than 60% inhibition at 24 uM were found to be 2,4-dichloroflavone and its derivatives. Substitution of chlorine at 2nd position of flavones was observed to be significant for Aldose Reductase inhibition. The present paper describes the effect of halo-substituted flavones on AR activity.

P-78

Simple Spectrophotometric Detection Of Anticancer Drug In Pharmaceutical Samples Using Novel Reagents

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A simple and sensitive spectrophotometric method for the determination of flutamide (FLA) in either pure form or in pharmaceutical preparations is described. The methods are based on the diazotization of reduced flutamide, followed by coupling with alcoholic 4,4'-methylene-bis-(p-amino-3'-hydroxybenzanilide) in acidic medium to give orange red colored product having wavelength of 500 nm. In second method, the diazotization of reduced flutamide followed by coupling with 3-methoxy-4-hydroxy-benzaldehyde in neutral medium to give orange yellow color product having wavelength of 481 nm. Beer's law is obeyed at concentration of 0.3- 17 ppm and 0.2-15 ppm respectively. Common excipients used as additives in pharmaceutical preparations do not interfere in the proposed method. Both the methods are highly reproducible and have been applied to a wide variety of pharmaceutical preparations and results compare favourably with reported method.

Keywords: Flutamide (FLA), 4,4'-methylene-bis-(p- amino-3'-hydroxybenzanilide), 3-methoxy-4-hydroxy-benzaldehyde, pharmaceutical preparations, diazotization, and spectrophotometer.

P-79
Determination Of Mosapride Using Spectrophotometry In Pharmaceutical Preparations

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A facile, novel rapid selective and sensitive spectrophotometric method was developed for the determination of mosapride in either pure form or in its formulations in pharmaceutical preparations is described. The proposed method was based on the diazotization coupling reaction of mosapride with piperzine in acidic medium pH-3.7-4.5 to give red colored product having wavelength of 497nm and is stable for more than 15 hours at optimum condition. Beer's law is obeyed at concentration of 0.1-16 ppm at the wavelength of maximum absorbance. Common excipients used as additives in pharmaceutical preparations do not interfere in the proposed method. The developed method is highly reproducible and applied to wide variety of pharmaceutical formulation and the results were compared favourably with the reported method.

Keywords: Mosapride citrate, pharmaceutical preparations, piperzine, diazotization, and spectrophotometer.

P-80

Synthesis Of Potential Fibrinolytic & Cardiovascular Analeptic Tetrazolo [1,5-A]Quinoxaline Derivatives

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Quinazoline derivatives are of special importance because of their versatile biological and pharmacological activities especially Anti-inflammatory, Anticonvulsant, Hypnotic, Anthelmentic, Hypotensive, Antibacterial agents etc. Similarly, Tetrazoles possess diverse biological activities like antimicrobial, antibacterial, antifungal, anti-inflammatory, anticancer, antiallergic etc. Here we describe an easy and an efficient method to synthesize 2-Hydrazino-3-phenyl-3H-quinazolin-4-ones, which are predicted to be excellent Anorexic, Antiobesity, Anxiolytic and Psychotropic agents. Thus, due to the commendable biological importance of above heterocycles, we report the synthesis new tetrazolo [1,5-a] quinoxalines. The strategy employed for the synthesis of desired tetrazoles involved synthesis of 4- chloro tetrazolo[1,5-a] quinoxaline which was transformed into 4-arylamino tetrazolo [1,5-a] quinoxalines by interacting with aromatic amines. Further, the compound with hydrazine hydrate yielded 4-hydrazinotetrazolo [1,5-a] quinoxaline, subsequently transformed to 4-substituted thiocarbamoyl hydrazinotetrazolo [1,5-a] quinoxaline on reaction with phenyl thiocynate.

The structures of the synthesized compounds have been established on the basis of IR, PMR, Mass Spectral and elemental analyses. These compounds were further subjected to computer programme PASS for prediction of biological activities. Thus, tetrazolo [1,5-a] quinoxalines are expected to be potential fibrinolytic and cardiovascular analeptic agents.

P-81

Parallel Combinatorial Synthesis And Evaluation Of Ester And Amide Prodrugs Of Ibuprofen, Flurbiprofen And Ketoprofen

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Various ester and amide prodrugs of non-steroidal anti-inflammatory drugs (NSAIDs) viz. ibuprofen, ketoprofen, and flurbiprofen were synthesized using the parallel combinatorial synthesis technique. Five alcohols were selected viz. methyl (m), ethyl (e), propyl (p), butyl (b), and benzyl (be) alcohol, for esterification. Five amines were selected viz., propylamine, isopropylamine, butylamine, aniline and benzylamine, for amidation. N, N-dicyclohexylcarbodiimide (DCC) based coupling in the presence of dimethylaminopyridine (DMAP) was used for accomplishing esterification/amidation. All the ester and amide prodrugs were characterized by TLC, UV, FT-IR spectroscopy and HPLC. The yield (not optimized) of ester/amide prodrugs (a total of 30 prodrugs) was found to be in the range of 38-77%.

To verify the potential *in vivo* efficacy of the prodrug, *in vitro* enzymatic hydrolysis of ester prodrugs was evaluated in 50% human plasma; with the non-enzymatic hydrolysis in 0.01 M phosphate buffer pH 7.4 serving as a control. The samples analyzed by HPLC.

The $t_{1/2}$ for hydrolysis of ester prodrugs in 50% human plasma was found:

- Flu-bu (9.73 hr), Flu-p (13.23 hr), Flu-e (15.19 hr), Flu-m (20.3 hr) and Flu-be (35.07 hr).
- Ibu-bu (7.59 hr), Ibu-p (8.63 hr), Ibu-e (9.64 hr), Ibu-m (13.74 hr) and Ibu-be (20.46 hr).
- Ket-be (0.34 hr), Ket-bu (0.83 hr), Ket-p (1.69 hr), Ket-m (2.23 hr) and Ket-e (3.98 hr).

In contrast to the ester prodrugs, the amide prodrugs of flurbiprofen, ibuprofen and ketoprofen were not hydrolyzed to any significant extent in 50% human plasma.

P-82

Knoevenagel Condensation Reactions 1,2-Dihydro-1-Phenyl-3-Propylpyrazol-5-One Of 3- Formyl Chromones And 4- Formyl Pyrazoles With Pyrazolone By Conventional And Non-Conventional Methods.

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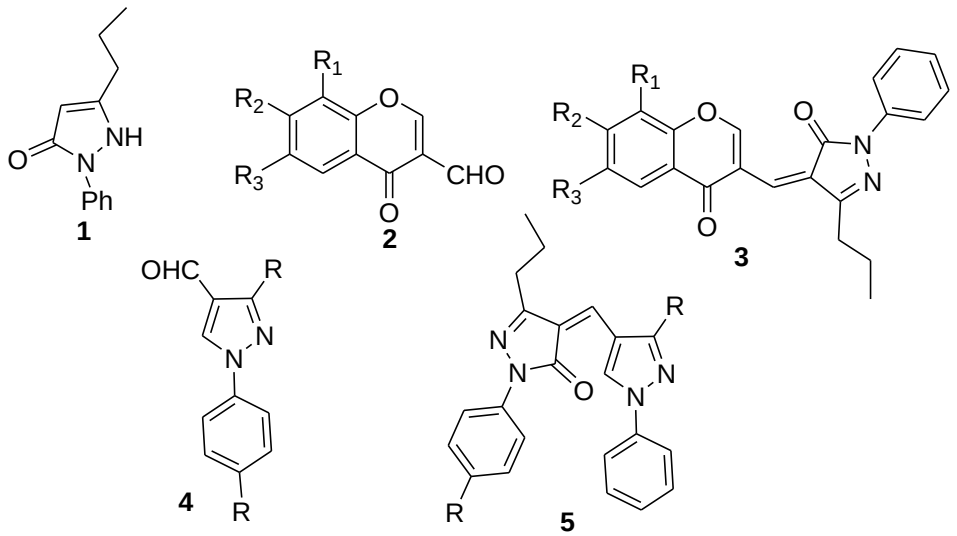
3-Formyl chromone **2** when heated with 1,2-dihydro-1-phenyl-3-propylpyrazol-5-one **1** in presence of acetic acid afforded the compound 4-((4-Oxo-4*H*-chromon-3-yl)methylene)-1-phenyl-3-propyl-1*H*-pyrazol-5(4*H*)-one **3**. 4-Formyl pyrazol **4** on treatment with compound **1** in presence of acetic acid gave compound (4)-1-phenyl-4-((1-phenyl-1*H*-pyrazol-4-yl)methylene)-3-propyl-1*H*-pyrazol-5(4*H*)-one **5**. These compounds are synthesized by conventional and ultrasonic irradiations.



P-83

Synthesis, Characterization And Antimicrobial Activities Of Some Fluorinated Pyrazolyl Compounds

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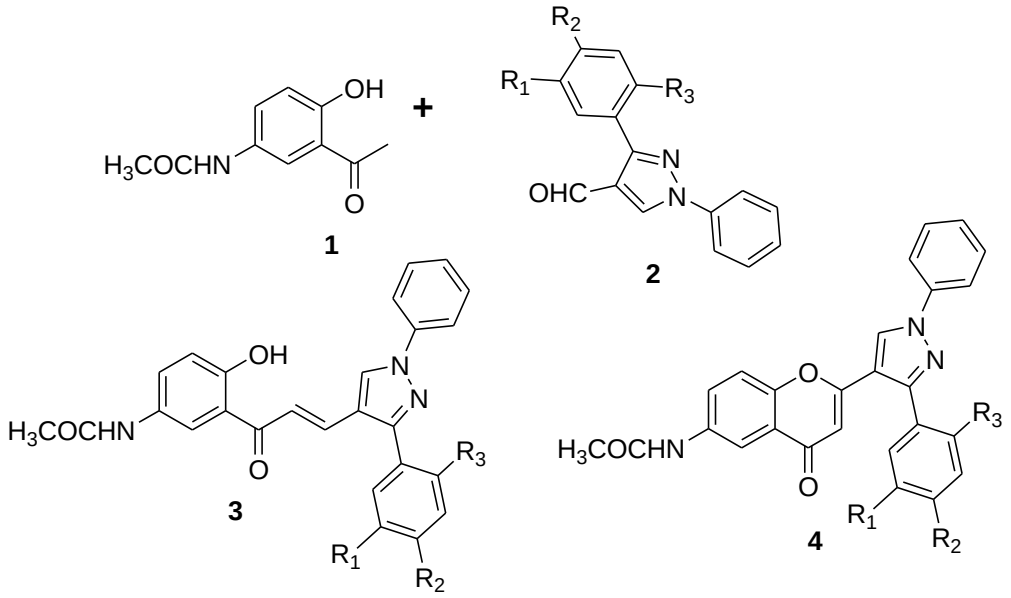
Base catalyzed condensation of **1** with **2** gave compound **3.** Compound **3** on oxidative cyclization with DMSO-I_2 gave compound **4.** The compounds **3** and **4** were characterized by IR, ^{1}H NMR and mass spectroscopy. Some of these compounds were tested for their biological activities.



P-84

Synthesis Of Some Biologically Important Thiadiazoles, Triazoles And Oxadiazoles By Ultra Sound Irradiation Technique

S K Narwade & B K Karale*
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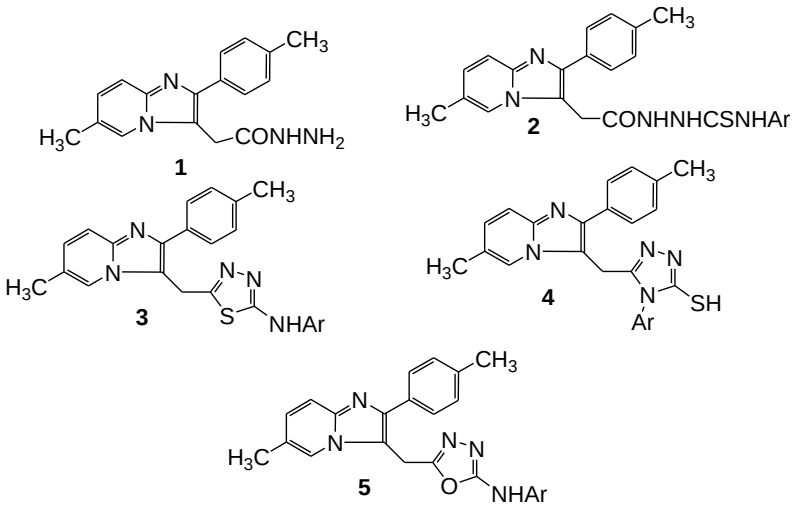
Acid hydrazide **1** when treated with aryl isothiocyanates gave the compounds **2.** These compounds **2** on in acidic medium gave compounds **3** i.e. thiadiazoles and in basic medium gaves compounds **4** i.e. triazoles. These compounds **2** on treatment with I_2/KI & NaOH gave compounds **5** i.e. oxadiazoles. These compounds are synthesized by conventional method as well as ultra sound irradiation method.



P-85

Studies in synthesis of DL-Tyrosine.

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DL- Tyrosine (α-Amino *p*-hydroxydihydrocinnamic acid) is an important intermediate in the synthesis of many classes of compounds. For example, compounds containing tyrosine moiety are potent PPAR-α / γ agonists and are useful in treating Type-2 Diabetes and Dyslipidemia. Tyrosine has been obtained by hydrolysis of casein and also by a combination of synthetic and enzymatic methods. Present work involves convenient and improved methods of synthesis of DL-Tyrosine with potential for upgradation to large scale synthesis. During the study anisaldehyde was condensed in turn with malonic acid, hydantoin, acetyl glycine and benzoyl glycine. The condensed derivatives were reduced either catalytically using Raney nickel or H_2 at atmospheric pressure or by using red P/HI. Reduction with red P/HI had advantage of achieving demethylation in the same step compared to the catalytical method. The condensed derivative with malonic acid was reduced catalytically and then brominated, aminated, and demethylated to get DL-Tyrosine, while the condensed derivative with hydantoin was hydrolysed and demethylated after catalytic reduction. The oxazole-5-one derivatives (from acyl glycines) on reduction with red P/HI gave DL-Tyrosine. DL-Tyrosine was obtained in a yield of 60% to 65% in the final step while yields in the earlier steps ranged from 70% to 98%. Progress of all reactions was monitored by TLC. All intermediates and DL-Tyrosine were characterized by their melting points and IR spectroscopy. DL-Tyrosine was also characterized by ^{1}H NMR.

P-86
Identification Of Yeast Mitochondrial Atp Synthase Using Maldi-Tof-Mass Spectrometry

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Proteomics is a rapidly evolving field for the separation, identification and characterization of proteins. The technologies for genome analysis are simpler than proteome. Out of these matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS) is one of the advanced technique which has changed paradigm of protein sequencing. In the present study we have initially used high throughput technique, one dimensional gel electrophoresis (1-DE) to characterize protein expression in altered yeast mitochondrial and to examine the proteomic profiling to understand the mechanisms behind alterations. The phenobarbitone drug was used to altered gene as well as protein expression levels. The altered proteins were resolved by 1-DE. These proteins were then subsequently digested and identified by MALDI-TOF-MS analysis using peptide mass fingerprinting (PMF) and database searching. Proteome data indicates that phenobarbitone alters the protein level of ATP synthase (or called as F_0F_1 ATPase) in mitochondrial membrane. This enzyme plays a vital role in oxidative phosphorylation reaction of a fundamental theme of bioenergetics i.e. the transmission of free energy by proton gradients.

Key words: MALDI-TOF-MS, ATP synthase, Yeast mitochondrial proteome etc.

P-87

Studies On Biochemical Basis Of Arteether Resistance In A Rodent Malaria Model

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*Division of Parasitology and *Biochemistry, Central Drug Research Institute, Lucknow.*

Artemisinin based drugs offer a ray of hope in treatment of drug resistance in malaria. Unique antimalarial activity of artemisinin derivatives is due to presence of endoperoxide bridge. Heme, iron and other oxidant promotes cleavage of this peroxide bridge in artemisinin derivatives, and ultimately leads to the formation of C-centered free radicals which alkylate some proteins of parasites and also forms covalent adducts with heme preventing formation of hemozoin. Heme, which is toxic to the malaria parasite, is formed when the intraerythrocytic malaria parasites ingest and digest the hemoglobin inside the food vacuole and convert it into nontoxic hemozoin. The non - polymerized heme in the food vacuole is subsequently degraded by glutathione. Glutathione (GSH) plays a critical role in detoxification and protection of cells against oxidative stress. In present work arteether resistant *Plasmodium vinckei* parasites were selected by continuous drug pressure and glutathione metabolism was compared in arteether resistant and sensitive parasites. We found that the level of GSH and activities of GR, Catalase, and G-6-PDH increased while SOD activity decreased in resistant parasites when compared to sensitive parasites. For resistance reversal studies three agents namely Doxorubicin, Fluconazole and Ketoconazole were used in combination with arteether which showed suppression of the ED_{90} values of arteether by 9, 6, and 7 fold respectively in resistant strain of parasites. As Doxorubicin is known to deplete the glutathione levels, it is hypothesized that it decreases the glutathione level and increases the oxidative stress in resistant parasites thus leading to reversal of arteether resistance. Antifungal azoles (Fluconazole and Ketoconazole) have a high binding affinity for heme which may lead to heme-azole complex formation thereby protecting heme from degradation by reduced glutathione, Heme-azole complex is known to damage the cell membrane more vigorously than the free heme.

P-88

Applications Of Diazofluoroborate Organic Synthesis.

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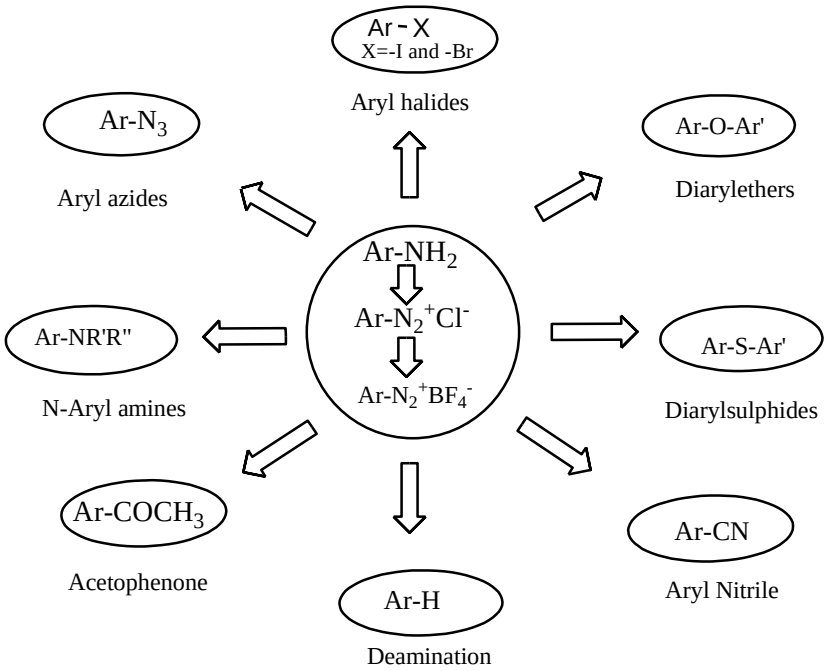
The solid diazofluoroborate salts of primary aromatic amines were utilized for the different targets such as aryl azides,aryl nitriles,diaryl ethers,diaryl sulphides,N-aryl amines from sec.amines, aryl halides, deaminated products of amines and various acetophenones in tap water under mild condition is discussed. Short reaction time, ecofriendly solvent systems are the important features of the present methodology.

Scheme



References:

1. Lawson J.K., Easley W.K. and Wagner W.S., *Org.Synthesis, 4, 892, 1963*.
2. H.Roseky, D.Glemser,*Chem.Ber*.,97,1710,1964
3. Woodward R.B., *Tetrahedron*, 2, 1958, 1.

P-89

Receptor Based Design Of Novel Dihydrofolate Reductase Inhibitors As Potential Anticancer Agents

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Molecular modeling and docking thechniques are becoming increasingly important in drug design for the anticancer therapy. Dihydrofolate Reductase (DHFR) enzyme plays a major role in the De novo purine synthesis and is an important target for the anticancer agents belonging to the class of antimetabolites. We here report the *in silico* screening, conducted before the actual synthesis and plan to conduct *in vivo* screening of some 'best fit' quinazolinone moieties as the possible inhibitors of DHFR enzyme for anticancer activity. Literature survey reveals that quinazolinones have an anticancer potential as inhibitors of DHFR enzyme and thus receptor based design of a series of thirty 6,6'-methylene-bis-2-methyl-3-((2'-aryl)-imidazolidine-4'-one)- quinazolin-4- (3H)-one analogues was performed using Glide® as the docking module. The prediction of ADME properties was obtained with the QikProp® 2.5 module. The 3D ligand-protein complex structure of human DHFR (1HFQ) was obtained from the Protein Database Bank (RCSB PDB) and processed for the docking using the Protein preparation wizard module. Methotrexate a potent inhibitor of DHFR enzyme was included in test sets, to compare the Glide score (G score) of designed analogues. The binding affinities of different ligands were compared to give score values .Twenty analogues showed comparative G scores with Methotrexate. Those twenty analogues were subjected to predict ADME properties by using QikProp® 2.5 module. QikProp settings determine which molecules are flagged as being dissimilar to other known drugs. Four analogues out of twenty analogues lie within the QikProp limits of ADME properties.
The microwave assisted synthesis of four designed quinazolinone analogues by using substituted anthranilic acid as a starting material to carry out Nimentowski reaction to construct quinazolinone nucleus is in progress. Synthesized analogues shall be evaluated for anticancer activity by *in vivo* tumor inhibition method.

P-90

A Novel Heterogenious Catalyst for Nucleophilic Opening of Epoxide Rings

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The nucleophilic opening of epoxide ring is an extremely useful transformation as the resultant C-2-substituted alcohols are building blocks for a wide range of pharmaceuticals such as β-adrenergic blockers, rennin inhibitors, antihypertensive agents, cholrectic drugs, dipeptide isosters etc. This encouraged us to develop various catalytic processes for electrophilic activation of the epoxide ring to render it susceptible to nucleophilic cleavage under mild conditions.[1] In the pursuit of a new catalyst, we were influenced by the tight legislation on the maintenance of greenness in synthetic pathways and processes.[2] Since the use of solid acid catalysts address adequately the aspect of maintaining greenness,[3] we reported for the first time $HClO_4$-SiO_2 and HBF_4-SiO_2 as extremely effective electrophilic activation agents for heteroatom acylation.[4] The versatility of $HClO_4$-SiO_2 was subsequently demonstrated for dithiolane/carbamate/acetal formation and thia-Michael addition.[5] The present study describes the development of a novel heterogeneous catalyst system for the desired transformation.[6]

References

1. Shivani, A. K. Chakraborti *J. Mol. Catal. A*: *Chem.* **2006**, doi:10.1016/j.molcata.2006.08.047. A. K. Chakraborti, A. Kondaskar, S. Rudrawar

Tetrahedron **2004**, *60*, 9085. A. K. Chakraborti, S. Rudrawar, A. Kondaskar *Eur. J. Org. Chem.* **2004**, 3597. A. K. Chakraborti, S. Rudrawar, A. Kondaskar *Org. Biomol. Chem.* **2004**, *2*, 1277. A. K. Chakraborti, A. Kondasker *Tetrahedron Lett*. **2003**, *44*, 8315.

2. Tundo, P. Anastas, D. S. Black, J. Breen, T. Collins, S. Memoli, J. Miyamoto, M. Polyakoff, W. Tumas *Pure Appl. Chem***. 2000**, *72*, 1207.
3. K. Wilson, J. H. Clark *Pure Appl. Chem*. **2000**, *72*, 1313.
4. K. Chakraborti, R. Gulhane *J. Chem. Soc. Chem. Commun*. **2003**, 1896. A. K. Chakraborti, R. Gulhane *Tetrahedron Lett*. **2003**, *44*, 3521. A. K. Chakraborti, R. Gulhane *Indian Patent* 266/DEL/2003 (10-3-2003).
5. S. Rudrawar, R. C. Besra, A. K. Chakraborti *Synthesis* **2006**, 2767. A. K. Chakraborti, S. V. Chankeshwara *Org. Biomol. Chem.* **2006**, *4*, 2769. R. Kumar, D. Kumar, A. K. Chakraborti *Synthesis* **2006**, DOI: 10.1055/s-2006-xxxxx; Art ID: Z19706SS. G. L. Khatik, G. Sharma, R. Kumar, A. K. Chakraborti, *Tetrahedron* **2006**, doi:10.1016/j.tet.2006.11.050.

P-91

Characterization Of Hexokinase From Filarial Parasite

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Hexokinase plays an important role in glucose utilizing tissues and parasites. Metabolic modeling and experimental studies indicate that hexose phosphorylation may be of major importance in regulation of carbon flux. The reason for not having ideal drugs against filaraisis is that chemotherapeutic targets in filarial parasites are not well characterized. Therefore it is an utmost need to identify new targets for drug development to make it possible to control the disease. For filarial parasites glycolysis is an important metabolic pathway for energy production. Hexokinase, the regulatory enzyme of glycolytic pathway, catalyses the transfer of phosphate moiety from ATP to hexose sugar producing glucose-6-phosphate which serves as a substrate for pentose phosphate pathway. The NADPH produced maintains the redox potential of the cell and pentose sugars are utilized for biosynthesis of nucleic acids. Therefore hexokinase may be potential chemotherapeutic target. The hexokinase from wide variety of organisms have been cloned and characterized. Although the eukaryotic hexokinase and glucokinase genes appear to have arisen from a common ancestor, the kinetic and regulatory properties of corresponding proteins vary considerably.
The hexokinase of filarial parasite *Seteria cervi* was purified and kinetic properties studied. The purified protein has a molecular mass of ~55 kDa. The enzyme phosphorylated a wide variety of substrates and showed high affinity for glucose and fructose. The filarial enzyme was inhibited by known inhibitors of mammalian hexokinase to different extent. The enzyme was utilized screening of antifilarial compounds synthesized in our institute and significant inhibitory activity was observed for few of these compounds.

P-92

Isolation and characterization of thioredoxin reductase of filarial parasite.

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** Medicinal chemistry, Central Drug Research Institute, Lucknow-226001*

Glutathione (GSH) and thioredoxin constitute the most important cellular thiols, participating in a variety of processes. Due to relatively high concentration GSH is mainly involved in maintainance of proper redox environment and also serves as a substrate for a variety of enzymes involved in the defence against reactive oxygen species. Thioredoxin system consists of NADPH dependent disulphide oxidoreductase thioredoxin reductase and the small protein thioredoxin. This system is responsible for a more versatile role in cell physiology regulating the function of a number of protein factors and serving as an electron source for deoxyribonucleotide synthesis. The thioredoxin system has significant role in reduction of reactive oxygen species by interaction of thioredoxins and peroxidoxins and is one of the major peroxide detoxifying proteins. The enzymes play important role in helminths and malarial parasites where it is the key enzymatic system to deal with hydrogen peroxide.
The thioredoxin reductase was isolated and characterized from filarial parasite *Setaria cervi.* The enzyme was purified from the parasite by anion exchange and affinity chromatography. Kinetic properties of the purified enzyme were studied. The K_m value for the substrate DTNB was found to be 2.5 ± 0.5mM. The thioredoxin reductase was utilized as chemotherapeutic target for synthesis of antifilarial compounds. The results showed significant inhibition of enzyme activity by some of these compounds. Further evaluation of parasitic thioredoxin reductase as a potential target for chemotherapy of filaria appears to be more feasible when using the natural substrate of the enzyme in inhibitor studies.

P-93

Design and Synthesis of Potential Anti-fungal Agents

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The study involves the design, synthesis and evaluation of some novel antifungal agents against the target N-myristoyl transferase enzyme (Nmt). N-myristoyl transferase is a cytosolic monomeric enzyme that myristoylates a number of eukaryotic cellular proteins altering the protein functions. The literature reveals the importance of this enzyme for the growth, survival and viability of the pathogenic fungus <u>*C. albicans*</u>. Thus inhibition of Nmt could be detrimental to the survival of the pathogenic fungus.
The computations were carried out in *Sybyl 7.1* (Tripos Inc., USA), molecular modeling software on the Linux RedHat Enterprise WS platform and *Gold 3.0.1* (CCDC, UK) docking software on the Windows platform. A novel series of benzothiazoles and benzofurans analogs was designed; as the benzothiazoles and benzofurans analogs have profound anti-bacterial and anti-fungal activities, as quoted in the literature. The docking protocol was validated being able to reproduce the binding pose of several inhibitors as seen in the crystal structures and by a docking study of the known inhibitors. The designed benzofuran and benzothiazole analogs were docked into the active site of the Nmt using the same docking protocol program *Gold 3.0.1*.
Based on the GoldScores, and their orientation in the binding pocket, molecules were prioritized for the synthesis and evaluation. The molecules were synthesized by aldol condensation of 2-substituted benzofuran and benzothiazole with various substituted aromatic

ketones. Structures of the synthesized compounds were confirmed by NMR and IR spectroscopy. The compounds were tested for antifungal activity by the cup plate agar diffusion method against *C. albicans*.

P-94

Advanced Materials for Organic Electronics

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In the last few decades; conducting polymers (CP) have been very actively pursued. Several discoveries brought CPs to full commercialization with applications in polymer light emitting diodes, solar cells, sensors, and electtochromic devices. Polymer light emitting diodes (PLED) are an emerging and exciting new technology. In the future, these PLEDs have the prospect of competing with or replacing current LCD technology. Also, they have the potential to revolutionize data transmission between computers. (i.e. the internet). They are easier to manufacture, cheaper to produce, and more efficient than normal inorganic LEDs. Organic materials, especially polymers, can be applied over a large area and patterned by lithography. The development of new conjugated polymers with improved performance is a major challenge for material chemists. This seminar will outline design and synthesis of new derivatives of conjugated polymers and copolymers for PLED, memory devices and photovoltaic applications.

References:

1. H. S. Nalwa, Handbook *of Organic conductive molecules and polymers,* John Wiley
2. & Sons, Vol. 1-4, 19.97
3. J. H. Burroughes *et al., Nature,* **1990,347,539-541**
4. Horowitz G., *Adv. Mater.,* **1998,** *10,* 365
5. D. Witker *et al., Macromolecules,* **2005,** 38, 7636

P-95

Virtual Screening Of P-Secratase Inhibitors Using Docking And Pharmacophore Models

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Docking and pharmacophore tools were used to examine the binding of ligands in the active site of β-Secratase, which is the major cysteine protease, expressed in osteoclast is involved in Alzheimer's disease. 105 molecules of benzamide containing aminonitrite analogues were docked to the receptor-using ligand fit software. Docking analysis suggests the role of hydrogen bonding and other weak interactions in the enzyme activity. A three dimensional chemical-feature based pharmacophore model was developed using 26 β-Secratase inhibitors with Hypogen algorithm of Catalyst software, which produced 10 pharmacophore hypotheses. The 1st hypothesis (Hypol), which consisted of hydrogen bond donor (HBD), hydrogen bond acceptor (HBA) and two hydrophobic (HY) features shows a correlation coefficient (0.954)

with training set and has high prediction of activity Jor a set of 79 test molecules with correlation of 0.804. Also a good agreement between pharamacophore (hypothesis) features and docking interactions was observed. The model was validated by screening the database containing active compounds. The model picked the active compounds with goodness of hit 0.91. The validated pharamacophore and docking method which shows rather good corrections between the inhibitory activities and the

P-96

"Taste masking and formulation of some Bitter Drugs"

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In the last decade competition in Pharmaceutical arena has revolved around Improving physiochemical properties of drug formulation to given patient a better Product[1]. Recent trends in pharmaceutical industries are showing more patient concern. Formulations are being prepared which are more acceptable to patients in terms of palatability, ease of administration and aesthetic appearance.

Many drugs are not able to see the day of light because of their bitter taste and so masking of bitter taste of drug is gaining high important in order to provide a formulation, which is having good taste and is palatable to the patient. Many drugs can not be formulated into liquid formulation because of their limited solubility thus making them inconvenient drugs for uncooperative patients. Also the onset of action of such drug is slow because of their poor solubility.

Cyclodextrin in Bitter taste masking

Cyclodextrin provide a drug delivery system capable of masking the bitter taste of the drug by engulfing the drug and improving the solubility of the poorly soluble drugs by their solubilising powers. Cyclodextrin have been known for about one hundred year". In the year 1953 the first patent on CDs and their complexes were. registered, but until the 1970s not much work could be done because they could not be manufactured in high amounts and pure states. At present a monograph for BCD is available in both the US Pharmacopeias/ National formulary and monograph of cyclodextrin are available in many copendia.. Thus more then a century after their discovery, CDs are now recognized as important pharmaceutical excipients.

Apart from Cyclodextrins many techniques are also available for bitter taste masking of drugs. The present work represents masking of the bitter taste of certain drugs by complexation with BCD. The work also involve masking the bitter taste of the drug by methods other than cyclodextrin complexation. Al1 the taste masking techniques are compared for Industrial feasibility.

P-97

Synthesis, Characterization and antimicrobial activity of 1,3-di (5-phenyl-1 ,3,4-thialdiazolo)-6-methyl-2- thioxo-4-(2- hydroxy-5- chlorophenyl)pyrimidi-5-ethyl carboxylate.

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Thiadiazolo pyrimidin-2-thiones have been found pharmacologically important as antitumour, antiallergic, antiviral, antifungal, anti-inflammatory and antihypertensive agents. 1,3-di (5-phenyl-1 ,3,4-thialdiazolo)-6-methyl-2-thioxo-4-(2hydroxy-5-chlorophenyl)- pyrimidi~6-ethyl carboxylate is synthesized by the condensation of disubstituted thiourea, ethylacetoacetate and 5 chlorosalicylaldehyde. The structure of the compound has been investigated by elemental analysis, IH-NMR, IR ,UV-visible and mass spectral data.The antimicrobial activity of the compound has been screened *in vitro* against the several microorganisms.

P-98

Synthesis And Characterization Of Some New Nitrosubstituted 3,5 - Diaryl Isoxazoles, Tiho Isoxazoles And Their Derivatives

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Isoxazoles are well known to have a number of biological and antimicrobial activities. Earlier workers have reported 2-bromo-β-diketone derivatives . and 4- bromoisoxazole 4- Isoxazole derivatives have been reported to possess antibacteria, antitubercular, antiviral and antifungal activity. Flavones, thiochromones and also chalcones have been used in the synthesis of 3-5 diaryl isoxazoles. The reaction of chalcone dibromide with hydroxylamine hydrochloride in presence of alkali gives 3,5- diaryl isoxazoles. Many earlier workers have been reported synthesis of 3,5 diaryl Isoxazole by the reaction of chalcone dibromide or flavone with hydroxylamine hydrochloride and piperidine/ KOH/NaOH as the reaction medium by using ethyl alcohol, pyridine methyl alcohol as the solvent. Chalcones, chalcone dibromides and flavones26 are prepared by reported method.
Literature survey indicates that title compounds have not been synthesized from 1-(2-hydroxy-3-nitro-5-methylphenyl)-3-(substituted phenyl)- 2,4 dibromo propen - 1 - one & 2 - (Subsituted phenyl) -6-methyl-8-nitro-flavone. Hence it was thought of interest to prepare and characterized some new nitrosubstituted 3,5-diaryl isoxazoles, thioisoxazoles, and their derivatives. All synthesized compounds were characterized based on their elemental and spectral analysis.

P-99

Ormeloxifene, A Selective Estrogen Receptor Modulator, Inhibits Osteoclast Differentiation and Induces Apoptosis

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Osteoclasts are cells responsible for bone resorption while osteoblasts are cells that form bone. To maintain normal bone physiology, body maintains a homeostasis between number of osteoclasts and osteoblasts. During osteoporosis, this dynamic equilibrium is disturbed and

the former increase in number. Ormeloxifene, an established anti-implantation agent, was tested for its effect on osteoclasts. Osteoclastogenesis was significantly inhibited at 10 pM, 10 nM, 100 nM and 1 μM concentrations as evidenced by reduced number of TRAP positive cells in culture from bone marrow progenitors. It also induced significant apoptosis in osteoclasts collected on 5^{th}, 4^{th} and 3^{rd} day of culture at concentrations ranging from 1 pM to 2 μM. In both experiments, estrogen served as positive control. Additionally, the iNOS gene expression in osteoclast cell culture was seen to be upregulated significantly on treatment with ormeloxifene at 100 nM concentration comparable to those treated with estrogen. Generation of Nitric Oxide too showed an increase at 1 nM, 100nM and 2μM concentrations. Estrogen was used for positive control. Nitric oxide "NO" is an important signalling molecule in bone which is produced in response to diverse stimuli including sex hormones. High concentration of NO inhibit bone resorption by inhibiting osteoclast formation and by inhibiting the resorptive function of mature osteoclasts. The findings indicate that in bone, ormeloxifene mimics the action of female sex hormone estrogen.

P-100

Formulation And In- Vitro Characterization Of Niosomes Bearing Frusemide

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Cardiovascular diseases represent a major cause of mortality worldwide with a wide occurrence in the developed world. In the present study, niosomes of Frusemide, a diuretic and antihypertensive were prepared. Frusemide has a short half life of 45-60 minutes and has poor bioavailability (40-70%) due to the presence of a biological window comprised of the upper GI tract as its absorption is site-specific, taking place mainly in that region. An attempt had been made to sustain the release of frusemide, which may be useful in the treatment of hypertension, fluid retention like in the case of cardiac and pulmonary edema, etc. As Frusemide is a potent loop diuretic controlled diuresis means less toxic effects like electrolyte imbalance, ototoxicity, etc.
Niosomes were prepared using spans, cholesterol and DCP by film hydration method. The process variables studied include type of spans, ratio of cholesterol and DCP, concentration of drug, type of solvent and time of hydration. The formulated niosomes were characterized for various parameters viz. surface morphology, size, entrapment efficiency, in- vitro release rate and storage stability.
SEM and TEM revealed that the niosomes were round and discrete in shape. The maximum entrapment efficiency of 77.13% was obtained in the case of niosomes formulated from Span 60: Cholesterol: DCP (47.5:47.5:5) at the hydration time of 1hr. A direct relationship between the percentage leaching of the drug out of the vesicles and temperature was observed. The findings revealed that niosomes may be useful for designing a sustained release delivery system of frusemide and the potential of niosomes to enhance the therapeutic effectiveness and simultaneously minimizing the adverse side effects.

P -101

Unexplored Potential Of Bisindole Alkaloids As Antileishmanial Agents

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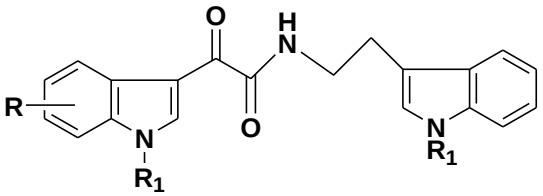
Marine organisms have proven to be rich source of compounds that may prove highly beneficial for the development of new pharmaceutical agents. A growing number of bisindole alkaloids are being discovered from variety marine invertebrates, sponges and tunicates. Their unique structure and the high degree of biological activity have made them the cynosure of scientific attention.

As part of our interest in the synthesis of biologically active compounds we undertook and synthesized a series of indole alkaloids. Among these alkaloids bisindole alkaloids (**I**) found to be more active against leishmania as compare to those simple indole alkaloids (**II**).



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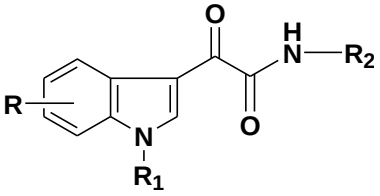

II

This research proposes to concentrate on hitherto untapped potential of bisindole alkaloids as new targets for leishmania.

P-102

Synthesis of 2,4,6-trisubstituted pyrimidine and triazine heterocycles as antileishmanial agents

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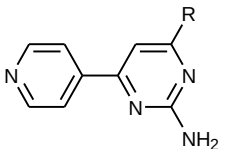
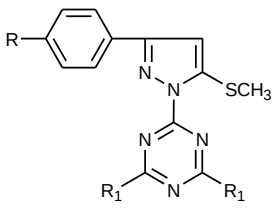
Leishmaniasis is caused by different species belonging to the genus Leishmania, a protozoan which is transmitted to humans by the bite of an insect vector, phlebotomine sandfly.





Dihydrofolate reductase (DHFR) is an important target site in most of the parasitic diseases. Most of the clinically used DHFR inhibitors show less selectivity for leishmanial enzymes. This is due to the fact that the gene for pteridine reductase (PTR1) is amplified in some leishmanial mutants. PTR1 can reduce pterins and folates and therefore act as a bypass for DHFR inhibition. This implies that antifolate drugs must simultaneously target both DHFR

and PTR1 to be successful antileishmanials. A number of compounds having pyrimidine and triazine moiety are reported to be potent inhibitors of PTR1 in Leishmania. Pyridine, pyrimidine, and triazine class of compounds are previously reported to be potential antileishmanial agents. Based on these observations we hypothesized and synthesized a series of 2,4,6 trisubstituted pyrimidines and triazines and screened for its in vitro antileishmanial activity profile in promastigote model. Nine compounds have shown >94% inhibition against promastigotes at a concentration of 10 μg/mL.

P-103

Synthesis and evaluation of antimalarial activity of 4-aminoquinoline triazine derivatives

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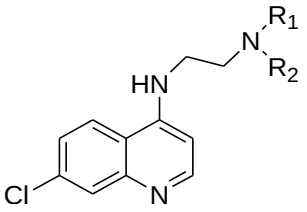
[a] *Medicinal and Process Chemistry Division,* [b] *Parasitology Division, Central Drug Research Institute, Lucknow –226001 (INDIA)*

Despite over 100 years of drug developments efforts, malaria remains one of the most devastating infectious diseases in the world. The current epidemic is fueled by the development of drug resistant strains of plasmodium falciparum, the parasite responsible for the most deadly cases of malaria. Historically, Chloroquine has been thedrug of choice for antimalarial chemotherapy because it is highly effective, less toxic and cheap drug but the emergence of chloroquine resistant parasites created a tremendous therapeutic void. There are several reports indicating that several chloroquine analogues and derivatives maintain significant activity against chloroquine – resistant plasmodium falciparum strains. This has suggested that resistance mechanism does not involve any change to the target of this class of drug but rather involves a compound specific resistance. So there is still significant potenial to discover new quinoline antimalarials.



A series of 21 compounds of quinoline triazine derivatives have been synthesized and evaluated showing the activity in the range of 1.00 μM to 0.125μM.

P-104

Synthesis and antimalarial activity of new 1, 2, 3-trisubstituted tetrahydro-β-carbolines.

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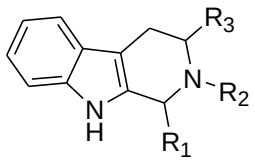
[a]*Medicinal and Process Chemistry Division,* [b]*Parasitology Division, Central Drug Research Institute, Lucknow, India*

A series of new 1, 2, 3-trisubstituted tertahydro-β-carbolines has been synthesized and screened against antimalarial activity. A few compounds have shown interesting antimalarial activity.



P-105

Derivatisation Of Aplysinopsin To Generate Lead For Antimicrobial Activity.

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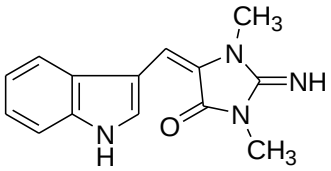
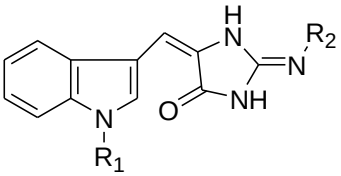
[a]*Medicinal and Process Chemistry Division,* [b]*Parasitology Divison, Central Drug Research Institute,Lucknow-226001, India*



(I)



(II)

Aplysinopsin, (I), a marine natural product and its other naturally occurring analogues have a range of biological activities. These include antimalarial, monoamine oxidase inhibitor, $5HT_A$ receptor inhibitor (targets involved in antidepressant activity) [1] and antileishmanial activity [2].

We describe here SAR of a series of molecules, based on aplyinopsin scaffold with substitution pattern shown in figure II, and the discovery of a lead for leishmaniasis infection.

References: -

1. Hu et al. *J. Nat. Prod.* **2002,** *65,* 476-480
2. Gulati, D.; Chauhan, P.M.S. et al *Ind. J. Chem.* **1994**, *33B*, 4-9

P-106

Synthesis And Antibacterial Activities Of A-Hydroxyphosphonates And A - Acetyloxyphosphonates Derived From 2-Chloroquinoline-3-Carbaldehyde

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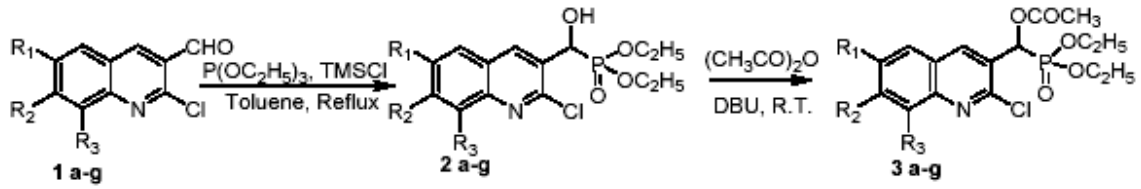
Quinolines are an important class of heterocyclic compounds. Several compounds of this class have been screened for biological activities such as bactericidal, antitumor, anti-inflammatory, antimalerial etc. Among quinolines, 2-choloroquinolin-3-carbaldehydes occupy a prominent position, as the latter are key intermediates for further annelation of a wide variety of ring and for various functional group interconversions.



In continuation of our work on synthesis of Bioactive compounds comtaining phosphates herein we wish to present synthesis of α -Hydroxyphosphonates derived from 2-chloroquinolin-3-carbaldehyde by modified Abramov reaction using chloro(trimethyl)silane (TMSCl). Subsequent α-hydroxyphosphonate produced were acetylated using acetic anhydride in the presence of 1,8-Diazabicyclo-undec-7-ene (DBU) to afford the α -acetyloxyphosphonate in high yields. The synthesized α -hydroxyphosphonate and α -acetyloxyphosphonate compounds were screened for antibacterial activities. Some of the Synthesized derivatives have shown comparative activity against their standard Streptomycin.

P-107

Design, Synthesis and Evaluation of novel N-substituted-6-methoxynaphthalene-2-carboxamides as potential Chemosensitizing agents for cancer.

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Cancer chemotherapy may be impaired severely by the presence of drug resistance. The main reason being, membrane protein, P-glycoprotein, which efflux cytotoxic agents from cells. The agents used to combat this resistance were called as chemosensitizers. Earlier studied chemosensitizers were non-specific in their action and produced toxicity. Therefore, non-toxic chemosensitizing agents were developed and among them Elacridar showed good promise.
Based on this we developed a pharmacophore for chemosensitizing activity and a series of 6-methoxynaphthalene with 4-alkyl/aryl-1-piperazinopropyl substituents on amide nitrogen were synthesized and evaluated and found to exhibit promising activity.
In the present work we propose to replace the piperazine nucleus with various heterocyclic substituents to study their role in chemosensitizing activity. The various heterocycles used were pyrrolidine-2-one, benzimidazole, methyl benzimidazole, benzotriazole, 1,2,3,4-tetrahydroisoquinoline and 4-amino-3-methylthio-5-phenyl-1,2,4-triazole.
The required 6-methoxy-2-naphthoic acid was synthesized from 2-naphthol, which was brominated to form 6-bromo-2-naphthol. Methylation with dimethyl sulfate in alkaline condition gave 6-methoxy-2-bromonaphthalene. This was then converted to Grignard and treated with DMF to obtain 6-methoxy-2-naphthaldehyde. Oxidation of this with ammonical silver nitrate gave the 6-methoxy-2-naphthoic acid. The N-(3-bromopropyl)phthalimide was

condensed with different heterocycles in DMF in presence of base and hydrolysed to obtain substituted propylamines. The 6-methoxy-2-naphthoic acid was converted to 6-methoxy-2-naphthoyl chloride by reacting with oxalyl chloride in dichloromethane. This was then condensed with different substituted propylamines to obtain the titled compounds. The yields of the compounds were in the range of 71-76 %. Compounds were characterized by IR & NMR spectroscopy.
Synthesized compounds were evaluated in P388 murine lymphocytic leukemia cell line and in adramycin resistant cell line. All compounds reversed adriamycin resistance when evaluated in resistant cell line, with significant potency at 10 & 20 μg/ml, a quality that is desired in a good chemo-sensitizing agent.

P-108

Synthesis & Pharmacological Screening Of Gaba-Nergic Agonist Using Hybrid Approach

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The term epilepsy is derived from the Greek word "Epilambenein" which means to seize or convulsions. The term seizure refers to a transient alteration of behavior due to disordered, synchronous and rhythmic firing of population of brain neurons. Epilepsy is one of the CNS disorders where selectively acting drugs are still lacking. In many cases of epilepsy the exact etiological reasons are not yet understood. The only insight available to rectify the continuous firing og neurons. Most of the currently used ant-epileptic agents are found to act by potentiating the GABA-nergic responses in CNS.
From literature survey we had observed that the pseudohydantoin have much better activity so we clubbed together substituted pseudohydantoin group & barbituric acid to yield potential anticonvulsant agent.
In the present work the authors have the objective of developing more selective drugs acting on GABA nergic receptors. In this paper the Design, synthesis, and pharmacological evaluation of the more effective and selective drugs than the currently used anticonvulsants in the market will be highlighted.

EXPERIMENTAL WORK:
The N-substituted 2-phenylimino-4- thiazolidinone was synthesized and condensed with barbituric acid as per mentioned standardized reaction conditions. The physico-chemical studies of synthesized compounds were done by thin layer chromatography, elemental analysis, FTIR and NMR-spectroscopic studies. The reaction monitoring, purity and structural characterization of the synthesized compounds were done by thin-layer chromatography and melting point determination at each step of synthesis. Pharmacological testing of synthesized compound was done by actophotometer and rotarod apparatus[Ref]. Anticonvulsant activity was evaluated using electoconvulsiometer. LD_{50} determinations were done by Graphical method of Miller and Tainter[Ref] using Phenobarbitone as reference standard.

RESULTS AND DISCUSSION:
The structures of synthesized compound were confirmed by interpretation of TLC, FT-IR and NMR spectral study. All the reactions yielded quantative yields and the anticipated compounds were confirmed. From the results of Pharmacological studies it was concluded

that out of 5 derivatives 3 were found to have significant locomotors and muscle relaxant activity. Similarly 3 out of 5 showing better protection agents electrically and chemically induced seizure & one compound have shown moderate protection. The LD50 values were found to lie between 553-to 750-mg/kg bodyweight indicating better therapeutic window for the newly synthesizes anti-convulsant compounds..

CONCLUSIONS:

As per our objective the combined hybrid of thiazolidine 4-one nucleus and barbiturates were synthesized & found to be pure, containing no unreacted intermediates, Pharmacological testing have also shown significant motor depressant activity and better protection against electrically and chemically induced seizures. The higher LD_{50} values support to less toxicity and better therapeutic safety. So we conclude that the hybrid molecule shows good potential development of novel Antiepileptic agents.

P-109

Studies on Reductive cleavage of Isooxazolines

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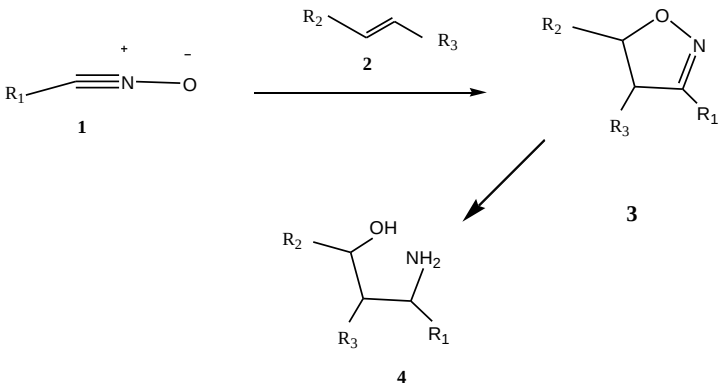
Due to their intrinsic biological activities and applications as conformational modifiers for physiologically active peptides, unnatural and nonproteinogenic amino acids have become very important and attractive targets .Among amino acids, proline[1] analogues, with their unique structural constraints (cyclic and a secondary amine), play an important role in the investigation of structure, receptor affinity, and biological activity of amino acids chimeras and peptides. Furthermore, heterocyclic pyrrolidine rings are valuable scaffolds and precursors in natural products and in drug discovery, i.e., kainoid, carbapenems, captopril, and gramicidin. Consequently, routes to and applications of proline-based amino acids and derivatives have received much attention in both chemistry and biochemistry[2]. We herein report our attempts on ring transformation of isoxazoline **3** to synthesize of pyrrolidone derivatives and 5–substituted 4-hydroxyproline ester . Thus dipolar cycloaddition of nitrile oxide **1**. with olefins **2** furnished isoxazolines **3** in excellent yield and diastereo-selectivity.



The details of ring transformation of **3** through the intermediacy of **4** would be presented.

Reference:

1. Tamaki, M.; Han, G.; Hruby, V. *J. Org. Chem.* **2001**, *66*, 3593.
2. (a) Bowers-Nemia, M. M.; Joullie, M. M. *Heterocycles* **1983**, *20*, 817.

(b) Ma, D.; Wu, W.; Deng, P. *Tetrahedron Lett*. **2001**, *42*, 6929.
(c)Sabol, J. S.; .; Flynn, G. A.; Friedrich, D.; Huber, E. W. *Tetrahedron Lett*.**1997**, *38*, 3687

P-110

Synthesis And Biological Activity Of Mercaptobenzoxazole Based Thiazolidinones And Their Arylidenes

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Arylidenes of thiazolidines with mercaptobenzoxazole, namely [(Aryl-4-oxo-1,3-thiazolidin)-hydrazinoacetyl-mercaptobenxazole]; (5-arylidene)-2-aryl-4-oxo-1,3-thiazoliden hydrazinoacetyl-mercaptobenxazole were synthesized. Their chemical structure have been confirmed by ^{1}HNMR, IR, mass spectra and also by microanalytical data. Antimicrobial evaluation was done by agar dilution method against three pathogenic bacteria viz. Bacillus substilis, *Escherichia coli* and *Klebsiella pheumonia* and three pathogenic fungi viz. *Aspergillus niger*, *candida albicans* and *Fusarium oxisporium*. Among new derivatives evaluated, the chloro derivatives exhibited higher potency as compared to the standard drugs streptomycin (for bacteria) and griseofulvin (for fungi) against the tested organisms.

P-111

Prodrug Concept Beyond The Issue Of Availability

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Prodrugs, the pharmacologically inactive derivatives of active drugs, are designed to maximize the amount of active drug that reaches its site of action, through manipulation of the physicochemical, biopharmaceutical or pharmacokinetic properties of the drug.
Prodrugs can be designed to target specific enzymes or carriers by considering enzyme-substrate specificity or carrier-substrate specificity in order to overcome various undesirable drug properties. Recently, advances in gene cloning and controlled gene expression techniques in mammalian cells allow the elucidation of the molecular nature of enzymes and carrier proteins and make possible more rational design of "targeted - prodrugs."
The new approaches which attempt the localization of prodrug activation enzymes into specific cancer cells prior to prodrug administration mainly include ADEPT (antibody-directed enzyme prodrug therapy) and GDEPT (gene-directed enzyme prodrug therapy). Gene-directed enzyme prodrug therapy (GDEPT) is a suicide gene therapy approach that aims to improve the selectivity of chemotherapy by enabling cancer cells to convert non-cytotoxic prodrugs to cytotoxic drugs.[1,2]
Dendrimer-based prodrugs were used to enhance the transepithelial permeability of naproxen, a low solubility model drug. The stability of the dendrimer-naproxen link was assessed. Naproxen was conjugated to G0 polyamidoamine (PAMAM) dendrimers either by an amide bond or an ester bond.[3]
The other therapeutic strategies utilizing targeted prodrug approach include PDEPT (polymer-directed enzyme prodrug therapy) which utilizes a combination of a polymeric prodrug and

polymer-enzyme conjugate to generate cytotoxic drug selectively at the tumour site, ADAPT (antibody-directed "abzyme" prodrug therapy) in which the bacterial enzyme catalyst of ADEPT is replaced by catalytic antibody that can be “humanized”, VDEPT (Virus-directed enzyme prodrug therapy), and PTAPT (Peptide Transporter Associated Prodrug Therapy) in which the peptide transporters have been targeted.[4]
Several prodrug strategies have been developed, but the kinetics and mechanisms of the deprotection of potential prodrug candidates are still often poorly known.

Reference:

1. Viral vectors for gene-directed enzyme prodrug therapy, Schepelmann, S.;
1. Springer, C. J. *Curr Gene Ther.* **2006**, 6, 647-70.
2. Prodrug approaches of nucleotides and oligonucleotides, Poijarvi-Virta, P. *Curr Med Chem.* **2006**,13, 3441-65.
3. In vitro evaluation of dendrimer prodrugs for oral drug delivery, Najlah, M.; Freeman, S.; Attwood, D.; D'Emanuele, A. *Int J Pharm.* **2006**, (In press).
4. Diethylstilbestrol glutamate as a potential substrate for ADEPT. Pedone, E.; Searle, F.; Brocchini, S. *J Drug Target*. **2006,** 6, 437-43.

P-112

***In vitro* cultivation of *Plasmodium falciparum*: Protein profile of parasites grown in RPMI and RPNI (modified) media with human and animal sera.**

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RPNI, a combination of three commercially available growth media (RPMI-1640, NCTC-135 and IMDM) has been found to support long term continuous cultivation of laboratory maintained strain of *P. falciparum* in the presence of 10% bovine calf serum. The present study was under taken to compare the protein profile of the parasites grown in RPMI as well as RPNI media. Different sera such as human serum, bovine calf serum (BCS) and horse serum were supplemented in RPNI medium while only human serum was supplemented in RPMI medium. The laboratory maintained NF-54 and 3D7 strains of *P. falciparum* were used during study. The cultures were maintained in candle jars protocol. Parasites grown in different medium supplements were pooled and isolated using 0.1% saponin. The parasites were sonicated in PBS, mixed with sample buffer, boiled for 3 minutes and centrifuged at 10000 rpm for 10 minutes. These samples were run on SDS gel electrophoresis (SDS-PAGE). The protein patterns obtained with parasites grown in RPNI medium were compared with that of the parasites grown in RPMI medium. The results revealed identical protein profile of the parasites grown either in RPMI medium supplemented with 10% human serum or in RPNI medium supplemented with 10% human serum / BCS / horse serum .

P-113

Discovery of Novel 2-thiophene-5-yl-3H-quinazoline-4-one derivative as dual inhibitors of NFκB and AP-1

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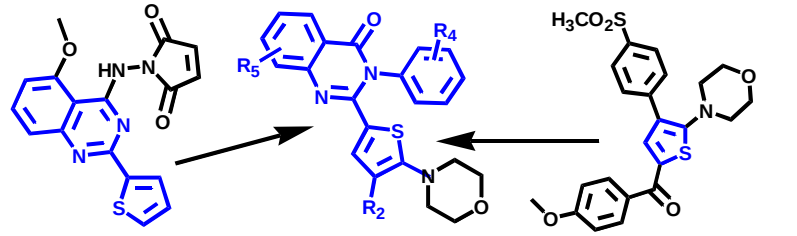
Transcription factors are regulatory proteins which bind to specific DNA sequences in the gene promoter or enhancer regions and hence activate or inhibit transcription. Transcription factors NF-kB and AP-1 are the central control points of tissue and organ homeostasis and important regulators for immune response leading to inflammation and tumorigenesis. Therefore, their controlled regulation may provide a suitable cure for a disease without the often encountered adverse reactions (ADRs) of standard drugs.
Several literature exits that highlight the fact that when two minimum structural features necessary for activity are incorporated into one single molecule, the activity increases manifolds. Based on this understanding we have designed and synthesized 2-thiophene-5-yl-3H-quinazoline-4-one derivative as depicted in scheme-1.

OUR DESIGNED MOLECULE



IC_{50} = 8nM for NFkb and AP-1 PMCH-16 IC_{50}= 3.3mM for NFkb and AP-1

Scheme 1

Based on the above rationale the compounds designed and synthesized by us have been tested on *in vivo* model of inflammation as well as *in vitro* assays for NFkB and AP-1 inhibition.

As a significant outcome of this hypothesis we have obtained a potential lead molecule (**PMCR-66**) which has not only shown a very promising dose response in the *in vivo* model of acute inflammation but also a **dual inhibitory** activity for **NFkB (99.0%)** and **AP-1 (66%)** in their *in vitro* assays. Further, these results are also supported by the **molecular modeling study of PMCR-66**. To the best of our knowledge, this is **the first 2-thiophene-5-yl-3H-quinazoline-4-one derivative that has been reported to show NFκB and AP-1 inhibitory activity.**

P-114

Synthesis of Novel Thiazole Derivatives as a Potential TNF- α Inhibitor

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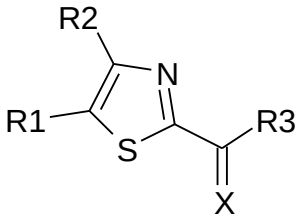
The proinflammatory cytokines tumor necrosis factor-α (TNF- α) and interleukin-1β (IL1β) contribute to the regulation of the body's response to infection and cellular stress. However, chronic and excessive production of TNF- α and IL-1β are believed to underlie the progression of many autoimmune diseases such as rheumatoid arthritis (RA), Crohn's disease and psoriasis. Analysis of cytokine mRNA and protein in rheumatoid arthritis tissue revealed

that many proinflammatory cytokines such as TNF-α, IL-1β and chemokines are abundant in all patients regardless of therapy. In rheumatoid joint cell cultures that spontaneously produce IL-1β, TNF-α was the major dominant regulator of IL-1β. Subsequently, other pro-inflammatory cytokines were also inhibited if TNF-α was neutralized, leading to the new concept that the pro-inflammatory cytokines were linked in a network with TNF-α at its apex. This led to the hypothesis that TNF-α is of major importance in RA and hence is an important therapeutic target.

There are a large number of small-molecule agents that are in various stages of preclinical and clinical development that inhibit the synthesis of TNF-α Several small-molecule TNF-α inhibitors that have been developed like thalidomide derivatives, thiazole derivatives, imidazole derivatives etc. by various companies. The therapeutic rationale behind development of above drugs is the reduction of pro-inflammatory actions of the cytokine TNF- α, which is found, elevated with other cytokines in autoimmune lesions.

GENERAL STRUCTURE OF DESIGNED COMPOUND



The compounds designed and synthesized by us on the above rationale have been tested on *in vivo* and *in vitro* assay systems. Most of the compounds show potential anti-inflammatory effect in acute and chronic models of inflammation. Moreover, they are not active in COX-1, COX-2 and cPLA-2 assays. But these compounds show a very good TNF- α inhibitory activity in PBMC (peripheral blood mononuclear cell) cell line based assay. Amongst the several compounds that have been synthesized in this series, PERD-12 has shown the best *in vivo* and *in- vitro* results with over 61% TNF- α inhibition in PBMC cell line based assay system. Hence, further studies need to be performed to develop a potential anti-inflammatory drug based on TNF- α inhibitory mechanism.

P-115

3D QSAR and DFT Based study of Dihydropyridodiindoles

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The 3D QSAR of a series of Dihydropyridodiindoles have been made with the help of CoMFA and CoMSIA techniques on Sybyl 7.2. This series has a compound of quite rigid structure with highest activity. The Same compound has been used as template for whole series to for possible active conformation. This study provide significant results. In the next step semiemperical (AM1 and PM3) and DFT descriptors like molecular weight (Mw), hardness (□), chemical potential (□), total energy, and electrophilicity index (□). Various regression models have been made and regression quality indicates that these descriptors provides valuable information and have significant role in assessment of activity. The DFT

calculations have been performed by using BLYP energy functional with the 6-31g** basis set on Gaussian03 over linux cluster. This study gives a significant view for drug designing and their receptor interaction.

P-116

Comparative evaluation of the methanolic extract of *Gmelina arborea* L leaves, root and stem bark for free radical scavenging activity.

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Oxidative stress that results from the increased generation of reactive oxygen species has been implicated in many human ailments including cardiovascular diseases, cancer and neural disorders and in the process of aging.The present study is aimed to evaluate the free radical scavenging of the leaves, root and stem bark of *Gmelina arborea* L. This plant is one of the constituents of herbal products like 'Dashamula' and 'Bramharasayana'.*Gmelina arborea* L. is a deciduous broad base tree which has been reported for its anti-inflammatory, antidiabetic, antiviral and wound healing activities. The dried powders of leaves, root and stem bark of *Gmelina arborea* L. were extracted separately to get their methanolic extracts. This was followed by phytochemical testing of the individual extracts. The three extracts were studied for their interaction with $DPPH^{\cdot}$ radical in the concentration range of 10-1000 µg/ml and their activities were compared. The study showed that all the extracts possess free radical scavenging activity and the order of scavenging of $DPPH^{\cdot}$ radical was - Leaves extract > root extract > stem bark extract. Thus we may conclude that the methanolic extract of the leaves of *Gmelina arborea* L. possesses maximum free radical scavenging activity in the concentration range of 10-1000 µg/ml. Further research needs to be done to explore the antioxidant potential of this indigenous plant as it can be exploited in reducing free radical induced pathophysiological abnormalities.

P-117

Picroliv Imparts Immunomodulatory Effect In Balb/C Mice In a Dose Dependent Manner

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Ayurveda has recommended several plants of medicinal value, some of these may improve the host immune system. Most of the plants recommended in Ayurveda exert their effect as antioxidants. Notably *Andrographis paniculata, Withania somnifera, Tinospora cardifolia, Curcuma longa* and *Ocimum sanctum* have shown their immunostimulant potential. *Picrorhiza kurroa* Royle (Scrophulariaceae) popularly known as 'Kutki' or 'Kurro' in Hindi, is one of such plants, from which Picroliv has been developed. Earlier *in vivo* and *in vitro* studies have shown the excellent hepatoprotective and immunomodulatory efficacy of

Picroliv (which is exerted by modulation of free radical-induced lipid peroxidation) in a number of laboratory studies against various toxins. Thus Picroliv could be useful as an adjunct to chemotherapy or as a short term prophylactic agent.
The present study was planned to evaluate the dose dependent immunostimulatory efficacy of Picroliv and to find out the molecular mechanism of its action. Picroliv was fed to Balb/c mice in different doses once daily by oral route for 14 consecutive days. It exerted highly significant immunostimulation response at a dose of 10mg/kg. It was found to significantly induce antibody mediated immune response demonstrating increase in antibody forming cells (PFC), CD19, antibody titre (HA) as also cellular responses like T cell proliferation at 1 mg/kg, both CD3+/CD4+ and CD3+/CD8 lymphocyte counts decreased while there was significant increase in the Nitric oxide production by peritoneal macrophages of Balb/c mice. Picrolive was also found to induce IFN-γ production and suppression in IL-4 production thus demonstrating induction of inflammatory cytokines. These studies strongly suggest picroliv to be a promising agent as an immunostimulant which may be used as adjunct to chem

P-118

In-Vitro Antileishmanial Activity Of Few Naturally Occurring And Synthetic Chalcones

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Visceral Leishmaniasis (VL) or Kala-azar caused by *Leishmania donovani* is one of the major public health problems in many tropical countries of the world and about 1.5 to 2.0 million new cases arise every year. Around 90 % of total VL cases occur in India, Nepal, Bangladesh and Sudan.[1] The control of VL remains a challenging problem because no vaccine exists and the available chemotherapeutics have serious side effects including variable efficacy, toxicity, parenteral administration, requirement for long courses of administration and emergence of resistance in parasite to various existing drugs[2]. Moreover, immuno-suppression in this disease also leads to inadequate efficacy of existing drugs.
In this scenario a novel drug, which can be easily synthesized and economically viable with less side effects is urgently required. Natural product based new leads are proving quite useful in this area. Chalcones are secondary metabolites of terrestrial plants, precursors for the biosynthesis of flavonoids, exhibit various biological activities.[3] For example the licochalcone A isolated from roots of licorice reported for its *in-vitro* and *in-vivo* antimalarial and antileishmanial activity,[4] 3-methoxy,4-hydroxyloncocarpin isolated from the roots of *Loncocarpus utilus* inhibits the NADH: ubiquinone oxidoreductase activity[5] and synthetic chalcones such as 2,4-dimethoxy, 4'-allyloxychalcone, 2,4-dimethoxy, 4'-butoxychalcone have been reported as antileishmanial agents.[6] In continuation of our program on development of natural products based antileishmanial agents, we have isolated few chalcones from the *crotalaria* genus and studied their antiparasitic activity.[7] The poster describes the isolation, synthesis of few natural chalcones and evaluation of their antileishmanial activity.

References

1. Anon ,**1996**. *World Health Organization* . Inf. Circ. WHO Mediterr. Zoon Control. Cent. **40,11**.
2. Sundar,S., Goyal,, A.K., More, D.K., Singh, M.K., Murray, H.W., **1998**. Treatment of Antimony- Unresponsive Indian visceral leishmaniasis with ultrashort courses of amphotericin-B lipid complex. *Ann. Trop. Med. Parasitol*. **92 (7), 755**.

3. Hsieh, H.-K.; Tsao, L.-T.; Wang, J.P., **2000** *J. Pharm. Pharmacol*., 52, 163.

4. Chen, M.; Christensen, S. B.; Blom, J.; Lemmich, E.; Nadelmann, L.; Fich, K;
   a. Theander, T. G.; Kharazmi, **1993,** A. *Antimicrob. Agents Chemother*.,
   b. 37, 2550.
5. Fang,N.; Casida, J.E. **1999,** *J.Nat.Prod*., 62,205.

6. Chen, M.; Zhai, L.; Christensen, S. B.; Theander, T. G.; Kharazmi, A. **2001,**
   i. *Antimicrob. Agents Chemother*., 45, 2023

7. Kumar, J. K.; Narender, T.; Rao, M. S.; Rao, P. S.; Toth, G.; Balazs, B.;
   a. Duddeck, H. **1999,***J. Braz. Chem. Soc*., 10, 278.

P-119

Asymmetric Synthesis of Phenyl-Isoserine Derivatives and Anticancer Taxane Drugs

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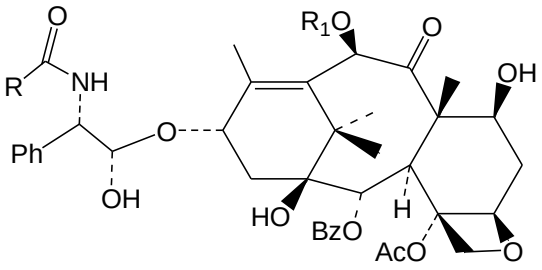
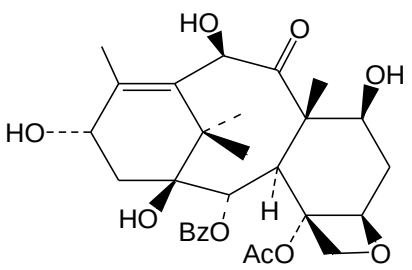
Paclitaxel, a natural molecule with taxane diterpene skeleton having N-benzoyl-phenyl-isoserine side chain, displays potent anticancer activity against various forms of leukemia and solid tumours in the breast, brain, lung and ovary in humans. Paclitaxel was first isolated from the bark of the pacific yew tree (*Taxus brevifolia*) in 1971. The antitumour activity of paclitaxel has stimulated intense research efforts over recent decade including the search for other taxanes with improved properties and the development of semisynthetic route to avoid rapidly exhausting its original source. These efforts have led to the symisynthesis of taxane drugs such as paclitaxel and docetaxel, which consists of esterification of 13-OH group of protected-10-deacetyl-baccatin-III (obtained from leaves of *Taxus baccata*, European yew) and final deprotections. Our efforts in asymmetric synthesis of side chains of these drugs will be presented.



Paclitaxel R= Ph, R_1= Ac;
Docetaxel R= *t*-butoxy, R_1=H



10- Deacetyl-baccatin III (10-DAB)

References

1. Suffness M., Taxol Science and Applications, CRC Press, 1995.
2. Zaitsev, A. B. and Adolfsson, H. Synthesis 1725-1755, 2006.
3. Chantepoup L. et al. US patent 2002/0068833 A1 June 2002.

4. Naidu R. US patent 2005/0272807 A1 Dec. 2005.

P-120

DNA Binding Studies And *In Vitro* Experiments Of Chiral Heterotrimetallic Series Of Complexes [Bis(Aquo-2-Aminoethanol Tryptophanato)M^{II}- Sn^{iv}] Chloride Where M=Co^{ii} , Ni^{ii} ,Cu^{ii} & Zn^{ii} .

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A new series of chiral complexes [bis(aquo-2-aminoethanol tryptophanato)M^{II}- Sn^{IV}] chloride where M= Co^{II} **1**, Ni^{II} **2**,Cu^{II} **3** & Zn^{II} **4** were prepared and characterized by various physico- chemical techniques. A well-tailored synthetic strategy via a three-step pathway under anhydrous conditions was employed. The complexes are novel as they exhibit discriminating power of transition and non- transition metal ions (strong lewis acids) in a single chemical entity in heterotrimetallic species towards DNA, which is the cellular target of most anti -cancer drugs. A transition metal ion preferably binds at the N7 position of guanine while non-transition viz. tin metal ion prefers to bind to the phosphate backbone of DNA double helix. This feature together with chirality induced by the tryptophan ensures strong stereoselective binding of the potential drug candidates **1-4** to DNA. In this work, we have demonstrated the binding event of the complexes1-3 with CT DNA by using various spectroscopic and electro- analytical techniques viz. UV-vis, fluorescence, spectrophotometry & cyclic voltametry. Viscosity measurements were also carried out as supporting evidence for exploring the binding modes of the complexes with CT DNA.

P-121

Drug Design , Synthesis and Characterization of a New Bimolecular Complex with an N-Glycosidic moiety: in vitro Cytotoxicity,Electrochemistry and Binding Studies with Calf-Thymus DNA.

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The modulation of the new bimolecular complex of the type St-1a was done by interaction of the Compound St-1 and by St-2 the formation of new complex (St-1A) will takes place via hydrogen bond and coordinate bond formation .The complex was characterized by various physico-chemical techniques. Molar-conductance measurements showed that complex St-1A is ionic in nature. On the basis of spectroscopic data, the complex was assigned a octahedral geometry and found to be highly stable. The copper complex St-1A was found to bind to CT-DNA, with a binding constant K_b of $1.4x10^3$ $M^{-1,}$ as derived by UV/VIS titration, and confirmed by CV, circular dichroism (CD), and viscosity measurements.. In an in vitro

antitumor MTT assay, St-a1 exhibited significant anticancer activity against the SY5Y and PC-12 cell lines, with an estimated IC(50) value in the micromolar range for SYSY.

P-122

Evaluation Of Anti-Oxidant Effect Of Melatonin In LPS And Rotenone Induced Oxidative Stress

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Oxidative stress is considered as an important underlying cause of many acute and chronic diseases. Lipopolysaccharide (LPS, an endotoxin) a component of bacterial cell wall and Rotenone a natural cytotoxic compound, are known to damage neurons through oxidative stress. Melatonin, the primary secretory product of the pineal gland, is known to possess free radical scavenging and antioxidant properties and display pronounced neuroprotective effects. This study was undertaken to evaluate *in vitro* anti-oxidant effect of melatonin in different brain regions against LPS and rotenone induced oxidative stress in brain regions of adult SD rat. Reduced Glutathione (GSH) and Malondialdehyde (MDA) concentration were measured as indices of oxidative stress. In one set of study, homogenates of different brain regions Striatum, Midbrain, Frontal cortex, and Hippocampus were incubated with LPS or rotenone at concentrations of 1, 25 and 50 µg/ml and 1, 2 and 4 mM for 60 minutes respectively. In another set, homogenates of different brain regions were incubated with melatonin (0.75, 1.5 and 3 mM) alone as well as with LPS (50mM) or rotenone (4mM) in separate groups. LPS and Rotenone showed significant oxidative stress as indicated by decrease in GSH and increase of MDA in all the brain regions except hippocampus in case of LPS. Melatonin (3mM) suppressed significantly oxidative stress produced by LPS and Rotenone. Melatonin per se did not affect GSH but decreased MDA significantly in Striatum and Frontal cortex. Melatonin showed better protective effect against rise of MDA as compared to GSH particularly in Hippocampus. Thus, anti-oxidant effect of melatonin may vary among the brain areas.

P-123

Coumarin Analogues of 1,2,3,4-Tetrahydro Papavarine and Protoberberine Alkloids Skeleton.

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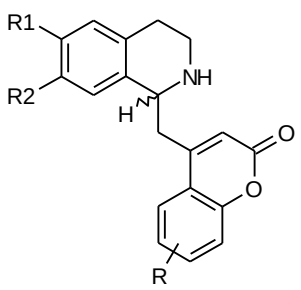
The isoquinoline nucleus is a part of alkloids like Papavarine, Tetrahydro papavarine, Emetine, Protoberberines, etc,. The present synthetic sequence employs Bischler-Napieralski reaction utilizing Coumarin-4-acetic acids to generate (molecular structural motifs) a molecular library **1.** The one carbon homologation has also been achieved by

hydroxymethylation leading to the protoberberine skeleton **2.** The structures of all the intermediates have been confirmed by spectral methods.



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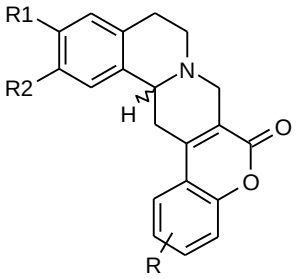

2

P-124

Synthesis And Biological Activity Of New Heteryl Phenoxy Propanes

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1,5-benzothiazepines exhibit a wide variety of pharmacological activities[1-4]. Isoxazolines[5, 6] are biologically active, synthetically useful and important heterocycles having a wide role in medicinal chemistry. It is reported that pyrazolines exhibit anti carcinogenic, anti diabetic anticonvulsant, anti-inflammatory, antibacterial, anti fungal, antiviral, analgesic and antioxidant activities[7-10]. Considering the applications of above mentioned heterocyclic compounds, we report here in the synthesis of new symmetrical and unsymmetrical phenoxy propanes having 1,5-benzothiazepines, isoxazoline and pyrazoline moieties coupled together and their anti microbial evaluation.
The cyclo condensation of the chalcones **1** separately with 2-aminobenzene thiol , hydroxyl amine and hydrazine hydrate were carried out to obtain substituted 1,5- benzothiazepines **2**, substituted isoxazolines **3** and substituted pyrazolines **4**, respectively. The compounds **2, 3** and **4** in methanolic NaOH were stirred separately with dry DMF and 1, 3-dibromo propane using phase transfer catalyst to give the products 1,3-bis-[4'-(2"-substitted phenyl) –2,3-dihydro-1,5- benzothiazepin-4"-yl)-phenoxy] propanes **5** , 1-[4'-(2"-substitted phenyl) –2,3-dihydro-1,5- benzothiazepin-4"-yl)-phenoxy] –3-[3'- (5"-substituted isoxazolinyl) phenoxy] propanes **6** and 1-[4'-(2"-substitted phenyl) –2,3-dihydro-1,5- benzothiazepin-4"-yl)-phenoxy] –3-[3'- (5"-substituted pyrazolinyl) phenoxy] propanes **7,** respectively.
Key Words: Cyclo condensation, 1,5-benzothiazepines, isoxazolines , pyrazolines , 1,3-dibromopropanes.

P-125

Synthesis Of Steroidal Derivatives As Potential Anti-Oxidant and Anti-Dyslipidemic Agents

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The development of medicine, both traditional and modern are fascinating. Infact human progress and development of newer medicines are inseparable. Chemistry of steroids and more particularly its C-21 derivatives commonly known as **pregnanes** is full of surprises. These potent derivatives have been found to posses cytotoxic, anti-feedant , lipid lowering activity, anti-inflammatory and anti-viral activity.

Owing to immense importance of these medicinally important pregnane derivatives, considerable attention is being devoted to the synthesis and biological evaluation of this important class of compound.

With the objective of synthesizing model compounds for use in biological studies and as part of our programme devoted to the synthesis of novel pregnane derivatives, we have adopted simple , expeditious and convenient methods for the introduction of various activating groups at C-16 position. Through these C-16 substituted derivatives various modifications have also been made at the C-20 position by introducing hydroxy and alkyl group in the side chain of the steroidal moiety. These newer pregnane derivatives were also conjugated with different sugars yielding medicinally important pregnane derivatives.

Steroidal oximino ether derivatives have used for the treatment of breast cancer in women. Synthesis of a number of novel steroidal oximino ether derivatives has also been accomplished.

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Synthesis, Chracterisation, Antioxidant and Antimicrobial Activities of Different Heterocycles Derived From 3-Formyl Chromones

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On condensation compound I and 2 in alcoholic KOH for 3 hI' affords (1-(4-(pyrdin-2-yl)benzyl)-1H-pyrazol-4-yl)(2-hydroxyphenyl)methanone 3. While compound 3 on stirring with hydroxylamine hydrochloride in presence of KOH afforded 2-hydroxyphenyl (\-(4-pyridin-2-ylbenzyl)-1H-pyrazol-4-yl)methanone oxime 4. Compound 4 on heating in POCI3 gave 2-(1-(4-(pyridin-2-yl)benzyl)-1 H-pyrazol-4-yl)benzo[d]oxazole 5. Compound I on condensation with 6 in dry pyridine gave 3-(2-(6-chloro-7-methyl-2-oxo-2H-chromen-4-yl)vinyl)-4H-chromen-4-one 7. All compounds has been characterized by fR, 'H NMR and mass spectral studies. These compounds are tested for their antioxidant and antimicrobial activities.

P-127

Knoevenagel Condensation Reactions 1,2-Dihydro-L-Phenyl-3-Propylpyrazol-5-0ne Of 3- Formyl Chromones And 4-Formyl Pyrazoles With Pyrazolone By Conventional And Non-Conventional Methods.

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3-Formyl chromone 2 when heated with 1,2-dihydro-l-phenyl-3-propylpyrazol-5-one 1 in presence of acetic acid afforded the compound 4-((4-0xo-4H-chromon-3-l)methylene)-1-phenyl-3-propyl-lH-pyrazol-5(4H)-one 3. 4-Formyl pyrazol 4 on treatment with compound 1 in presence of acetic acid gave compound (4)-1-phenyl-4-((l-phenyl-l H-pyrazol-4-yl)methylene)-3-propyl-lH-pyrazol-5(4H)-one compounds are synthesized by conventional and ultrasonic irradiations.

P-128

A validated stability indicating UPLC method for Primaquine phosphate

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A new isocratic reverse phase chromatographic method was developed using ultra performance liquid chromatograph (UPLC) for primaquine phosphate bulk drug. The newly developed method is applicable for assay and related substance determination of the active pharmaceutical ingredient. The chromatographic separation of primaquine and impurities was achieved on Waters acquity BEH C18, 50 mm x 2.1 mm, 1.7 µm column within a short runtime of 5 min. System suitability of the analysis established the validity of chromatographic separation. The method was validated according to regulatory guidelines with respect to specificity, precision, accuracy and linearity. Forced degradation studies were also performed for primaquine phosphate bulk drug samples to demonstrate the stability indicating power of the newly developed UPLC method. Peak purity of these samples was verified using a photodiode array (PDA) detector.

Poster -129

Heteropolyacid Catalyzed Syntheses of Coumarins Via Pechmann Condensation Reaction

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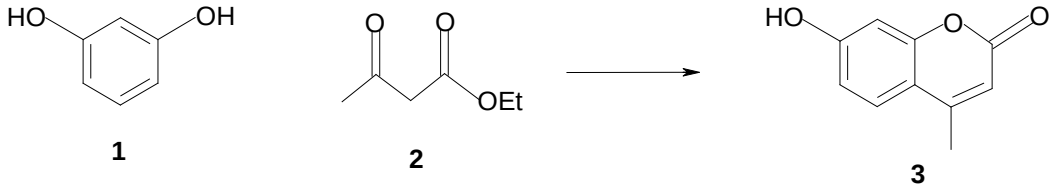
Coumarin and its derivatives have been attracting great interest because of their importance in synthetic organic chemistry. Many of the coumarin derivatives exhibit diverse biological activities useful to mankind. [1] These compounds find their application in pharmaceuticals, fragrances, agrochemicals, and insecticides.[2–4] In the recent years, one method which has been vastly investigated for the synthesis of coumarins is the Pechmann reaction, which starts from phenols. In the conventional production of coumarins by Pechmann condensation, concentrated sulfuric acid is used as the catalyst.[5] There are other acid catalysts like P_2O_5, $FeCl_3$, $ZnCl_2$, $POCl_3$, $AlCl_3$, PPA, HCl, phosphoric acid and trifluoroacetic acid, which are known to effect this condensation.[6] Among the heterogeneous catalysts which have been reported for Pechmann condensation, the most prominent ones include Nafion-H,[7] zeolite H-BEA, Amberlyst 15,[8] and some other solid acids.[9,10] Laufer et al have reported nafion resin/silica nanocomposites for the synthesis of 7-hydroxycoumarins by Pechmann reaction.[11] Recently, microwave irradiated solventless synthesis of coumarins in quantitative yields by

Pechmann condensation has been reported, catalyzed by chloroaluminate ionic liquid.[12] Maheswara et al[13] have reported excellent yields of coumarins via Pechmann condensation using silica supported perchloric acid ($HClO_4 \cdot SiO_2$).

Heteropolyacids are polynuclear complexes of Mo^{VI}, W^{VI} and V^{V}, which can also involve other elements as central atoms or ligands. HPA are multi-electron oxidants and, at the same time, are strong Brönsted acids. Infact, the acidity of concentrated aqueous and nonaqueous solutions of $H_3PW_{12}O_{40}$ is higher by 1 - 1.5 units of the Hammett acidity function (Ho) than that of $HClO_4$ and H_2SO_4. (14). Therefore, HPAs have been used as catalysts in several acid catalyzed reactions, like Friedel-Craft alkylation, esterification, hydrolysis, condensation, etc.[15]

In the present study, we report Keggin type heteroplyacids as efficient catalysts for the synthesis of coumarins via Pechmann condensation reaction between a phenol and ethyl acetoacetate. The HPAs screened were phosphotungstic acid, phosphomolybdic acid and phosphovanadic acid. Phosphotungstic acid (PTA) was found to be the most effective catalyst. The model reaction in this study, Pechmann condensation of resorcinol **1** with ethyl acetoacetate **2**, in toluene under reflux conditions, to obtain coumarin **3**, is shown in the scheme below.



1 **2** **3**

Good yields of coumarin were obtained using this catalyst. The product was isolated form the reaction mixture by column chromatography and characterized by ^{1}H and ^{13}C NMR, IR and elemental analysis.

The quantification of the substrates and product was done on a HP 6890 series Gas Chromatograph, using a Restek-5 capillary column. Since the product could be separated on GC, the GC-MS of the product was also done as a tool for the confirmation.

A few more phenols were screened for the Pechmann condensation with ethyl acetoacetate using the HPA catalyst. The products in all cases were isolated by column chromatography, and characterized by the techniques mentioned above.

References:

1. R.D.H. Murray, J. Medez, S.A. Brown, The Natural Coumarins: Occurrence, Chemistry and Biochemistry, Wiley, New York, 1982.
2. E.A. Gunnewegh, A.J. Hoefnagel, R.S. Downing, H. van Bekkum, Recl. Trav. Chim. Pays-Bas 115 (1996) 226.
3. W.-C. Sun, K.R. Gee, R.P. Haugland, Bioorg. Med. Chem. Lett. 8 (1998) 3107.
4. J. Oyamada, C. Jia, Y. Fujiwara, T. Kitamura, Chem. Lett. (2002) 380.
5. E.C. Horning, in: Organic Synthesis, Vol. III, Wiley, New York, 1955, p. 281.
6. (a) H. Appel, J. Chem. Soc. (1935) 1031;
7. (b) L.L. Woods, J. Sapp, J. Org. Chem. 27 (1962) 3703;
8. **(c) Z.S. Ahmad, R.D. Desai, Proc. Indian Acad. Sci. Chem. Sci. 5A (1937) 277; Z.S. Ahmad, R.D. Desai, Chem. Abstr. 31 (1937) 5785;**
9. (d) R. Robinson, F. Weygand, J. Chem. Soc. (1941) 386;

(f) A.J. Nadkarni, N.A. Kudav, Ind. J. Chem., Sect. B 20 (1981) 719.

10. D.A. Chaudhari, Chem. Ind. (1983) 568.

11. E.A. Gunnewegh, A.J. Hoefnagel, H. van Bekkum, J. Mol. Catal. A: Chem. 100 (1995) 87.
12. B.M. Reddy, V.R. Reddy, D. Giridar, Synth. Commun. 31 (2001) 3603.
13. T.S. Li, Z.H. Zhang, F. Yang, C.G. Fu, J. Chem. Res. (S) (1998) 38.
14. M.C. Laufer, H. Hausmann, and W.F. Hölderich, J. Catal 218 (2003) 315-320.
15. V. Singh, S. Kaur, V. Sapehiyia, J. Singh, G. L. Kad, Catal. Commun. 6 (2005) 57-60.
16. M. Maheswara, V. Siddaiah, G.Lakishmi V. Damu, Y. K. Rao, C. V. Rao, J. Mol. Catal. A: Chem 255 (2006) 49.
17. I.V. Kozhevnikov, K.I. Matveev Appl. Catal,, 5 (1983) 135.
18. Kozhevnikov, I. V. Chem. Rev. 1998, 98, 171.

P-130

Impurity Profile Of An Aryl Cyano Drug Intermediate.

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Impurities in pharmaceuticals are unwanted chemicals that remain with the Active Pharmaceutical Ingredients (APIs), or develop during formulation, or upon aging of both API and formulated APIs. Impurity profiling is the common name of analytical activities, the aim of which is detection, identification or structure elucidation of impurities. The present study aims to isolate and characterize the impurities present in aryl cyano drug intermediate.

The impurities were detected by analytical HPLC using Hio Sil Kyatek C_8 column. Acetonitrile: water (60:40) pH adjusted to 3.0 with dilute ortho phosphoric acid was used as the mobile phase with a flow rate of 1ml/min and detection at 220nm.

The detected impurities were then isolated by preparative HPLC using the same mobile phase and UV detection. The column used was TSK gel ODS 80 Tm with a flow rate of 10ml/min. The isolated impurities were further freeze dried and characterized by IR and NMR spectrometric analysis.

The two impurities interpreted from IR and NMR spectrometric data were found to be –

1) 3-[(1'-methyl-1'-carboxymethyl)]-5-[(1'-methyl-1'-cyanoethyl)]-1-methyl-benzene.
2) 3-[(1'-methyl-1'-cyanoethyl)]-5-[(1'-methyl-1'-cyanomethyl)]- 1-methyl-benzene.

P-131

Cloning, Sequencing And Characterization Of *SRRG-1* Gene Of *Leishmania donovani*

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Leishmania parasites are pathogenic trypanosomatid protozoa that cause a group of disease globally known as Leishmaniasis. There is no vaccine in routine use and chemotherapy the sole treatment still relies on toxic penatavalent antimonials.The situation is compounded by development of drug resistance to this first line treatment.Therefore there is an urgent need for the development of new drug, and also to unravel the mechanism of antimony

resistance.Mechanism of drug resistance in the field isolates is less understood and the studies on laboratory generated metal resistant mutants suggest a multiplicities of the resistance mechanism, most prevalent being gene amplification and thiol metabolism. Present study deals with identification and characterization of a novel gene *SRRG-1*(SAG Related Resistance gene-1) using DNA microarray tool. The gene consistently showed upregulation in non responsive isolates. Complete ORF of *SRRG-1* was amplified from *L. donovani* genomic DNA using primers designed from *L. infantum* sequence and cloned in pCR-TOPO vector. An open reading frame of 870 bp encoding 290 amino acid with predicted molecular weight of 33.3 kD and pI 8.37 was observed .The gene was expressed as His tagged recombinant protein in *E. coli* cells (BL-21 plys) using pXP-NT expression vector. Purification and characterization of the recombinant protein is underway.The study may help to unravel the mechanism of clinical resistance.

P-132

Isolation and molecular characterization of filarial Acetylcholinesterase

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Filariasis is a one of the world's most disabling and disfiguring diseases affecting millions of people in tropical and sub-tropical regions of the world. The isolation and characterization of parasite-specific enzyme targets is essential for developing effective control measures against filariasis. Acetylcholinesterase (E.C. 3.1.1.7, AchE), an important enzyme of neuromuscular transmission, has been shown to be present in a number of helminth parasites including filarial parasites and may be playing a role in host-parasite interactions. This enzyme appears to be a suitable candidate for development of drugs/vaccine targets against filarial parasites, but major stumbling block is the lack of sufficient knowledge about the structural differences between the parasite and mammalian Ache. The molecular characterization of filarial parasite AchE (pAchE) may help in identifying the differences between the parasite and the host enzymes and ultimately in rationale design of suitable anti-filarial drugs. In our previous studies we have demonstrated two molecular forms of AchE in human (*Brugia malayi*) and bovine (*Setaria cervi*) filarial parasites different from the host enzyme. In the present study, we have isolated and characterized the filarial parasite acetylcholinesterase. The *S. cervi* AchE was purified using a combination of gel filtration and affinity columns. The two isoenzymic forms of filarial parasite AchE were separated and isolated by preparative polyacrylamide gel electrophoresis and electro-elution. Both the molecular forms of *S. cervi* enzyme were true AchE as both preferentially utilized acetylthiocholine iodide as substrate and were strongly inhibited by the true AchE inhibitor and not by pseudolcholinesterase inhibitor. The polyclonal and monoclonal antibodies against parasite AchE showed significant level of reactivity with both the molecular forms of parasite AchE but not with the host enzyme. These findings suggest that the parasite AchE isoforms are biochemically and immunochemically different from the analogous host enzyme. The filarial AchE gene was amplified using specific primers based on conserved sequences of AchE from related parasites and *B. malayi/W. bacnrofti* cDNA library and *S. cervi* genomic DNA. The *B. malayi* and W. *bancrofti* cDNA gave one PCR product (0.8 kb) and 2 PCR products (0.8 and 0.6 kb) were observed with *S. cervi* genomic DNA. These PCR products were cloned in pGEMT cloning vector and transformed in *E. coli.* The presence of insert was verified by restriction analysis.

P-133

Spectrophotometric determination of Isoniazid and ritodrine hydrochloride using novel reagents

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Novel coupling reagents were used for simple, rapid and sensitive spectrophotometric determination of isoniazid (INH) and ritodrine hydrochloride (RTH) in pure form or in pharmaceutical preparations of it. The proposed method was based on the diazotization of 4,4'-methylene-bis-(p-amino-2'-carboxybenzanilide) and 3,5- dimethoxy-4-hydroxy-2-aminoacetophenone (3,5-DMHAA) followed by a coupling reaction with either INH or RTH in hydrochloric acid medium. The resulting colored products have absorption maxima at 492 and 481nm for INH and 487 and 472nm for RTH respectively. Beer's law is obeyed at concentration of 0.1-24 ppm, 0.1-18 ppm for INH and 0.1-15 ppm, 0.1-19ppm for RTH. The method is applied for the analysis of INH or RTH in pharmaceutical preparations and the results agree favorable with the official and reported data. Common excipients used as additives in pharmaceutical preparations do not interfere in the proposed method. The developed methods offer the advantages of simplicity, rapidity, and sensitivity without the need of extraction or heating.
Keywords: Isoniazid (INH), Ritodrine hydrochloride (RTH), 4,4'-methylene-bis-(p- amino-2'-carboxybenzanilide), 3,5- dimethoxy-4-hydroxy-2-aminoacetophenone (3,5-DMHAA), pharmaceutical preparations, diazotization, and spectrophotometer.

P-134

Immunochemical characterization of *Setaria cervi* microfilarial antigen

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Filariasis is a chronic debilitating disease affecting millions of people worldwide. The specific diagnosis and control measures are essential for effective control and management of the disease. The production of antibodies against intact parasites would be helpful for identifying and characterizing the surface antigens having immunoprophylactic potentials. *Setaria cervi*, a bovine filarial parasite, has been shown to have some antigens common to human filarial parasites. In the present study we have produced antibodies against *S. cervi* intact microfilariae and used these antibodies for immunochemical characterization of microfilarial antigens. The *S. cervi* microfilariae (ScMf) were isolated by dissecting adult female worms and incubating the uteri in salt solution containing 0.5% glucose at 37^{o}C for 4-5 h. The ScMf were purified using Percoll gradient. The immunization of the rabbits with *S. cervi* intact microfilariae with and without adjuvant was done. The immune rabbit sera were tested in ELISA and showed antibody titre of 1:128,000 with both microfilariae somatic (ScMf) and adult somatic (ScA) antigens. These immune rabbit sera (immunized with intact microfilariae with and without adjuvant) were further tested for qualitative analysis of ScMf and ScA

antigens by crossed immunoelectrophoretic analysis and it showed the presence of 5-6 and 7-8 precipitin peaks in ScMf and ScA antigens respectively.

P-135

Exploring Structural Biology In Drug Discovery

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It has been recognized that knowledge of the 3D structures of proteins has potential to accelerate drug discovery. The recent developments in genome sequencing and bioinformatics have radically transformed the opportunities. X-ray crystallography, comparative models based on homologous is been exploited in lead optimization. Advent of knowledge of 3D structures of globins, enzymes and polypeptide hormones enabled us in finding new therapeutic targets.

A homology model of $P450_{14DM}$ from C*andida albicans* is generated at BioMed CAChe (v6.1) workstation. 1Ea1 (NCBI protein databank) of *Mycobacterium tuberculosis* is used as a template. Active site is characterized. Azole derivatives like fluconazole, miconazole have been docked and dock scores are generated. Dock score evaluation has enabled us to study the mutual interactions between the ligands and the binding site.

The structure based design method is used to optimize the existing drug candidates for better potency and efficacy. Virtual screening of newly designed molecules is done. Synthesis and *in vitro* evaluation is on anvil as future study. Homology model proved efficient for design of new antifungal.

P-136

Green Procedure For The Preparation Of New Schiff Bases Having Thiazole Moiety

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Thiazoles are an important class of natural and synthetic compounds. Thiazole derivatives display a wide variety of biological activity such as cardiotonic, fungicidal sedative anasthetic, bactericidal and antiflammatory.
With the increasing environmental concerns and the regulatory constrains faced the chemical and pharmaceutical industries development of environmentally benign organic reaction has become a crucial demanding research area in modem oraganic chemical research. Therefore more and more chemists systhetic endeavors and devoted toward green synthesis. Which means the reagent, solvent and catalyst are environmentally friendly.
In recent year to~minimizethe amount ofhamlful organic solvents used in chemical processes much attention has been devoted to the use of alternative reaction media. Besides the use of supercritical fluids water and ionic liquids the posiibility of performing chemical process in the absence of solvent (solvent - free) conditions has been receiving more attention. The reported examples demonstrate that no solvent reaction are generally faster, give highly selectivity and yields and usually require work up procedure and simpler equipments. In view of these recent emphases aimed at developing new selective and environmentally friendly

methodologies for the preparation of fine chemicals herein we report expeditious synthesis of imines having thiazole moiety by the one pot condensation of haloketones, thiourea derivatives and substituted Acetophenone under solvent free conditions. All the products were dtaracterized by IR, NMR and Mass spectral analysis.

P-137

Improved Synthesis of 6-Halo Substituted 3-Cyano-4-Styryl Coumarins & Their Biological Activity

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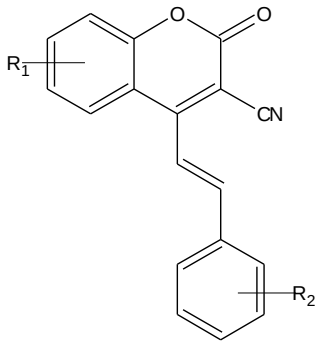
3-Cyano-4-methyl coumarins are conviniently synthesized by Kendale & Axford method and in continuation to our work earlier on this moiety, efforts were towards improved synthesis of the starting material (I) to obtain 3-cyano-4-styryl coumarins derivative.

In current work, the cyclizations by different base catalysis were compared and a direct, efficient and operationally simple approach to the synthesis of novel styryl derivatives was successfully employed. Under mild temperature condition using alkali metal alkoxide, the products are obtained in very good yield.

The title compounds were screened for their biological activity for antibacterial & anti-tubercular against *Mycobacterium Tuberculosis* ($H_{37}RV$).



P-138

Preparation & Biological Activity of Small Library of Substituted 4*H*-1,4-Benzothiazines

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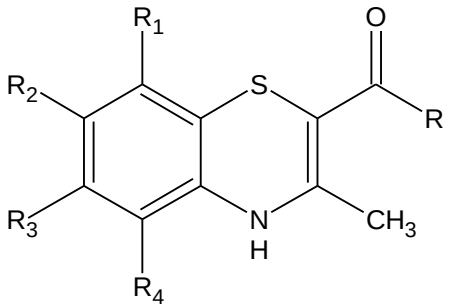
Thiazine systems are endowed with different pharmacological activity related to various receptors like GABA,, calmodulin , serotonin,tyrosine kinase and also as, dopamine receptor antagonist, α-adrenergic receptor blocker and histamine H_1, H_2 receptor antagonist, thyroid stimulating hormone receptor & N-methyl-D-asparate receptors & also voltage dependent potassium channel.

In the current work, various 2-aminobenzothiazoles were synthesized to obtain 2-amino benzene thiols & the later were subjected to condensation under optimized reaction conditions with different β-diketones & β-diketo esters to obtain substituted 1,4-benzothiazine derivatives.

All the compounds were well characterized by IR, NMR and Mass Spectra and screened for their preliminary biological activities.



P-139

Clean Synthesis of 2-Methyl Indole Using Various Condensing Agents

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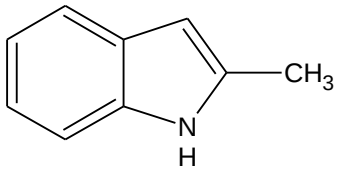
2-Methyl indole being an important starting material in many drug molecules and very few processes are known for its mass scale preparation, we initiated various approaches towards laboratory methods & synthesis of 2-methyl indole-3-carboxaldehyde.

In the current work, for the synthesis of 2-methyl indole, the starting materials like N-acetyl-o-toluidine, hydrazones of phenyl hydrazine were used and these substrates underwent cyclocondensation with different six condensing agent like 1) sodium ethoxide, 2) sodamide, 3) acetic acid, 4) zinc chloride, 5) polyphosphoric acid and 6) potassium bisulphate. Comparative yield optimization was afforded successfully.



P-140

Synthesis and Antiviral Study of Some Novel Substituted Phenyl-1*H*-[1,2,4]-Triazolo [3',4':3,4] [1,2,4] Triazino [5,6-b]-Indoles.

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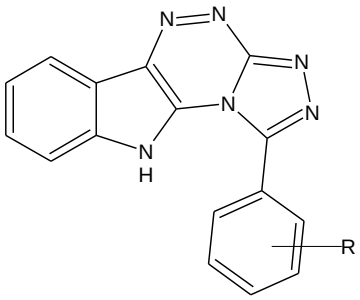
In recent years, several tetracyclic pharmacologically active compounds have been studied for their wide range of biological activities. The current work aims at four step preparation of angularly fused triazino indoles from penultimate 3-hydrazino-as-triazono [5,6-b]-indoles. Several cyclization approaches are in literature to afford either angularly or linearly fused triazino indole molecules depending upon versatility of cyclizing agents. The driving force of such molecules in the penultimate stage is electronically controlled cyclization to arrive at the final products leads to investing reaction mechanism.

All title compounds were investigated for their promising antiviral activity under standard protocols and some of these compounds have shown wonderful activity due to their "drug like" structures.



P-141

Novel Dihydropyrimidines (DHPM) with Carbamoyl Side Arm: An Unusual Planar Conformation

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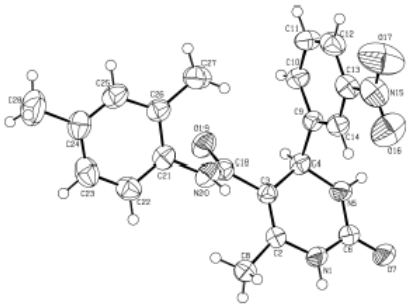
The aza analogs of dihydropyridines such as dihydropyrimidines belong to a class of biologically important molecules. DHPM's of the Biginelli type are inherently asymmetric molecules and influence of the absolute configuration at stereogenic center at C4 on biological activity is well documented. A novel DHPM derivative bearing a carbamoyl moiety was synthesized by an efficient three component Biginelli reaction & was characterized spectroscopically & confirmed by x-ray crystal structure. The unusual phenomena are revealed as the molecule is planar insted of boat like confirmation. The substituted phenyl ring is orthogonal to the 3,4-DHPM ring in the carbonyl group is in an anti-clinical confirmation.

These structural intrigues may lead to generate several new libraies of bioactive novel compounds.



ORTEP of the molecule with thermal ellipsoids drawn at 50% probability

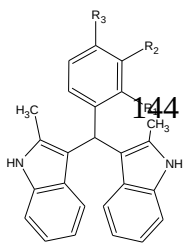
P-142

Synthesis, X-Ray Crystallography and Biological Activity of Bis Indole Dimers

Vijay Virsodia[1], Akshay Pansuriya[1], Dhaval Joshipura[1]Chirag Bhuva[1]& Naval Kapuria[2]
[1]*Department of Chemistry, Saurashtra University, Rajkot-360005,* [2]*Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan.*

A low toxicity and a marked activity in inhibiting both the tumor growth and the metathesis process are required. A very important pharmaceutical profile of bis-indoles has attracted researches to produce an efficient synthesis of these compounds. Literature, related to bis-indole reveals that they are active as antitumor, anti-inflammatory, and antifibromylgia agents, the compounds having core moiety-A-(linking the heterocycles) as a substituted phenyl scaffold is not much reported.

In current investigations, bis-indole (substituted) phenyl methane derivatives have been prepared by the electophilic substitution of indoles with iminium systems. Aldehyde condenses with 2-methyl indole, with elimination of water to a form a dimer. The analogues reaction of indole with other aromatic or aliphatic aldehyde and ketene produces azafulvenium salt, which undergoes the further addition with another indole molecule to afford bis -indole methane. The X-ray crystallographic data of the 3-[(4-chlorophenyl) (2-methyl-1*H*-indole-3-yl) methyl]-2-methyl-1*H*-indole supports the shifted patterns of protons. Efforts to study the symmetry aspect of these dimers and to select a more active catalytical system are in progress.



P-143

A Novel Series of 4-(2'-Hydroxy-3-Isopropylaminnopropoxy)-Substituted Benzopyran-2-Ones As Cardiovascular Agents

Y. T. Naliapara[1] and Dinesh Sureja[2]
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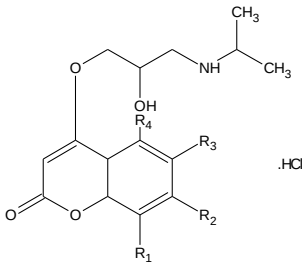
Many calcium channel antagonists are reported for the cardiovascular activity, especially propanolol, atenolol, mettoprolol, celiprolol, esmolol & many others. The only molecule which has seen day light from coumarins heterocyclic system is bucumolol, where the side chain is extended at the benzanoid part at the C_7-hydroxy group. In current work, several new derivatives of bucumolol are prepared by modifying non benzenoid part of coumarins nucleus at C4 position. By treating variously substituted 4-hydroxy coumarins with epichlorohydrin & subsequently with isoproplyamine & then converted to respective hydrochloride.

All compounds were well characterized by IR, NMR & mass spectral data. The preliminary calcium channel antagonist data are encouraging for this modified structural class.



P-144

Synthesis and Anti-microbial Activity of 4-(Substituted Phenyl)-Bis (4-Fluorophenyl)-2,6-Dimethyl-1,4 Dihydropyridine-3,5 Dicarboxamides

Jitender Bariwal[1], Jalpa Trivedi[1], Hrishikesh Acharya[2] and Anamik Shah[1]
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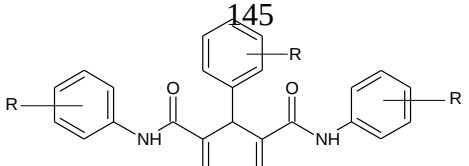
1,4 Dihydropyridine (DHP) are an important class of drugs able to block the Ca^+ current through voltage dependent L-type channels. In literature, large number of modifications have been reported particularly at 3,4 and 5 positions to enhance the potency.
Recently, we have reported the DHP as potent anti-tubercular agents. QSAR study of this series suggest that bulkier group at C_4 contribute positively, electronic influence of substitutions at carbonyl phenyl ring present at 3 and 5 position of DHP are important and electron withdrawing group on meta or pare position increases the activity as anti TB. On the basis of these findings, new series of DHP has been designed and evaluated for their anti-



tubercular activity. All compounds were characterized by MP., TLC, ^{1}H NMR, Mass Spectra and Elemental analysis.

P-145

Synthesis Of Some Novel Heterofused Pyrazolopyrimidines For Biological Activity

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Several pharmacological activities like mitotic, CNS stimulant, analgesic, antipyretic, anti-inflammatory, antiasthmatic and antibacterial activities have been attributed to condensed triazoles. Heterofused pyrazolopyrimidines possesses various biological activities such as CNS depressant, neuroleptic, tuberculostatic, antimicrobial, adenosine receptor antagonistic, antinociceptive, anti-inflammatory, non-narcotic analgesic, anticancer and leishmanicidal activity.
The above observations prompted us to synthesize some novel triazolopyrazolopyrimidines as possible antibacterial agents.
Herewith we are reporting the synthesis of some novel 1-phenyl-8-substituted-6-thiomethyl-1,2,4-triazolo[4,3-*c*]pyrazolo[4,3-*e*]pyrimidines as possible antibacterial agents both by conventional and microwave assisted route hitherto unreported in the literature**.** All the synthesized compounds were characterized by preliminary laboratory techniques like melting point, R_f value and further confirmed by UV, IR, NMR and Mass spectroscopy. The title compounds were screened for antibacterial activity by cup plate method using Streptomycin as the standard drug against *Klebsiella* (Gram –ve), *Escherichia coli* (Gram –ve), *Staphylococcus aureus* (Gram +ve) and *Bacillus subtillis* (Gram +ve). All the compounds showed weak to moderate activity against all four microorganisms.

P-146

Synthesis and Biological Evaluation of Isoxazoles Derivatives

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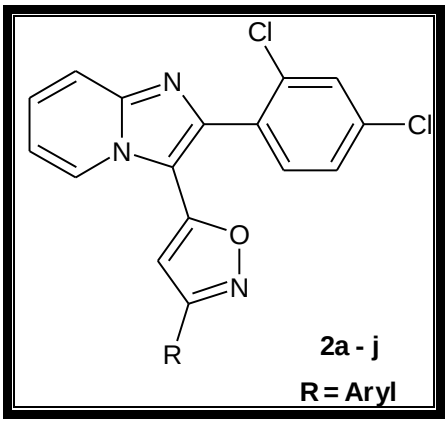
Large number of biologically active compounds possess imidazo[1,2-a] pyridine moiety. Isoxazoles are reported for many therapeutic applications which are anticonvulsant, anticancer, muscle relaxant, antibacterial and hypoglycemic etc. In the study of developing new targets, a skeleton structure based on isoxazole is determined.
The strategy employed for the synthesis involves the cyclocondensation of (2*E*)-3-[2-(2,4-dichlorophenyl)imidazo[1,2-*a*]pyridin-3-yl]-1-aryl-prop-2-en-1-one **(1a-j)** with hydroxylamine hydrochloride and sodium acetate in glacial acetic acid gives 2-(2,4-dichlorophenyl)-3-[3-aryl-isoxazol-5-yl]imidazo[1,2-*a*]pyridine **(2a-j)**.



All the synthesized compounds have been characterized by Elemental analyses, IR, ^{1}H-NMR and Mass spectral studies and purity of the compounds have been checked by thin layer chromatography. Screening of these new heterocycles for their various biological activities is in progress.

P-147

Synthesis, antimicrobial and antitubercular activity of some 1,3,4-thiadiazole derivatives.

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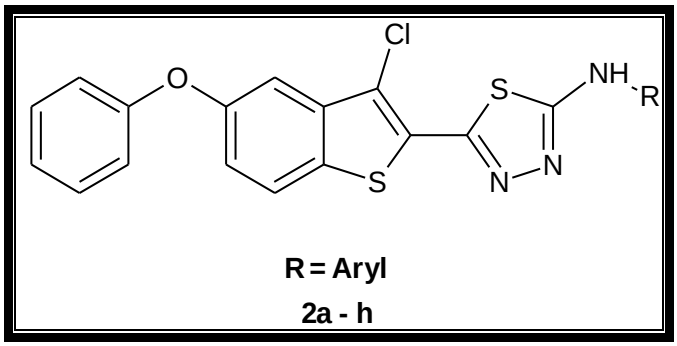
Interesting biological activities of a heterocycle like benzo(b)thiophene have stimulated considerable research work in recent years leading to the synthetic utility of derivatives of this ring system. Moreover, 1,3,4-thiadiazoles nucleus possess several biological activities like anticonvulsant[1], CNS depressant[2], antibacterial[3], antifungal[4], antiinflammatory[5] and antiviral[6]. These fact prompted us to investigate some 1,3,4-thiadiazole derivatives bearing benzo(b)thiophene nucleus.



The title compound (2a-h) have been synthesized by the cyclization of N^{1}-(3'-chloro-5'-phenoxy-benzothiophen-2'-yl)-N^{4}-aryl-thiosemicarbazide in Con. H_2SO_4.
The constitution of all the compounds have been characterized using Elemental analyses, IR, ^{1}H NMR and Mass spectral studies. Purity of all the compounds have been checked by thin layer chromatography. The products have been screened for their *in vitro* biological activity

like antitubercular and antibacterial activities towards Gram +*ve* and Gram –*ve* bacterial strains and antifungal activity towards Aspergillus niger at a concentration 40 μg/ml.

P-148

Piper Betle L.: The Female Plant Stimulates Immune Functions in Mice

***Meghna Singh** *Vishal Kumar Soni, *Rajnish Sahoo, *Anil Dangi, **Nikhil Kumar and *Shailja-Misra Bhattacharya
**Division of Parasitology, Central Drug Research Institute, M.G. Marg, Lucknow-226001, India; **Betel Vine Biotechnology Laboratory, National Botanical Research Institute, Rana Pratap Marg, Lucknow-226001, India.*
Email: meghna.biotech@gmail.com

Piper betle L. (betel vine, family Piperaceae) is a dioecious plant associated with tradition and culture of South East Asia including India. As per estimates nearly one billion people use it daily in one form or the other. Leaves of betel vine are widely used for chewing purposes and the attributed properties are digestive, carminative, stimulant, antiseptic and antifungal. In spite of its importance, the plant has largely remained unexplored. More than hundred landraces are known to be under cultivation in different parts of India. On the basis of chemical constituents of leaf essential oils, five prominent groups of betel vine landraces, namely, Bangla, Kapoori, Meetha, Sanchi and Desavari were recognized. Recent molecular characterization on the basis of RAPD (Verma *et al*. 2004) has shown two major groups based on gender namely Kapoori (male) and Bangla and rest others (Female). We have recently reported landrace/gender-based differences in the antiparasitic activity, which was evident only in the female plant of *P. betle* (Tripathi *et al.,* 2006). There is no report in the literature on its immunomodulatory activity.

In the present study, the crude extract from the leaves of female plant of *P. betle* and its various fractions viz. hexane, chloroform, n-butanol and aqueous, were evaluated for their immunomodulatory activity employing both humoral and cellular immune assays. The parameters used for assay included macrophage function assay, lymphoproliferation, haemagglutinin antibody titer, plaque forming cell enumeration and delayed type hypersensitivity reaction. The crude methanolic extract and its hexane fraction induced both cellular and humoral immune functions in mice as revealed by significant lymphocyte proliferation index with a marked increase in nitric oxide production by peritoneal macrophages. It also led to significant rise in antibody level and number of antibody forming cells. The crude extract in addition induced strong delayed hypersensitivity response in mice while hexane fraction was comparatively less effective. The chloroform fraction possessed low immunostimulatory efficacy when compared with the hexane fraction or the crude methanolic extract. The crude water decoction failed to demonstrate good immunostimulation at the doses tried.

Thus, present study for the first time demonstrates strong immunostimulation properties in the leaves of female plant of *Piper betle*, which was largely localized in the hexane fraction. The findings are significant in view of the widespread use of betel leaves in day-to-day life by both rural and urban Indian population.

References:

1. A. Verma, N. Kumar, and S. A. Ranade. J. Biosciences, **29**, 319-328 (2004).

2. S. Tripathi, N. Singh, S. Shakya, A. Dangi, S. Misra-Bhattacharya, A. Dube and N. Kumar. Current Science, **91** (6) 746-749 (2006).

P-149

Flavonoids And Phenol Glycosides From *Boerhavia diffusa*[+]

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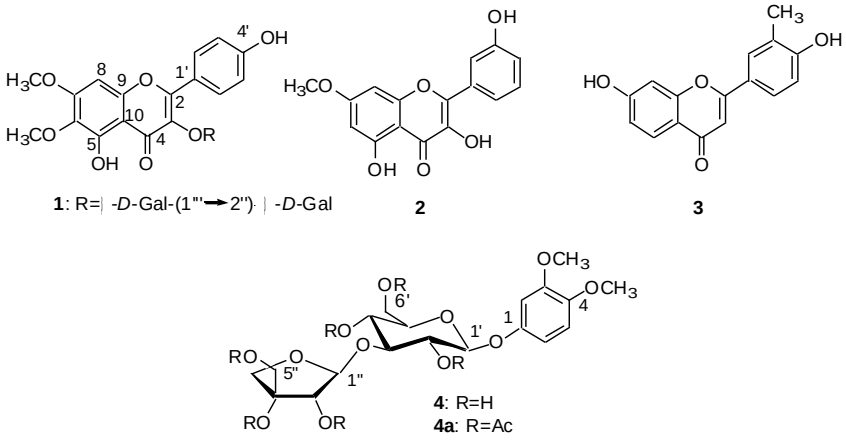
Boerhavia diffusa Linn. (Nyctaginaceae) popularly known as 'Punarnava' is an important rejuvenative drug of Ayurvedic system of medicine in India [1,2]. The plant has variety of biological properties including antiinflamatory, antiproliferative, antioxidant, antiviral and more importantly immunomodulatory properties [3,4]. The eirlier phytochemical studies on this plant reported to have variety of chemical constituents such as rotenoids, xanthone, phenolic glycoside, lignans and flavonoids. In the present study, we report the isolation and characterization of four new compounds namely eupalitin 3-*O*-β-*D*-galactopyranosyl-(1,2)-*O*-β-*D*-galactopyranoside (1), 3,3,5-trihydroxy-7-methoxyflavone (2), 4,7-dihydroxy-3□-methylflavone (3) and 3,4-dimethoxyphenyl-1- *O*-β-*D*-apiofuranosyl-(1,3)- *O*-β-*D*-glucopyranoside (4). The structures of new compounds were elucidated by detailed spectroscopic analysis.



References

[1] V.V. Sivarajan, I. Balachandran (1994). *Ayurvedic drugs and their plant sources*, Oxford and IBH Publishing Co. Pvt. Ltd: New Delhi, p 387.
[2] S.S. Handa, M. Deepak, A.K. Mangal (1998). Indian *Herbal Pharmacoepia* Volume I. IDMA and RRL: Mumbai, p 38.
[3] S. Mehrotra, K.P. Mishra, R. Maurya, R. C. Srimal, V.K. Singh (2001). *Int. Immunopharmacology*, **2**, 979-988.
[4] S. Mehrotra, V.K. Singh, S.S. Agarwal, R. Maurya, R. C. Srimal (2002). E*xp. Mol. Pathol*., **72**, 236-242.

P-150

Development of Process for Preparing Chiral Drug Intermediate:

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University Institute of Chemical Technology (UICT), Mumbai.: pcbb_83@yahoo.co.in

A more economical way of making compounds as single enantiomer is to manufacture them using an enantiomerically pure natural product as a starting material, rather than using one as a resolving agent. For the synthesis of chiral drugs, chiral drug intermediates play an important role. One such molecule is (S)-3-hydroxy-gamma-butyrolactone. (S)-3-hydroxy-gamma-butyrolactone was synthesized from an easily available carbohydrate source (Amaranth seeds) and the reaction condition was studied using enzymes. Starch was extracted from the Amaranth seeds and the pH, temperature, enzyme concentration and reaction time for the enzymes (α-Amylase and Pullulanase) were optimized. α- 1, 4-linked oligosaccharide was prepared from Amaranth starch using the enzymes. This oligosaccharide was then used to prepare (S)-3, 4-dihydroxy butyric acid. (S)-3, 4-dihydroxy butyric acid was separated from the reaction mixture. It was then lactonized to the final compound (S)-3-hydroxy-gamma-butyrolactone. This final compound was then separated using chromatography and characterized.

P-151

Synthesis of Paroxetine Analogs:

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University Institute of Chemical Technology (UICT), Mumbai.,: pcbb_83@yahoo.co.in

Paroxetine, a phenyl piperidine derivative is a potent and selective inhibitor of neuronal 5-HT reuptake. Its selectivity for 5-HT is more than that of other Selective 5-HT reuptake inhibitors like Fluoxetine, Sertraline and Fluvaxamine. We have synthesized Paroxetine analogs by condensation of 4-(4-fluorophenyl)-3-hydroxymethyl-piperidine with:

- xylose
- triazole moieties

4-(4-fluorophenyl)-3-hydroxymethyl-piperidine was synthesized from simple starting material Flurobenzene. The synthesized molecules were tested for antidepressant activity by despair swim test and 5-HT Head-Twist test. The synthesized molecules were also tested for antimicrobial activity by Cup-Plate method.

P-152

Investigation of Phytoconstituents Of *Solanum Xanthocarpum Schard And Wendl And Cassia Fistula Linn* For Anti-Inflammatory Activity

Milind bhitre* Miss Shraddha Anwikar and Harsha kadri
C.U.Shah College of pharmacy, SNDT University, Juhu, Mumbai.

The rheumatoid arthritis is not only the problem of elderly people but the younger generation may also show the first signs of the disease as aches and pains, strain type injuries, lower back, neck or joint pain. About 60% of the Indian Population of age between 40-60 shows problem of rheumatoid arthritis.

Arthritis literally means “Inflammation of joint”. Thus we tried to find plants which shows better anti-inflammatory activity than NSAID which has more side effects.
Fruits of *Solanum xanthocarpum schard and wendl(solanaceae) and cassia fistula linn(caseplinaceae)* was selected for the study. They were collected from local market and authenticated by Zandu pharmaceautical.Aqueous, methanol and chloroform extracts of the plants were carried out by soxhlet extraction. Phytoconstituents were confirmed by performing phytochemical tests.standardisation of extract was done by finding extractive values and also HPTLC fingerprinting was done.
Acute toxicity study of the extracts was done in rats as per OECD guidelines. Route of administration was oral. It was found out that extracts are safe up to 2gm/kg of body weight.Anti inflammatory activity of the extracts were tested in rats by Carageenan induced rat paw edema method by using Plethysmometer.Dose given was 150 and 300 mg/kg of body weight. Standard used was Aspirin 150mg/kg of body weight.
Results obtained were analysed by statistical analysis and it has been observed that extracts show better anti-inflammatory activity than standard aspirin. $p<0.05$Vs control (Normal saline).

P-153

L-Arginine Supplementation Does Not Increase Serum Cholesterol Level In Normal And Hyperglycemic Rats.

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1. Yash Institute of Pharmacy, Aurangabad., 2. Y.B.Chavan College of Pharmacy, Aurangabad. 3. University Department of Chemical Technology, Dr.B.A.Marathwada University, Aurangabad.

Objective: To study the effect of L-Arginine supplementation on serum Cholesterol level in normal and Hyperglycemic rats.

Materials and Methods: Diabetes was induced in albino rats by administration of a single dose of alloxan monohydrate (60mg/kg, through tail vein).Rats were divided into four groups two normal and two hyperglycemic. In each of the two groups one served as control (normal saline) and the other group was treated with L-arginine daily orally at the dose of 900mg/kg for a period of 24weeks. Blood sample was taken every 4weeks (upto24weeks) and the blood sugar level, serum cholesterol level was estimated using multichannel autoanalyser with standard kits. The protocol of the study was approved by the local Institutional Animal Ethics Committee.

Results: It was observed that administration of L-arginine for a period of 24 weeks continuously in normal rats did not significantly alter the cholesterol level. Alloxan induced hyperglycemic control has shown to increase the cholesterol level however, supplementation of l-arginine to hyperglycemic rats did not show an increase in the serum cholesterol level.

Conclusion: L-arginine supplementation does not increase serum cholesterol in normal and hyperglycemic rats as against the hyperglycemic control.

Key words: L-arginine, Cholesterol, Diabetes.

P-154

Convergent Synthesis of a Pentasaccharide Related to the Steroidal Saponin from *Calamus insignis*: Important for its Cell Cycle Inhibitory Activities

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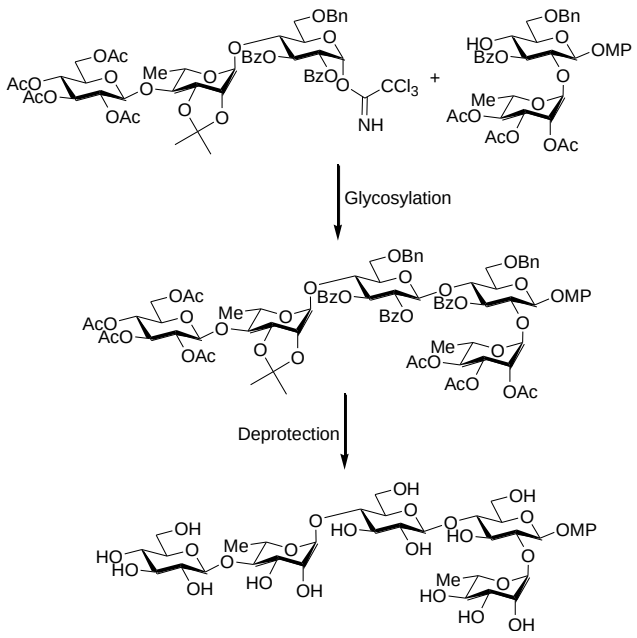
Steroidal saponins are attractive for their diverse bioactivity and often they promise potential drug candidates for specific actions. Unfortunately, isolation of these saponins is not easy and requires long time and labour. Therefore, chemical synthesis of certain saponin becomes inevitable when they found to be active. Recently Ishibashi and co-workers[1] have reported a spirostanol glycoside that showed cell growth inhibitory activity against HeLa cells at low concentration (IC_{50} value: <10 □ M). In the current poster describes the convergent chemical synthesis of the glycoside part of the saponin concerned. Synthesis of the pentasaccharide achieved commencing from commercially available D-glucose and L-rhamnose through rational protecting group manipulations.



Reference: [1]Ohtsuki, T.; Sato, M.; Koyano, T.; Kowithayakorn, T.; Kawahara, N.; Goda, Y.; Ishibashi, M. Bioorg. Med. Chem. 2005, 659-665.

P-155

In vitro antifungal activity of some Indian medicinal plants

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The ethanol extract of nine Indian medicinal plants belonging to different families were evaluated for *in vitro* antifungal activity against some yeasts viz. *Candida albicans (1)* ATCC2091, *Candida albicans (2)* ATCC18804, *Candida glabrata* NCIM3448, *Candida tropicalis* ATCC4563, *Cryptococcus luteotus* ATCC32044, *Cryptococcus neoformans* ATCC34664, *Trichosporon beigelli* NCIM3404, and some moulds viz. *Aspergillus candidus* NCIM883, *Aspergillus flavus* NCIM538, *Aspergillus niger* ATCC6275 and *Mucor heimalis* NCIM873. The *in vitro* antifungal activity was evaluated at three different concentrations by agar disc diffusion method. *Aspergillus flavus* was the most susceptible fungal strain while *Candida glabrata* was the most resistant one. The results were compared with the standard antifungals.

P-156

Antibacterial and anti-inflammatory activity of *Aristolochia indica* L. leaf

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Methanolic extract of *Aristolochia indica* L. was studied for antimicrobial and acute anti-inflammatory activity in carrageenan induced rat hind paw edema. Antimicrobial study was done against 15 different microbial strains by agar disc diffusion method at the concentration of 600µg/disc. The microbial strains were *Staphylococcus aureus* ATCC25923, *Staphylococcus epidermidis* ATCC12228, *Bacillus cereus* ATCC11778, *Bacillus subtilis* TCC6633, *Micrococcus flavus* ATCC10240, *Pseudomonas aeruginosa* ATCC27853, *E. coli* ATCC25922, *Klebsiella pneumoniae* NCIM2719, *Proteus mirabilis* NCIM2241, *Proteus vulgaris* NCTC8313, *Salmonella typhimurium* ATCC23564, *Citrobacter freundii* ATCC10787, *Candida albicans* ATCC2091, *Candida tropicalis* ATCC4563 and *Cryptococcus luteolus* ATCC32044. The results were compared with the standard antibiotics Piperacillin (100 µg /disc), Amikacin (30µg/disc), Flucanazole (10 µg/disc) and Amphotericin (100 units/disc). Anti-inflammatory activity was done in carrageenan induced rat hind paw edema at 400mg/kg concentration. The results were compared with standard drug Indomethacin 25 mg/kg. Gram positive bacteria were more susceptible than Gram negative bacteria. Methanolic extract of *Aristolochia indica* L. was given significant anti-inflammatory activity.

P-157

Effect of Different Dietary Essential Fatty Acids in a Low Fat Cereal-Legume Base Diet On Rats and Its Consequences

Bijoya Chatterjee
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There is a common notion that all fat is bad. In this context there have been many studies that have evaluated the role of different fatty acids in the body. Studies have evaluated that the levels of fatty acids in plasma are reflective of the fatty acids consumed in the diet. The fatty acid composition of plasma is closely related to fatty acid composition of platelet & erythrocyte function. The membrane fatty acid composition has a major to play in the pathogenesis of several diseases including cardiovascular disorders. Keeping this in mind the present study was designed to find out whether low levels of essential fatty acids influence erythrocyte & platelet count, plasma fatty acid composition & platelet function.

To carry out the study a low fat cereal legume base diet was given to rats along with 3% oil varying in Essential Fatty Acid compostion (EFAs): Sunflower (S), groundnut (G) & linseed (L) oil to three groups S, G & L respectively for six months. Each group was checked for erythrocyte & platelet count, plasma fatty acid composition & platelet function. From the result it was evident that the different oils influenced platelet count, plasma fatty acid composition & platelet function significantly.

So it can be said that it is the type & quantity of fat that influences various parameters in the body. Therefore there should be a balance in consumption of different EFAs as each of them are essential & have different roles in the body.

P-158

A Novel, Concise And Highly Diastereoselective Route Towards The Synthesis Of (-)Steganacin Aza-Analogues

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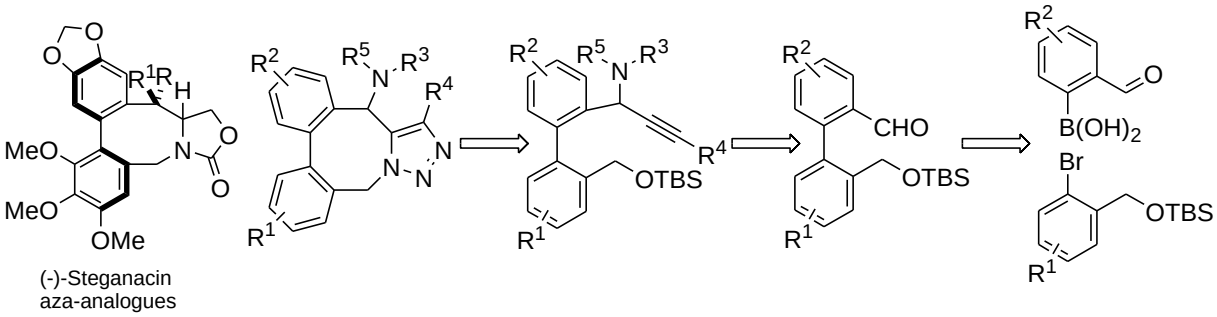
A novel, microwave-assisted, highly efficient protocol for the synthesis of *hitherto* unknown aza-analogues of (-)-Steganacin[1], a naturally occurring bisbenzo-cyclooctadiene lignan lactone with potent anti-leukemic and anti-tubulin polymerization activity, has been developed. Focused microwave irradiation is demonstrated to be highly beneficial in promoting the three crucial steps of the sequence; the Suzuki-Miyaura[2] cross-coupling reaction, the Cu (I)-mediated A_3-coupling as well as the intramolecular Huisgen 1,3-dipolar cycloaddition "Click Chemistry" to effect the final ring closure[3].



Retrosynthetic Analysis

References:

K. Koga et. al., *Tetrahedron Lett.* **1989**, *30* 2949-2952.
P. Appukkuttan, E. Van der Eycken, *Eur. J. Org. Chem.*, **2004**, *3277-3285*.
T. Beryozkina, P. Appukkuttan, E. Van der Eycken, *Org. Lett.* **2006**, *8* 487-490.

P-159

The effect of different diets on the Pharmacokinetics of Loracarbef in healthy human male volunteers.

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OBJECTIVE: To investigate the effects of different food on the pharmacokinetics of a single oral dose of Loracarbef 200mg. DESIGN: This was a randomized 3 treatment, 3 period open labeled crossover study in healthy human male volunteers. METHODS: loracarbef was administered to 24 subjects under 3 conditions: fasting, after a standardized high fat diet (diet A) and low fat diet (diet B) separated by a 1-week washout period. Concentrations of loracarbef in serum were determined by a validated high performance liquid chromatography procedure with fluorescence detection. OUTCOME MEASURE Parameters- Cmax, Tmax, AUC_{12h}, AUCinfinity, elimination half-life (t1/2) and elimination rate constant were estimated using noncompartmental methods. The natural log of AUC and Cmax were analyzed using ANOVA. Bioequivalence of the 3 treatments was determined at the 5% significance level with the two 1-sided tests procedure and limits of 80% and 125% for AUC and Cmax was applied.

RESULTS: The mean serum concentration versus time profiles were similar between the 2 diets but significantly different from the fasting state. The geometric mean Cmax values were significantly reduced by the diets 9.01 +/- 1.89 micrograms/ml versus 4.07 +/- 0.93 micrograms/ml and 3.73 +/- 0.75 micrograms/ml after fasting, diet A and diet B respectively. AUCinfinity values under fasted and fed conditions (diet A, diet B) were almost identical, 17.5 versus 16.5 and 16.7 mg/L x h, respectively [90% confidence interval (CI) of the ratio of fasted versus fed based on geometric least-square means was 2.34, 3.38 and 3.30]. The absorption of loracarbef was significantly delayed by the food; the median Tmax values were

0.85, 1.99 and 2.63 hours for fasted, diet A, diet B respectively. The mean half-lives of loracarbef was nearly identical for the diet A and the fasting state , suggesting that the elimination kinetics of this loracarbef remained unaltered when the drug was administered with a high fat food. However, it was slightly increased by the low fat diet. Thus as the rate of absorption of loracarbef was affected by the food intake but not the extent of its absorption, loracarbef can be administered with the food.

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Synthesis and Antimicrobial Studies Of Novel 5-N^2-[{6-Fluoro-7-(Substitutedanilino)Benzothiazolyl} Sulfonamido]- 2-Methoxy-N^3-[2-{(3, 4, 5- Tri Methoxy) Phenyl}-4-Oxo-Thiazolidino]Carboxamide

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5-N^2-[{6-fluoro-7-(substitutedanilino) benzothiazolyl} sulfonamido] 2-methoxy-N^3-[2-{(4-hydroxy) phenyl}-4-oxo-thiazolidino] carboxamide 4 $_{\mathbf{a\text{-}l}}$ have been synthesized by cyclization with thioglycolic acid of Schiff bases $\mathbf{3_{a\text{-}l}}$ from corresponding 5-N^2-[{6-fluoro-7-(substitutedanilino) benzothiazolyl}sulfonamido] 2-methoxy benzoyl hydrazine $\mathbf{2_{a\text{-}l}}$. Compounds $\mathbf{2_{a\text{-}l}}$ in turn is prepared by dehydroxyhalogenation followed by condensation with hydrazine hydrates of acids $\mathbf{1_{a\text{-}l}}$. Compounds $\mathbf{1_{a\text{-}l}}$ in turn is prepared by chlorosulfonation followed by condensation with 6-fluoro-7-(substitutedanilino)-2-amino benzothiazoles of acid (1). Final compounds have been characterized by their element analysis, IR, ^1H-NMR. All the synthesized compounds have been screened for their antimicrobial activity. Some of them show good activity.

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Effect of BacoMind™, an enriched phytochemical composition from *Bacopa monnieri*, on learning and memory in rats and mice

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Bacopa monnieri (*B. monnieri*) has been in use since time immemorial as nerve tonic for improvement of memory and concentration and to provide relief to patients with anxiety or epileptic disorders. An enriched phytochemical composition, BacoMind™, was developed from *B. monnieri* extract for use as a cognition enhancing agent and it differs from the previously reported standardized extracts, in that it has been standardized to specific bioactive constituents. Hence, the nootropic activity of BacoMind™ was evaluated in different learning and memory paradigms viz., elevated plus maze, passive shock avoidance test and object recognition test. BacoMind™ was administered for 7 days at the dose of 40, 60 and 80 mg/kg to albino Swiss mice in elevated plus maze and passive shock avoidance test and 27, 40 and 54 mg/kg to albino Wistar rats in object recognition test. Scopolamine (0.3 mg/kg) was used to induce amnesia and piracetam (100

mg/kg) served as reference standard. A significant ($p<0.01$) increase in inflexion ratio was observed with BacoMind™ administration in scopolamine treated mice using elevated plus maze. In passive shock avoidance test, BacoMind™ significantly ($p<0.001$) reduced the latency to reach the shock free zone and number of mistakes in 15 min in both normal as well as scopolamine treated mice. In object recognition test, BacoMind™ significantly ($p<0.001$) increased the discrimination index in both normal as well as scopolamine treated rats. Based on the findings of the present study, BacoMind™ revealed nootropic activity by enhancing acquisition and retention of memory and can be useful in enhancing memory in normal and cognition impaired subjects.

Keywords: *Bacopa monnieri*, BacoMind™, Nootropic activity, Elevated plus maze test, Passive shock avoidance test, Object recognition test.

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Evaluation of safety and tolerability of BacoMind in healthy volunteers

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Bacopa monnieri (*B. monnieri*), also referred to as *Bacopa monniera, Herpestis monniera,* water hyssop, Brahmi, has been used in the traditional system of medicine for centuries. In Ayurveda, it is used as a brain tonic to enhance learning and memory, to improve concentration; and also used in the management of anxiety and epileptic disorders. BacoMind™ is the standardized phytochemical composition of *B. monnieri* extract enriched with bioactive constituents developed as a cognitive enhancer. A phase I study was planned with an objective of evaluating the short term safety and tolerability of BacoMind™ in healthy adult volunteers. The design employed was randomized, open label, dose escalation study. A total of twenty three volunteers with mean age of 31.09 years, certified as healthy were recruited. The dosing schedule included administration of single capsule of BacoMind™ daily for 30 days i.e., 300 mg for first 15 days increased to 450 mg for next 15 days. The outcome was measured based on detailed examination of clinical, haematological, biochemical, and electrocardiographic parameters. The safety evaluation was done based on analyzing the pre and post treatment changes in clinical and laboratory parameters. BacoMind™ was tolerated well by the volunteers. No adverse events were reported other than mild gastrointestinal disturbances observed in three individuals, which subsided spontaneously without discontinuation of treatment. All volunteers exhibited good compliance till the completion of trial. The short term supplementation of BacoMind was found to be safe and tolerable at the doses administered for the given duration in healthy adult volunteers.

Keywords: *Bacopa monnieri,* BacoMind™, Safety, Tolerability, Healthy volunteers.

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Design and Synthesis Of Chromones And Evaluation Of Their Anti-Inflammatory Activity

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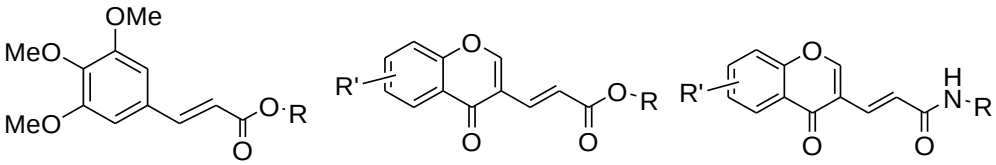
As a part of our on-going research program to design and synthesize novel heterocyclic compounds and evaluating their biological activity, we have synthesized a series of novel chromones. Chromone derivatives are the subject of considerable pharmaceutical interest, they are known to posses various biological activities.

It has been reported that substitution at C-3 position of chromone plays significant role in various type of activities, e.g. antigene and antibody reaction,[1] vaso relaxant,[2] anti allergic activity,[3] etc. and the cinnamic acid esters have also shown anti inflammatory activity[4]. On the basis of above we have designed and synthesized various novel 3-(4-oxo-4*H*-1-benzopyran-3)-acrylic acid esters and 3-(4-oxo-4*H*-1-benzopyran-3)-acrylic acid amides in which C-3 position of basic chromone moiety bears various acryl acid ester and amide moieties.



These compounds were screened for their inhibitory activities on TNF-α induced expression of ICAM-1 on HUVECs, some of these compounds have shown very interesting results. Such studies are important for understanding the mechanisms underlying the anti-inflammatory activities of these compounds of this class and for establishing structure-activity relationship. The preliminary interesting results will be discussed during the poster presentation.

REFRENCES

1. A. Nohara, T. Umetani and Y. Sanno *Tetrahedron* **30**, *1974*, 3553.
2. Z. Chen, Y. Hu, H. Wu and H. Jiang *Bioorg. Med. Chem. Lett.* **14**, *2004*, 3949.
3. A. Nohara, H. Kuriki, T. Saijo, H. Sugihara, M. Kanno and Y.Sanno *J. Med. Chem.* **20**, *1977*, 141.
4. S. Kumar, P. Arya, C. Mukherjee, B. K. Singh**,** N. Singh, V. S. Parmar, A. K. Prasad and B. Ghosh *Biochemistry* **44**, *2005*, 15944.

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Synthesis And Antimicrobial Studies Of Some Novel Quinoline Derivatives

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Quinolines and its derivatives have a wide range of biological activites such as antimicrobial, hypnotic, antiasthama, antimalarial, antiseptic, sedative and CNS activities. It is also a synthetic precursor for many naturally occurring quinolines.

Quinoline derivative have been repoted to display pronounced biological activities. In particular quinoline and structurally similar 4-amino quinolines have successfully been employed in treatment of prophylaxis of malaria.The high interest in new synthetic methodologies towards quinoline stems to some extent from an increasing demand for new highly efficient antimalarial drug. The synthesis of quinoline derivatives then continues to be an active area of heterocyclic chemistry.

Based on above obsersative we tempted to synthesized novel 2-methyl-4-[{2-(anilino)-2-oxyethyl} oxy]quinoline. The compounds have been tested for their antibacterial activity against different microorganism. The purity of product was checked by thin layer chromatography using different eluent. The structure of novel synthesized compound has been established on the basic of elemental analysis, ^{1}H NMR & IR spectral data.