Enterohepatic re-circulation of Bioactive Ginger Phytochemicals is Associated with Enhanced Tumor Growth Inhibitory Activity of Ginger Extract

Pooja yadav[1], Vibha Tandon[1,2], Sushma Gundala[3] and Dr. Ritu Aneja[3]

[1]*Department of Chemistry, University of Delhi*
[2] *Special Centre for Molecular Medicine, JawaharLal Nehru University*
[3]*. Georgia State University*

Ginger has a long history of medicinal use dating back 2500 years. Ginger has been traditionally used from time immemorial for varied human ailments in different parts of the globe, to aid digestion and treat stomach upset, diarrhoea, and nausea. Some pungent constituents present in ginger and other zingiberaceous plants have potent antioxidant and anti-inflammatory activities. The anticancer properties of ginger are attributed to the presence of certain pungent vallinoids, viz. [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols, zingerone etc. In our study we have purified the constituents of ginger by silica gel column chromatography using hexane and ethyl acetate as mobile phase and demonstrated in vitro effect among the most-abundant bioactive constituents of ginger extract (GE), viz., 6-gingerol (6G), 8-gingerol (8G), 10-gingerol (10G) and 6-shogaol (6S). We also comparatively evaluated in vivo efficacy of GE with an artificial mix formed by combining four active ginger constituents at concentrations equivalent to those present in whole extract. Orally-fed GE showed 2.4-fold higher tumor growth-inhibitory efficiency than Mix in human prostate tumor xenografts. Plasma concentration vs time revealed multiple peaking phenomenon for ginger constituents when they were fed as GE as opposed to Mix, indicating enterohepatic recirculation (EHR). Bioavailability of 6G, 8G, 10G and 6S was 1.6, 1.1, 2.5 and 3.4 fold higher, respectively, when dosed with GE compared to Mix. These data ascribe the superior in vivo efficacy of GE to higher AUCs, greater residence time, and enhanced bioavailability, of ginger phytochemicals, when fed as a natural extract compared to artificial Mix, emphasizing the usefulness of consuming whole foods over single agents.

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POSTER

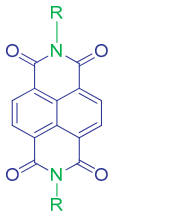
A Study of Novel Di-Substituted Naphthalene Diimides Stabilizing Inter and Intra-strand G Quadruplexes

Souvik Sur[1], Gopinatha Suresh Kumar[2] and VibhaTandon[3*]

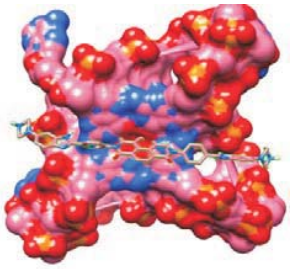
[1]*Chemical Biology Laboratory, Department of Chemistry, University of Delhi, Delhi-110007, India*
[2]*Biophysical Laboratory, Indian Institute of Chemical Biology, Kolkata-700032, India1,*
[1,3]*Special Centre For Molecular Medicine, Jawaharlal Nehru University, New Delhi-110067, India*

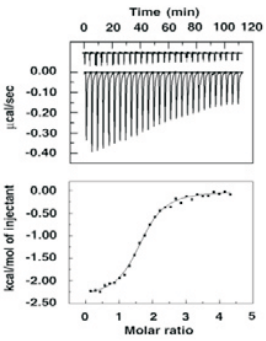
Email: vtandon@acbr.du.ac.in / vibhadelhi@hotmail.com

Human telomeres play a key role in protecting chromosomal ends; they are composed of *d*(TTAGGG) repeats. They form G-quadruplex DNA structures, stabilized by G-quartets in the presence of cations, and are involved in several biological processes. A series of novel disubstituted naphthalene diimides containing *N*-methylpiperazine end groups has been designed, effectively docked in both inter and intra strand G-quadruplex DNAs, synthesized and evaluated as G-quadruplex stabilizing ligands. Benzimidazole as side chain in ligands increases the stability of G-quadruplex DNAs over reported tetra- substituted NDI-ligand containing aliphatic side chains. Theirs theoretical recognition against G-quadruplex over dsDNA has been compared through thermal melting, Differential Scanning Calorimetry, Fluorescence and Isothermal Titration Calorimetric experiments. ITC and Docking data both suggest that an extra ~2 fold more stability of novel ligand **2** over reported analogues with G-quadruplex DNA and ~10 fold more specific binding over duplex DNA. A computational protocol was followed in order to investigate the conformational properties of a set of known G-quadruplex ligands and their molecular recognition against three different experimental models **1**, **2** and **3** of the human telomeric sequence. The average AutoDock correlation between theoretical and experimental data yielded an r^2 value ~0.9 among all the studied models.



R=aliphatic chain / aromatic chain / aliphatic-aromatic





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POSTER

Multistep Convenient Route for the Synthesis of New *N*-phenyl-3- (2'phenyl-4'-methylthiazole-5'-yl) -4-Tetrazolylpyrazoles as Anti-Inflammatory Agents

Lalit D. Khillare[a], Mahendra B. Bhalerao[a], Rahul A. Waghmare[b] and Ramrao A. Mane[*a]

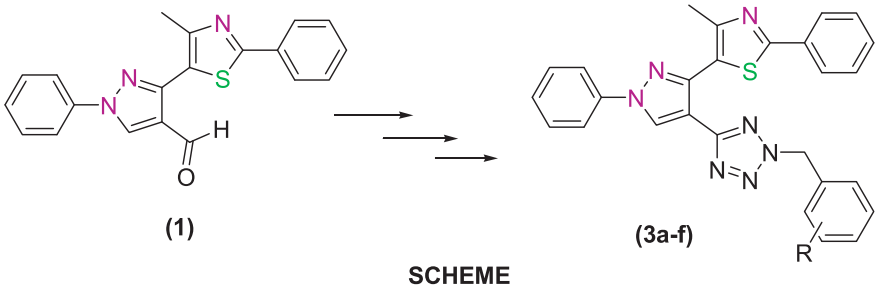
[a]*Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University,*
[b] *Milind College Of Science, Aurangabad, Maharashtra*
Aurangabad-431 004, Maharashtra, India

Email: manera2011@gmail.com

Non-steroidal anti-inflammatory drugs (NSAIDs) are amongst the most widely used therapeutic agents for the treatment of pain and inflammation. Most of the effective painkillers, including opioids and non-steroidal anti-inflammatory drugs, are generally not selective, only partially effective and prolonged exposure can cause side effects. Therefore continuous efforts are found to be directed towards search of novel therapeutics for pain control with alternative mechanism of action and to elicit side effects. The development of newer drugs with better safety profiles will always remain urgent need to relive saver inflammatory conditions.

Pyrazole derivatives are known to possess a wide spectrum of biological activities including anti-inflammatory. Celecoxib is well-known as NSAID which contain pyrazole nucleus and has less side effects. Thiazole and tetrazole heterocyclic nuclei are emerging as a potential anti-inflammatory agents.

Literature survey reveals that there is scanty information on the molecules having pyrazoles, thiazoles and tetrazoles in same molecular frame. Considering the pharmacological importance of the above biodynamic agent and also the side effects associated with the existing drugs here a series of new *N*-phenyl-3-(2'phenyl-4'-methylthiazole-5'-yl)-4-tetrazolylpyrazoles (**3a-f**) has been synthesized starting from 3-(4-methyl-2-substitutedthiazol-5-yl)-1-phenyl-1H-pyrazole-4-carbaldehydes **(1)**. The details of the multistep synthetic route, developed for the entitled products will be presented.



SCHEME

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POSTER

To Evaluate the *In Vitro* Anti-Neoplastic Potential of Chitosan Nanoparticles and Release Kinetics of Biopolymeric Nanoparticles against Cervical Cancer

Shweta Agarwal[1], Sadaf Fatima[2] and Anita K. Verma[1*]

[1] Nano-Biotech Lab, Kirori Mal College, University of Delhi, Delhi-110007*
[2] Department of Biotechnology, Jamia Millia Islamia, New Delhi-110025

Natural polymers like chitosan, gelatin, pectin and their conjugates have an established role as biomedical materials. We report preparation of positively charged chitosan nanoparticles (CHNP) by ionic gelation method using sodium tri polyphosphate (sTPP) as cross-linker. The terminal phosphate group of TPP binds with amine (NH_2) group of chitosan resulting in the the formation of nanoparticles. The mean diameter of the nanoparticles was ~115.4 nm with a PDI of 0.365, with a high surface charge of +19 mV stabilized them against aggregation and were stable over a wide range of temperature and pH. The characteristic peak of C-N (1250-1375 cm^{-1}) is present in FTIR of chitosan polymer along with other peaks. But in chitosan nanoparticles the peak was shifted to 1564.03cm^{-1} due to the wagging of NH_2 bond. The ionic interaction with the phosphate group of TPP indicated the conversion of chitosan polymer in the nano form, that forms a cross link with TPP. The strong and sharp peak of phosphate at 1092cm^{-1} in chitosan nanoparticles confirmed the involvement of TPP while making the nanoparticles. The observed encapsulation efficiency (E.E) was ~48% for doxorubicin (DOX). Release pattern of the drug was biphasic, releasing ~76% of the drug in pH 5.8 as against 80% in pH 7.4 within 24 h. *In vitro* cytotoxicity of void CHNP, DOX *per se*, and doxorubicin loaded chitosan nanoparticles (DLCHNP) after 24h, 48h and 72h was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay on SiHa (cervical cancer) cell line. Dose and time dependent evaluation of cytotoxicity was done on both HEK and SiHa cell lines. DLCHNP showed an increased inhibition of growth in SiHa cells as compared to DOX *per se* in 72h but in HEK and SiHa cell lines.

Keywords: Antineoplastic, Chitosan nanoparticles, Doxorubicin, Release kinetics, Biopolymers, Cervical cancer.

POSTER

Double Hetero-stranded Dinuclear Re(I)-based Helicates and Mesocates for Biological Applications

B. Shankar and M. Sathiyendiran*

Department of Chemistry, University of Delhi, Delhi 110007

Email: mvdiran@yahoo.com, msathi@chemistry.du.ac.in

The triple-stranded helical shaped, luminescent iron and ruthenium(II) supramolecular metal complexes have been demonstrated as a stable DNA binding and anti-cancer agents.[1] These are one of the few supramolecular systems applied for DNA recognition. The *fac*-$Re(CO)_3$ based metal complexes are under investigation for their rich photophysical properties. Herein, we represent phosphorescent helicate and mesocate shaped dinuclear Re(I)-based metallocycles that show dual luminescence both in solution and solid state. We envisage that helical shaped photo-active Re(I)-based metal complexes could be suitable as photo-toxic DNA binding agents due to their favourable photophysical properties and due to the fact that their helical conformation could facilitate DNA binding and intercalation.

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POSTER

Multicomponent One-Pot Synthesis of Novel Pyrazole Based Asymmetric 1,4-Dihydropyridine Derivatives for Evaluation of their Antihypertensive Activity

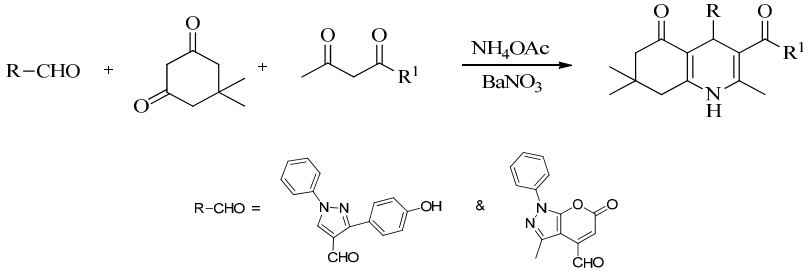
Rakesh Kumar[a,*], Neha Yadav[a], Jyoti Arora[a], R. P. Singh[c] and Ashok K Prasad[b]

[a]*Department of Chemistry, Bio-organic Laboratory, Kirori Mal College, University of Delhi, Delhi-110 007, India*
[b]*Department of Chemistry, Bio-organic Laboratory, University of Delhi, Delhi-110 007, India*
[c] *CFEES, Defence Research & Development Organisation, Delhi*

Email - rakeshkp@email.com

The 1,4-dihydropyridine (DHP) scaffold is very useful reducing agent and synthetic intermediates as well as an important pharmacophore found in a large number of biologically active and potential therapeutic compounds.[1] Their pharmacological activities include calcium channel blockers,[2] multidrug-resistance (MDR) reversing agents[3], HIV protease inhibition[4]. Hantzsch DHPs synthesis is one of the most broadly used methods for the preparation of DHPs. The 1,4-dihydropyridines are the most effective of the calcium antagonists or calcium channel blockers. There are even instances in which this reversal of activity is found between enantiomers.[5] Similarly, pyrazoles also act as N-type calcium channel blockers.[6] Also, one-pot multi-component reactions are of increasing academic and ecological interest due to the possibility of achieving high synthetic efficiency and reaction design.

Appreciation for the designing of new bioactive candidature by the hybridization of two active pharmacophore unit *i.e*. 1,4-dihydropyridine derivatives linked with pyrazole and their broad antihypertensive properties prompted us to synthesize new class of its derivatives and evaluate their potency against hypertension.



Scheme 1

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POSTER

Chemo-enzymatic Synthesis and Transport Potential Evaluation of Azido-glycerol Based Amphiphilic Polymeric Materials

Meena Kumari[a], Shiv Kumar[a], Abhishek Kumar Singh[a], Shilpi Gupta[a,b], Katharina Achazi[b], Christoph Böttcher[c], Paul Servin[d], Rainer Haag[b] and Sunil K. Sharma[a,*]

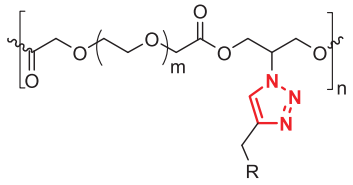
[a]*Department of Chemistry, University of Delhi, Delhi-110007*
[b]*Institute of Chemistry and Biochemistry, Freie Universität Berlin, Takustr. 3, 14195 Berlin, Germany*
[c]*Forschungszentrum für Elektronenmikroskopie, Institut für Chemie und Biochemie, Freie Universität Berlin Fabeckstraße 36a, 14195 Berlin, Germany*
[d]*Nanopartica GmbH, Takustr. 3, 14195 Berlin, Germany*

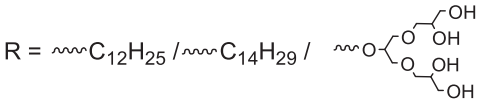
*Email:sk.sharma90@gmail.com

Polymeric micelles, which are supramolecular assemblies of block copolymers, with a characteristic core-shell structure, are useful nanocarriers for systemic delivery of drugs and genes.

As a part of ongoing research program, our focus has been to develop improved carrier systems.[1] We have adopted a cleaner and greener biocatalytic method to synthesize dendronized multiamphiphilic polymers by using biocompatible materials, e.g., poly(ethylene glycol), glycerol, polyglycerol (PG) dendrons, etc. Herein, we report on the synthesis of PEG-1000-diethyl ester and 2-azido-propane-1,3-diol based copolymers utilizing Novozym 435 (*Candida antarctica* lipase) using a bio-catalytic method. The linear base co-polymer was then functionalized with polyglycerol based regular [G1.0] and [G2.0] dendrons and C_{12}/C_{14} hydrophobic alkyl chains via an efficient 'Click approach'. The resulting amphiphilic dendronized polymers form well-defined micelles in aqueous solutions. The transport behavior of these polymers was studied by using Nile red as a fluorescent model dye. The cytotoxicity profiles of a few representative polymers were evaluated and the effect of hydrophobic alkyl chain length as well as hydrophilic polyglycerol dendron's generation on the biocompatibility of polymeric systems studied.

The synthetic methodology, characterization and transport study results will be discussed during poster presentation.





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POSTER

Synthesis of Two-Photon Active Cinnamoylcoumarins for High-Contrast Imaging of Cancer Cells

Preeti Yadav and Sunil K. Sharma*

Department of Chemistry, University of Delhi, Delhi 110007, India

Email: sk.sharma90@gmail.com

Among all the fluorescence microscopy techniques developed and optimized during last few decades[1], the two-photon-fluorescence (TPF) microscopy is of specific interest because of its potential applications in clinical imaging[2], immunology[3] and bio-engineering[4].The widespread applications of the TPF microscopy has led to several design strategies and synthesis of organic molecules with large TPA cross-sections (δ)[5]. However, most of the organic molecules reported in literatures have relatively small δ value to find a practical application.We have explored the possibility of using novel coumarin derivatives as molecular probes for confocal microscopy based bioimaging. A series of two-photon (TP) active 4-dimethylaminocinnamoyl coumarins were synthesized which exhibit red shift in absorption and large Stokes shift in emission in comparison to the parent coumarin.The TPF images confirmed the rapid uptake of the coumarins by the murine immature B lymphoma cell line WEHI 231. TP confocal microscopy revealed that these coumarin derivatives can be internalized by cancer cells rendering them a potential candidate as a bio-marker in TP confocal imaging. The recent research update in this area will be discussed during poster presentation.

Acknowledgement: We gratefully acknowledge University of Delhi for financial support. A part of the work was carried in the laboratories of our collaborators Professor Jayant Kumar at Center for Advanced Materials, University of Massachusetts Lowell, Lowell, Massachusetts 01854, USA and Dr. Akanksha Chaturvedi at LIG, NIAID/NIH, 12441 Parkway Drive, Twinbrook II, Rockville, Maryland 20852, USA.

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POSTER

Antigiardial Activity of the Ethanolic Extract and Fractions of Phlebophyllum *Kunthianum*

D. N. Singh* and Nisha Verma

K. S. Saket PG College, Dr. Ram Manohar Lohia Avadh University, Faizabad-224001, India.

Email: dnsinghsaket@ yahoo.com

Obtaining drugs from plants has been a traditional way in the Indian system of medicine and it is rightly said that ancient wisdom has been and will remain the basis of modern medicine, furthermore, synthetic drugs are limited in their spectrum pharmacological activity and efficacy and use may result in strain resistance. Hence, recognizing the need to revalidate the traditional system of medicine is urgently needed. Previously, we have reported the antifungal activity in the ethanolic extract of the aerial parts of S*aprosma fragrans* and leading to the isolation of the active constituents [1] followed by optimization of the activity of the isolated lead molecule [2]. In the continuation of our effort to search and identify the active constituent(s) of the traditional medicinal plants plants [3], recently, we have observed the antigiardial activity from the ethanolic extract of the phlebophyllum kunthianum [4]. On bioassay guided fractionation activity is concentrated in n-butanol fraction [4]. Here, we wish to present the detailed bioassay guided fractionation technique and antigiardial potency of the most active fraction of this plants. Isolation and identification of the active constituent(s) are under the process.

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POSTER

Synthesis and Characterisations of Some Novel Thiazolopyrimidines for Their Biological Potency

N. Verma, D. N. Singh* and L. P. Pathak

Department of Chemistry, K. S. Saket PG College, Dr. Ram Manohar Lohia Avadh University, Faizabad-224001, India

Email: dnsinghsaket@yahoo.com

The biological properties of heterocycles in general make them one of the prime interest of the area of drug discovery research and pharmaceutical industries. Due to development of drug resistant strain in parasitic area existing drug have limited in their pharmaceutical efficacy. Keeping in view importance of nitrogen heterocycles in the antiparasitic area [1-3], we envisioned our approach toward the synthesis of hybrid derivatives having fused 2, 3-dihydrothiazole and pyrimidine moieties for their biological activity. In the present work, we have synthesized some novel substituted thiazolopyrimidines by a series of chemical reaction. In this presentation, the detailed synthetic procedure, mechanisms of the reactions and characterizations of the synthesized compounds by their spectral data (^{1}H NMR, ^{13}C NMR, EIMS and IR) analysis will be discussed.

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POSTER

O_2-Dependent Efficacy of Novel Piperidine/Piperazine-Based Chalcones against the Human Parasite *Giardia Intestinalis*

Vijay Bahadur[a], Amit Kumar Singh, Daniela Mastronicola[b], Hemandra Kumar Tiwari[a], Yogesh Kumar[a], Alessandro Giuffrè[b] and Brajendra Kumar Singh[a,#]

[a] *Bio-Organic Laboratory, Department of Chemistry, Delhi University, Delhi 110007, India*
[b] *CNR Institute of Molecular Biology and Pathology, Rome, Italy*

Email: singhbk@chemistry.du.ac.in

Giardia intestinalis is the most frequent protozoan agent of intestinal diseases worldwide.[1] Though commonly regarded as an 'anaerobic pathogen', it preferentially colonizes the fairly oxygen-rich mucosa of the proximal small intestine.[2] Therefore, when testing new potential antigiardial drugs, O_2 should be taken into account, since it also reduces the efficacy of metronidazole, the gold standard drug against giardiasis.[3] In this study, forty-six novel chalcones were synthesized by microwave-assisted Claisen-Schmidt condensation[4], purified, characterized by high resolution mass spectrometry, ^1H and ^{13}C nuclear magnetic resonance and infrared spectroscopy, and tested for their toxicity against *G.intestinalis* in standard anaerobic conditions. As a novel approach, compounds showing antigiardial activity under anaerobiosis were also assayed under microaerobic conditions, and their selectivity against parasitic cells was assessed in a counterscreen on human epithelial colorectal adenocarcinoma cells. Among the tested compounds, three were more effective in the presence of O_2 than under anaerobic conditions, and killed the parasite 2-4 times more efficiently than metronidazole under anaerobiosis.

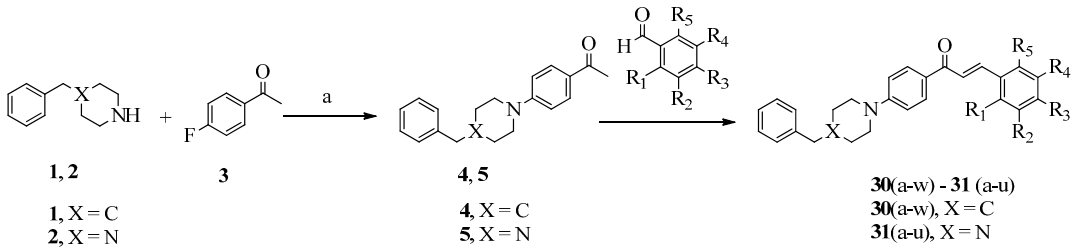

Figure 1: Synthetic route to compounds **30** (a-w) - **31** (a-u), **32** and **33**.
(a) K_2CO_3, DMSO 18h, 100°C. (b) NaOH, MeOH, Microwave (MW), 100W, 60°C, 15-30min

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POSTER

Folding and Unfolding property in Propylene linked Pyrazole Dimers

Sunil Kumar Rai and Ashish Kumar Tewari*

Department of Chemistry (center of advanced study), Faculty of science
Banaras Hindu University, Varanasi-221005

The non-covalent interactions in chemistry, biology, nanotechnology and crystal engineering play a subtle role in molecular recognition and molecular architecture.[1] Weak attractive intramolecular interactions between aromatic rings can play a significant role in determining the preferred conformation of flexible organic molecules.[2] Among various non-covalent interactions, C-H···O, C-H···N, C-H···π and π···π have been commonly observed in DNA, RNA and proteins which control the specific shape and geometry of such large molecules.[3] To illustrate the π···π interaction between purine and pyrimidine bases in DNA, Brown *et al.* (1968) used "propylene linker" for the promotion of intramolecular aromatic π···π interaction which was further studied by N. J. Leonard, L. F. Newcomb and S. H. Gellman.[4] The present study is based on the pyrazole system. Pyrazolone dimer **1** adopts open conformation while **2** adopted unusual folded conformation (Figure 1). The striking feature of compound **2** is its ability to display U-turn conformations stabilized by intramolecular non-covalent interactions.

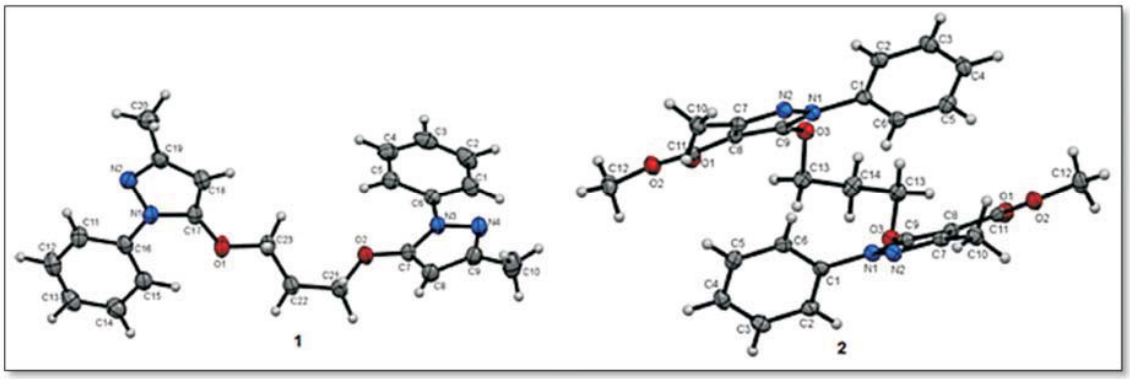

Figure 1. ORTEP diagram of compound 1 and 2, thermal ellipsoids are drawn at 30 % and 50 % probability level respectively.

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POSTER

DMA; A potent Radioprotector Mitigates DNA Damage in Radiotherapy by coactivation of Akt/ NFκB pathway

Vinod Tiwari[1] and Vibha Tandon[1,2]

[1]Department of Chemistry, University of Delhi, Delhi -110 007, India, [2]Special Centre for Molecular Medicine, JNU, New Delhi – 110 067.

Email:vtandon@acbr.du.ac.in

Ionizing radiation causes radiolysis of cellular water, generating reactive oxygen species (ROS), causing DNA damage. Cells exposed to ionizing radiation die via different mechanisms, including apoptosis and mitotic catastrophe. Radioprotectors protect the normal cells from the unwanted radiation damage. Since the beginning of the nuclear era, despite extensive research on the development of radioprotectors from natural and synthetic compounds, success has been limited. The only clinically acceptable radioprotector, amifostine, has inherent dose-limiting toxicities and has therefore stimulated extensive search for nontoxic, effective, and alternative radioprotectors. Akt (protein kinase B, PKB) is associated with cellular protection against ionizing radiation-induced apoptosis. DMA,(5- {4-methylpiperazin-1-yl}-2-[2'-(3, 4-dimethoxyphenyl)-5'-benzimidazolyl], a high therapeutic index molecule,with dual mode of action as free radical quencher and DNA binder, showed activation of NIK/IKKα/IKKβ mediated prosurvival NFκB pathway. DMA promoted activation and phosphorylation of GSK3β and DNA-PKcs through the activation of Akt. There was no significant radiation protection in DMA treated Akt siRNA transfected cells in comparison to only Akt siRNA transfected cells with increasing dose of radiation. Akt activation was found in a dose-dependent manner by DMA through Luciferase reporter assay. We found that in DMA (50 μM) treated HEK cells transfected with control siRNA , resulted less early apoptotic cells within 24h, but radiation (5 Gy) treated cells showed 20 % early apoptotic cells within 3h which were reduced to 12% at 3 h, 9% at 6h and 8% at 24h in DMA + radiation treated cells determined by Annexin V binding assay.Cell cycle experiments showed an accumulation of cells in G2-M phase in irradiated cells whereas DMA + radiation treated cells showed a significant G2-M arrest than the only irradiated cells at both 18and 24h.We observed reduced radioprotection in HEK 293 cells treated with LY294002(Akt inhibitor) alone and almost no radioprotection in presence of PS1145(NFκB inhibitor). These findings reinforce that DMA modulated the effects of radiation in the cells through activation of the Akt/ NFκB signaling pathway. On the basis of our studies we conclude that Akt is one of the signaling molecules affected by DMA.

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POSTER

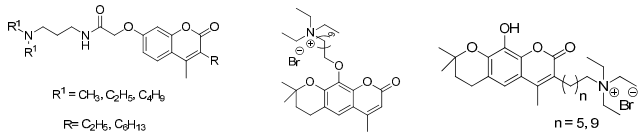
Synthesis of Quaternary Ammonium and Amido Derivatives of Pyranocoumarins and Coumarins and Evaluation of Their Antimicrobial Activity

Suchita Prasad,[1] Abhishek Kumar Singh,[1] Shiv Kumar,[1] Bipul Kumar,[2]
Hemant K. Gautam[2] and Sunil K. Sharma[1,*]

[1]*Department of Chemistry, University of Delhi, Delhi 110007, India*
[2]*CSIR-Institute of Genomics and Integrative Biology, South Campus, Delhi 110020, India*

Email: sk.sharma90@gmail.com

The search for compounds with antimicrobial activity has gained tremendous importancerecently, due to the alarming increase in the number of infections caused by antibiotic-resistant microorganisms. Coumarins and pyranocoumarins, a widely distributed class of compounds across the plant kingdom have been known to display diverse and interesting biological and pharmacological activities such as antimicrobial, anti-HIV, anti-inflammatory and anticancer.[1] Our research group has been involved in the synthesis of various analogues of coumarins and pyranocoumarins to study their pharmacological effects.[2] Further, ammonium compounds are known for their antibacterial activity against both Gram-positive and Gram-negative bacteria, as well as against some pathogenic species of fungi and protozoa.[3,4,5] The encouraging biological activity results of the two classes of compounds and based on the literature data on ammonium compounds and amides, we envisioned that coumarin and pyranocoumarin based amides & ammonium compounds may possibly act as potent antimicrobial agents. In lieu of this, the present work was undertaken here; we synthesized a series of long chain ammonium derivatives of pyranocoumarin & coumarin based amides and screened them for antibacterial activity against both Gram-positive and Gram-negative bacteria. The synthetic strategy and preliminary results will be presented as a poster.



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POSTER

Pharmacokinetics of S010-269, a potent anti-leishmanial Compound, in Rats

Abhisheak Sharma[1], Swati Jaiswal[1], Moni Sharma[2], Prem Man Singh Chauhan[2] and Jawahar Lal[1]

[1]Pharmacokinetics & Metabolism Division, [2]Medicinal & Process Chemistry Division, CSIR-Central Drug Research Institute, Lucknow – 226031, India

Email: j_lal@cdri.res.in

Leishmaniasis, a poverty-related disease, occurs in four continents and is considered to be endemic in 88 countries, 72 of which are developing countries. An estimated 2 million new cases (1.5 million cases of cutaneous leishmaniasis and 500000 of visceral leishmaniasis) occur annually, with about 12 million people currently infected [1]. The compound S010-269 has shown potent anti-leishmanial activity. Therefore, the pharmacokinetic study of the compound was carried out in rats to develop it as a potential candidate drug.

Young and healthy male *Sprague Dawley* rats were administered a suspension formulation of the compound at 10 mg/kg oral and intravenous administration. Blood samples were collected upto 48 h. An HPLC assay method was developed and validated and then applied for quantitative analyses of S010-269 in serum samples. Pharmacokinetic parameters were calculated from noncompartmental and compartmental models using WinNonlin program.

The lower limit of quantification for the analytical method was 10 ng/ml of S010-269 in serum. Recovery of the compound from spiked control serum was more than 95% with the variations (accuracy and precision) within acceptable limits [2]. The animals tolerated the treatment as no peculiarities in the animals' behaviour were observed. It was observed that after oral dosing, its absorption was rapid with two peak concentration (C_{max}) at 1 and 6 h and could be monitored up to 24 h. The compound exhibited low absolute bioavailability (2.94%). The clearance (0.3 L/h/kg) was smaller than the hepatic blood flow (2.9 L/h/kg, [3]) of the rat, suggesting an insignificant amount of extrahepatic elimination of this compound. The details will be presented.

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POSTER

Efficient Synthesis of Subphthalocyanines as Photo Sensitizers in Photodynamic Therapy

Poonam, Ritika Nagpal and S.M.S Chauhan

Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110007

Email: smschauhan@chemistry.du.ac.in

Boron-subphthalocyanines are cone-shaped 14 p-electron extended aromatic ring compounds. These subphthalocyanines are fluorescent properties having long triplet excited state lifetimes that efficiently produce singlet molecular oxygen, O_2 (^1D_g). Thus, subphthalocyanines are interesting candidates for use in photosensitization processes, especially in cases where absorption in the red part of the spectra is not required. PDT is based on the administration of a photosensitizer, which is preferentially accumulated in the microbial cell, subsequently irradiation with visible light, in the presence of oxygen produces singlet oxygen which inactivates the microorganisms.

The cyclocondensation of phthalonitriles in the presence of BCl_3, BBr_3 and other boron salts form the boron subphthalocyanines. UV-vis spectra of subphthalocyanines are comparable to phthalocyanines showing both Q- band and soret band, the soret band (300nm) and Q-band (520nm) are shifted to shorter wavelengths with respect to phthalocyanines as a consequence of the decrease of the p-conjugation system. The strongest absorption of the Q band attributed to the allowed p-p* transition of subphthalocyanines. The reaction has been performed in ionic liquid at 140èC and the results and spectroscopic data will be presented.

POSTER

Antimicrobial Resistance: Challenges and Perspectives

Antara Sharma

Kirori Mal College, University of Delhi, Delhi 110007 (India)

Antimicrobial resistance (AMR) is the ability of a microorganism to withstand the effects of an antimicrobial medicine to which it was originally sensitive. Though AMR is not a recent phenomenon, resistant strains are evolved through a natural process that happens when microorganisms are exposed to antimicrobial drugs. But today AMR is reaching alarming levels and its growth is a very significant health threat to the entire World. AMR not only hampers the control of infectious diseases, but also increases the costs of health care and threatens a return to the pre-antibiotic era. According to a recent WHO estimate there are about 6,30,000 MDR-TB cases in the world. The persistence of AMR is due to a host of factors that include biological, societal, industrial and legislative factors. AMR has economic consequences far beyond the health sector.

Undoubtedly, more information and new tools are needed, but available strategies and interventions can go a long way towards minimizing the scale and impact of AMR, and maximizing the effective lifespan of existing antibiotics. Much more could be achieved by better and more widespread applications of these measures, and there are many promising opportunities for innovation in this area. Thus, addressing the issue of antimicrobial resistance is one of the most urgent priorities to avert a developing global crisis in health care. We wish to make a poster presentation to engage all the principal stakeholders, including civil society to commit to a comprehensive national plan.

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POSTER

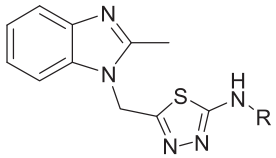
Development of Novel Benzimidazole Based 1,3,4-thiadiazoles as GSK-3β Inhibitors

Hinna Hamid*, Imran Khan, Mushtaq A Tantray and M S Alam

Department of Chemistry, Faculty of Science, Jamia Hamdard, New Delhi-110062 (India)

Email- hhamid@jamiahamdard.ac.in

GSK3 is a ubiquitous kinase that participates in a multitude of cellular processes, including cell membrane-to-nucleus signaling, gene transcription, translation, cytoskeletal structuring and cell cycle progression and survival. GSK3 controls the relevant substrates, such as glycogen synthase (GS), p53, p27, and β-catenin, which are associated with many diseases such as type II diabetes mellitus (T2DM), cancer, bipolar disorder, Alzheimer's disease, and schizophrenia [1]. Thus, modulation of GSK3 has been considered as one of the promising therapeutic ways for the treatment of the corresponding human diseases. Benzimidazole and thiadiazole derivatives have been reported as GSK3β inhibitors [2,3]. We therefore attempted to synthesize novel benzimidazole based 1,3,4-thiadiazoles as GSK-3 inhibitors. A series of 12 compounds of benzimidazole based 1,3,4-thiadiazoles have been synthesized. The synthesized compounds are being screened for their GSK-3 inhibitory activity and the potent compounds from screening will be evaluated further for various associated pathological disorders.



Key words: gene transcription, β-catenin, type II diabetes mellitus

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POSTER

Development and Validation of UV Spectrophotometric Method for Estimation of Agomelatine in Bulk and Pharmaceutical Dosage Form

Joshi Hitendra S.* and Reema H. Rupareliya

Department of Chemistry, Saurashtra University, Rajkot-360 005, Gujarat, India

Email: drhsjoshi49@gmail.com

A simple, rapid, accurate, precise, sensitive and economical UV Spectrophotometric method has been developed for estimation of Agomelatine from bulk and pharmaceutical formulation. The λ_{max} of Agomelatine in water was found to be 233 nm. The parameters linearity, precision, accuracy, limit of detection and limit of quantitation, robustness were studied according to International Conference on Harmonization guidelines. The drug follows linearity in the concentration range 2- 8µg/ml with correlation coefficient value 0.9981. The accuracy of the method was checked by recovery experiment performed at three different levels i.e., 50%, 100% and 150 %. The % recovery was found to be in the range 98.94%– 100.05%. The low values of % R.S.D. are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intra-day, inter-day variations and repeatability. The % R.S.D. value less than 2 indicate that the method is precise. The above method was a cost-effective quality- control tool for routine analysis of Agomelatine in bulk and in pharmaceutical dosage form.

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POSTER

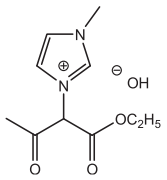
Ethylacetoacetate Tagged Bbasic Imidazolium Salt: Multi-task in Cui Nanoparticle Catalyzed Amination of Aryl Halides

Ananya Srivastava and Nidhi Jain*

Department of Chemistry, Indian Institute of Technology-Delhi, Hauz Khas, New Delhi-110016

Email: ananya.gkp@gmail.com

Copper catalyzed reactions suffer from harsh conditions of high temperature, high pressure, over-stoichiometric amount of copper reagents and use of expensive ligands. In an attempt to develop a mild, ef□cient and reusable system for copper catalyzed reactions, ethylacetoacetate was doped into ionic liquid (IL) by tagging it with imidazolium cation stabilized by a counter hydroxide or acetate anion (1a and 1b). The novel ligand-anchored ILs demonstrated high ef□ciency in generation and stabilization of uniformly dispersed Cu(I)I nanoparticles with particle size in range 9-12 nm (1c). Further, the catalytic system provided an ef□cient route to amination of aryl iodides, bromides and the less reactive chlorides under mild conditions with very low catalyst loading of only 2 mol % to yield primary aryl amines selectively. Furthermore, the reaction allowed easy isolation of products with recovery of ionic liquid containing an intact built-in ligand and base combination for further reuse.



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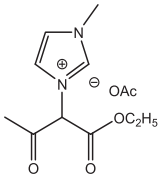

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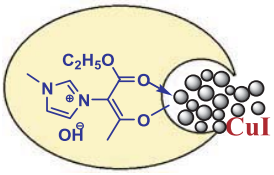

1c

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POSTER

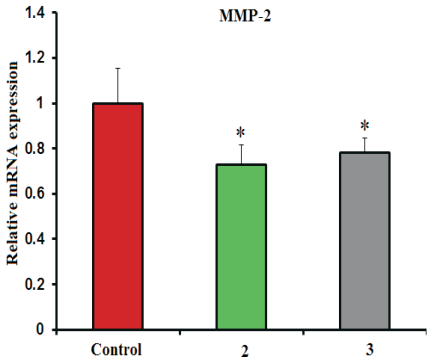
Molecular Drug Design Of Dimethyltin(Iv) Complex As Topo I Inhibitors: *In Vitro* Dna Binding, Cleavage Activity And Molecular Docking Studies

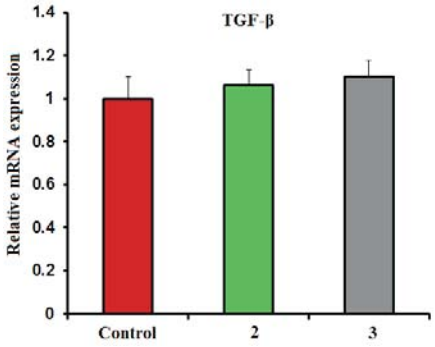
Shipra Yadav and Sartaj Tabassum*

Department of Chemistry, Aligarh Muslim University, Aligarh–202002, India

Email: tsartaj62@yahoo.com

Interaction of organotins has been extensively studied with a variety of ligands due to the importance of their antineoplastic activity. New dimethyltin(IV) chemotherapeutics **1–3**, were synthesized and thoroughly characterized by NMR spectroscopy, ESI mass spectrometry, elemental analysis and molar conductance measurements, and the molecular structure of **1** was studied by single crystal X–ray diffraction analysis. The i*n vitro* DNA binding profiling of the **2** and **3** was carried out by employing different biophysical methods to ascertain the feasibility of organotins(IV) complexes. Additionally, the cleaving ability of **2** and **3** was investigated by agarose gel electrophoretic mobility assay with supercoiled pBR322 DNA, demonstrated significantly good nuclease activity. Furthermore, both the complexes exhibited significant inhibitory effects on the catalytic activity of human Topo I at lower concentration. The computer–aided molecular docking techniques were carried out to correlate and rationalize the observed binding affinities with docking studies towards the molecular target DNA and Topo I. The cytotoxicity of the **2** and **3** against Huh7 cell line was evaluated, which revealed significant regression in cancerous cells. The antiproliferative activity of **2** and **3** were tested against the human hepatoma cancer cells (Huh7), which exhibited significantly good activity. Moreover, to validate remarkable antiproliferative activity of **2** and **3** complexes, specific regulatory genes expression (MMP–2 and TGF–β) was obtained by real time PCR.





POSTER

Enzyme-Degradable AMPS based hydrogel Cross-linked with Starch and Acrylamide – Preparation, Characterization andIn Vitro Blood Compatibility Study

Monali das* and Nirada Devi

Department of chemistry, Cotton College, Guwahati-781001, Assam, India

Biomaterials have an enormous impact on human health care. They are widely used in biomedical applications including drug delivery devices and tissue engineering matrices. While various types of hydrogels have been prepared as synthetic cellular matrices, designs offering both biocompatibility and biodegradability are limited. A partially enzyme degrable AMPS based hydrogel cross-linked with starch and acrylamide has been prepared in the present work which is also found to be bio compatible. The hydrogel is characterised by FT-IR, SEM, TGA and XRD. The Swelling study shows that the water uptake property of the hydrogel is dependent on composition of polymer, pH and ionic concentration of the medium. It is found to be partially degrable by α-amylase and celulase enzyme. The in vitro blood compatibility of the hydrogel were determined in terms of blood clot formation, percentage of haemolysis and protein *(bovine serum albumin, BSA)* adsorption tests. It is observed that on increasing concentration of AMPS in the blend, the amount of adsorbed BSA decreases implying a better biocompatible material. The observed decrease is consistent with the blood clot formation results. The extent of hemolysis decreases with increasing AMPS content. The observed results are attributed to the reason that with increasing concentration of AMPS in the blend, surface composition favorably changes which improves the blood compatible quality of the material. The hydrogel prepared in this study might be useful cell and tissue engineering applications.

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POSTER

Superoxide Ion Induced Multicomponent Synthesis of Spiro[(2-amino-3-cyano-5-oxo-5,6,7,8-tetrahydro-4H-chromene)-4,3'-oxindoles]

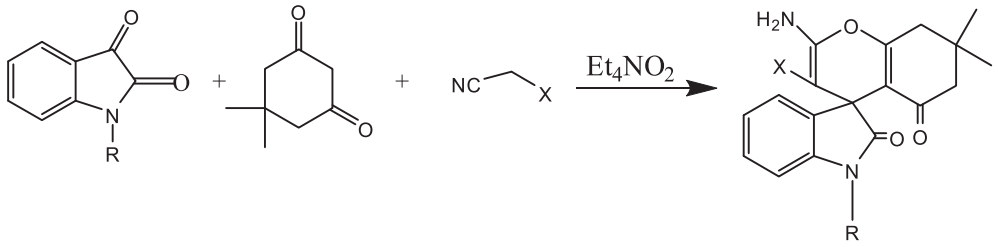
Sundaram Singh and Somaiah Gajaganti

Department of chemistry, IIT(BHU),Varanasi

Multi-component reactions (MCRs), in which multiple reactions are combined into one synthetic operation, have been used extensively to form carbon-carbon bonds in synthetic chemistry. Such reactions offer a wide range of possibilities for the efficient construction of highly complex molecules in a single procedural step, avoid the complicated purification operations and allow savings of both solvents and reagents. Although the scope of novel multicomponent reactions (MCRs) has widely increased over the last decade, they cover only a limited amount of the chemical space and much still remains to be accomplished.

The chemistry of superoxide ion, has come to the forefront of current interdisciplinary research owing to its demonstrated biochemical implications and as a species of relatively unexplored chemical reactivity. The ability of superoxide ion to function as a multipotent reagent has made the chemistry of this radical anion somewhat enigmatic.

The present report demonstrates a fast and selective multicomponent transformaton of cyclic 1,3-diketones, isatins, and malononitrile/ethyl cyanoacetate into spiro[(2-amino-3-cyano-5-oxo-5,6,7,8-tetrahydro-4H-chromene)-4,3'-oxindoles] under mild reaction conditions of superoxide ion at room temperature in excellent yields.



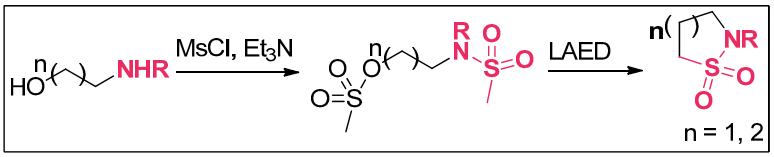
Scheme

POSTER

A New Synthesis of Sultams from Amino Alcohols

Nitin Lad[1], Rajiv Sharma[1], Victor E. Marquez[2] and Malcolm Mascarenhas[1]

[1]Department of Medicinal Chemistry, Piramal Enterprises Ltd., 1-Nirlon Complex, Goregaon (East), Mumbai 400063, India.
[2]Laboratory of Medicinal Chemistry, DBS, NCI, NIH,FCRDC, 376 Boyles Street, Bldg. 376, Rm. 104 Frederick, MD 21702-1201, USA.



A base-mediated cyclization of *N, O*-dimesylate derivatives of cyclic and acyclic amino alcohols provides a simple access to five- and six-member sultams: isothiazolidine-1, 1-dioxides and thiazinane-1, 1-dioxides respectively.

POSTER

Synthesis of Novel Guanidine Based Phthalimide as Effective Antimalarial Agents

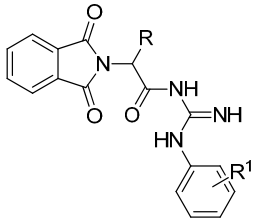
Prashant Kumar, Anil Kumar Singh, Brijesh Rathi and Brajendra Kumar Singh*

[§]*Bio-organic research Laboratory, Department of Chemistry, University of Delhi, Delhi-110007, India*

Email: prashanttomar972@gmail.com

Naturally occurring and synthetic compounds containing guanidine scaffold became one of the most valuable moieties due to both the hydrogen-bond mediated interaction of guanidinium ions and wide range of biological activities these substances display. The synthetic guanidines continue to be the subject of numerous reports: in physicochemical structural studies, as potentially useful drugs or pesticides, acting as catalysts, as selective oxoanion hosts, as flame retardants, in organometallic chemistry, as superpotent sweetners, in positron emission tomographic imaging, as water-soluble fluorescent probes, in molecular design, in sugar mimetics, in nucleotide mimetics and in peptide mimetics. Biguanide, Metformin, has been recognised as first line drug which manages glucose and lipid levels in the blood. Recently our group have synthesised hydroxylethylamine based phthalimides nanoparticles which showed good inhibitory activity against falcipain 3.

The strong biological efficacy of guanidine and phthalimide based compounds encouraged us to fuse these two moieties and compile a library of guanidino-phthalimides. The biological part of this work is in progress.



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POSTER

Synthesis and Biological Activity Evaluation of Coumarin Based 1, 2, 4-Oxadiazoles

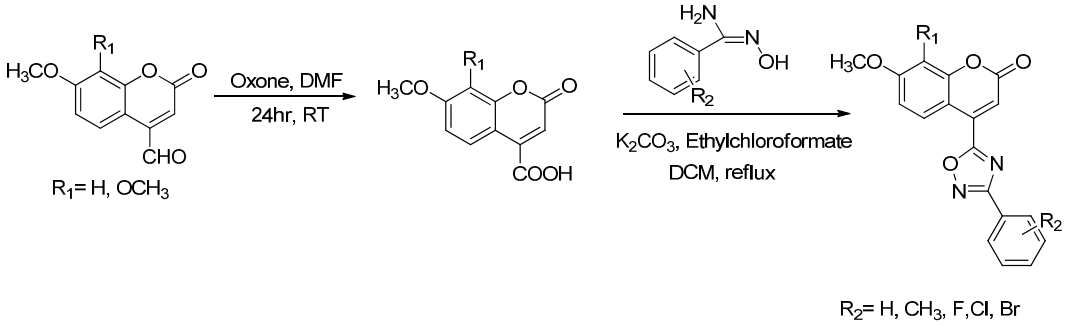
Akanksha Matta, Vijay Bahadur, Amit Kumar Singh and Brajendra Kumar Singh*

Bio-organic Laboratory Department of Chemistry, University of Delhi, Delhi 110 007, India

Email: singhbk@chemistry.du.ac.in

Century has passed since the first heterocycle was synthesized/isolated and remained trust area of research for the organic and the medicinal chemists. Among the various class of heterocycles oxygen and nitrogen containing heterocycles have gained much importance. In past few years, coumarin and oxadiazoles have been extensively investigated by biochemist and medicinal chemist. Many of these compounds have proved to be active as antitumor[1], antibacterial[2], antifungal[3] and antiinflammatory[4]. Hybrid molecules are highly active and effective and are used quite commonly medicinal chemistry. We have planned the synthesis of the coumarin based 1, 2, 4-oxadiazole hybrid molecule.

Library of novel coumarin based 1,2,4-oxadiazole of twenty compounds were synthesized (Scheme 1), purified and characterized by high resolution mass spectrometry, ^{1}H and ^{13}C nuclear magnetic resonance and infrared spectroscopy. The biological activity of these compounds will be illustrated later.



Scheme 1: Synthesis of Coumarin based 1,2,4-oxadiazoles

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POSTER

Beta-Peptide Based Functional Nanostructures

R. Goel, S. Gopal and A. Gupta*

Department of Chemistry, Dyal Singh College, University of Delhi

Email: alkaguptas@yahoo.co.in

Self-assembling peptides are one of the most attractive and useful building blocks in making nanostructures, like nanorods, nanovesicles, nanobelts, nanofibers and others due to their chemical diversity, biocompatibility, biodegradability and foldability into specific structures depending on the sequence and environmental responses.

Beta-amino acid oligomers and polymers represent an exciting opportunity in this area as their secondary structures are more stable than conventional peptides. Recent studies have indicated that chemical functionality can be patterned on the surfaces of nanostructures designed using beta-amino acids, presenting an important opportunity in nanoscience and nanotechnology.

In the present study we use computational methods to gain insight into hierarchical self – assembly process of a beta-alanine oligomer. HyperChem Release 8.0 has been used to obtain minimum energy structure and to explore the allowed conformational space. Molecular Dynamics (MD) simulations are performed to address the thermal stability and nature of intermolecular interaction of the putative assembly structure. The initial structure of peptide is geometrically optimized by Molecular Mechanics method using MM+ force field revealing that two peptides occupy two different regions of conformational space. The resultant structures are used as the starting point for MD simulations. The simulations studies have indicated a possibility β-Ala oligomer may form spherical nanovesicles vesicles on self assembly.

Peptides ate synthesized, characterized and nanostructuration is performed using a stirring-induced self-assembly method. The obtained structures are characterized using electron microscopy. Formation of spherical structures is clearly indicated. Effect of temperature on the stability of these structures is also investigated.

Temperature dependent CD studies reflecting high susceptibility of backbone conformation towards temperature of the environment of the parent peptide is also reported.

POSTER

MM-GBSA Calculations to Discriminate Actives and Inactives for *In-Vitro* Xanthine Oxidase Inhibition

Smriti Khanna,* Rajiv Sharma,# and Chandrika B-Rao*

**Discovery Informatics, Piramal Enterprises Ltd., Goregaon (E), Mumbai 400063, India*
#Department of Medicinal Chemistry, Piramal Enterprises Ltd., Goregaon (E), Mumbai 400063, India

Isocytosine has been recently discovered as a novel scaffold for xanthine oxidase inhibition implicated in the treatment of gout.[1] Many molecules in this series were docked, synthesized and tested in biochemical assays of which quite a few showed potent IC_{50} values in the nanomolar range. Isocytosine has a pyrimidine ring and one of the nitrogens forms H-bonds with the receptor whereas the other does not show any interactions as predicted from the docking studies. The position of the latter ring nitrogen of isocytosine was shifted to generate reverse pyrimidine moiety in order to get new core structure. Although the reverse pyrimidines docked very similar to normal pyrimidine compounds, they did not show any activity when tested in enzymatic binding assays. As the analysis of the docked poses and their interactions with the protein active site residues did not provide any rational justification, free energy calculations were done using Prime MM-GBSA module of Schrodinger. The ΔG binding energies also could not discriminate between the active pyrimidines and the inactive revere pyrimidine counterparts. The detailed split up of various energy terms showed one of the terms 'Ligand-in-Complex' energy that gave good correlation with the activity data. The energy values showed a consistent difference of ~20 kcal/mol between pairs of pyrimidines and corresponding reverse pyrimidine analogs. This energy term signifies influence of protein environment when the ligand is complexed to the active site of the receptor. Thus MM-GBSA calculations on the docked poses indicated that reverse pyrimidines experienced certain destabilizing interactions in the receptor which could not be predicted by dock scores.

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POSTER

Effect of Ala^{8,13,8}-magainin II Amide on Dynamics of First Trimester Villous Trophoblast Cell Turnover

Manisha Kar

Department of Physiology, All India Institute of Medical Sciences, Bhubaneswar, India

Ala^{8,13,8}-magainin II amide is a synthetic Anti-Microbial Peptide (AMP) which is modified from natural magainin 2. Magainin 2 was isolated from skin glands of African frog Xenopus leavis. It exhibits selective toxicity to bacterial and tumour cells because of its interaction with negatively charged cell surface phosphatidylserine resulting in membrane dysfunction. Placental villi are responsible for feto-maternal exchange processes and also elaborates important biomolecules. The maintenance of structural and functional integrity of this layer is of paramount importance and any perturbation specially during first trimester may lead to placental dysfunction. The placental villi consists of outer trophoblast lining and inner stromal core. The outer trophoblast lining in turn consists of two layers. The outermost layer is syncytium and innermost layer consists of mononuclear cytotrophoblast cells. Syncytiotrophoblast is derived from underlying cytotrophoblast cells. During the formation of syncytium, negatively charged phosphatidylserine gets exteriorized and thus may become vulnerable to magainin. In the present study the effect of Ala^{8,13,8}-magainin II amide was examined on dynamics of various processes of cell turnover namely proliferation, differentiation and apoptosis in trophoblast cells isolated from 6 to 8 week gestational placenta grown on collagen biomatrix for 24 h in serum-free supplemented culture medium. Following treatment, trophoblast cells were subjected to immunostaining for markers for housekeeping (cytokeratin-7), differentiation (hCG, hPL), proliferation (PCNA, Ki-67), fusion (Annexin V) and apoptosis (cytokeratin 18 fragment). The supernatant was analyzed for secretary β-hCG. Expression of PCNA was significantly higher ($P \leq 0.05$) in magainin-exposed group in comparison to control group. However, no such difference was observed for Ki-67. Annexin V was significantly ($P \leq 0.05$) higher in control group. Increased β-hCG synthesis, secretion and hPL synthesis ($P \leq 0.05$) was observed in control group. No significant difference was observed in expression for cytokeratin-7 and cytokeratin 18 fragment between two groups. Magainin attenuates syncytial fusion without marked effect on basal housekeeping activities.

POSTER

Structural Characterization and Kinetic Regulation of Guanylate Kinase, A Nucleoside Monophoshate Kinase of Filarial Parasite *Brugia Malayi*

Smita Gupta, Sunita Yadav, Nidhi Singh, M.I Siddiqi and Jitendra K. Saxena*

Division of Biochemistry, Central Drug Research Institute, Lucknow-226031

Email: smitagupta06@gmail.com

Nucleotide metabolism is a key pathway in life cycle of any organism and Nucleoside monophosphate kinases (NMPKs) play an important role in supplying DNA and RNA precursors, hence considered important target protein. Guanylate kinase (ATP: GMP phosphotransferase, guanosine monophosphate kinase, EC 2.7.4.8) belongs to NMPK superfamily and is critical for the synthesis of GTP/dGTP since it catalyses reversible phosphorylation of GMP/ dGMP to its diphosphate form GDP/dGDP. It's inhibition will modulate the synthesis of nucleotides, which are indispensable for any organism. In addition to being a critical enzyme in the biosynthesis of GTP and dGTP, Guanylate kinase functions in the recovery of cGMP and is, therefore, thought to regulate the supply of guanine nucleotides to signal transduction pathway components.

In the present study *Brugia malayi* Guanylate kinase (BmGK) was characterized. BmGK differs from its host enzyme in its kinetic parameters and showed specificity for ATP as a phosphate donor and GMP as phosphate acceptor. Mg^{+2} is essentially required for enzyme activity in form of Mg-ATP and in addition to this free Mg^{+2} unbound to ATP was found to activate the enzyme while GTP at high concentration showed end product inhibition. Thus, Mg^{+2} and GTP play a regulatory role in catalysis of BmGK. Since understanding the folding and assembly of the parasite enzyme may be of importance in designing molecules that can impede association of the subunits, unfolding study of BmGK was done. Effect of denaturant was tested and it was found that BmGK was denatured at 4M Urea and 2M GdnCl while complete loss of activity was seen at 1.5M Urea and 80mM GdnCl suggesting that inactivation of BmGK is prior to its structural denaturation. Molecular modelling study revealed that BmGK consist of three domains: the core, the lid and the NMP-binding domain like most NMP kinases. The core domain consists of a four-stranded β sheet flanked by α helices and also contains the P-loop which binds the ATP phosphate.

POSTER

Molecular Characterization of Immunomodulatory Protein from *Brugia malayi* and its Potential Immune Evasion Role in Human Classical Complement System

Sunita yadav, Smita gupta , Pravesh verma and Jitendra K. Saxena*

Division of Biochemistry, Central Drug Research Institute, Lucknow-226001

Email:lkosunita@gmail.com

Filarial parasites modulate effective immune response of their host by releasing variety of immunomodulatory molecules, which help in long persistence of parasite within the host. Most processes in immune system occur through an intricate network of biological protein-protein interactions, in which any disturbance can lead to pathological circumstance. In classical complement system after the interaction of IgG/IgM with C1q a sequential activation of C1q-bound C1r and C1s serine proteases promote proteolysis of C_4 to produce C4b that is responsible for complement cascade activation (MAC). Therefore, compounds that interfere with the C1q-$C1r_2C1s_2$ interaction will cause inhibition of classical pathway. The present study showed that *Brugia malayi* Calreticulin (BmCRT), a Ca^+ binding protein was responsible for the prevention of Classical complement pathway activation via its interaction with first component C1q of human host. This was confirmed by inhibition of C1q dependent lysis of immunoglobulin-sensitizes Red Blood Cells (S-RBCs) and Pull-down assay. BmCRT-HuC1q complex prevents cleavage of C4 into C4a and C4b causing inhibition of the entire cascade. A 3D model of BmCRT was constructed for not only analysis of whether two proteins interact, but also insight the physico-chemical profile of the interaction, and residues (sites) at the protein interface. Analysis of macromolecular interactions through protein-protein docking reveals that N and P domain of BmCRT was involved in complex formation. CD analysis indicates that BmCRT composed of 49.6 % α helix, 9.6 % β sheet and 43.6% randam coil. These findings signify that BmCRT may be a key factor contributing to ability of parasite to interfere at the earliest stages of complement activation which may help infectivity of parasites and long live host-parasite relationship.

POSTER

Synthesis of Different Derivatives oOf [1,2,4] Triazole-3-Thiol Based Schiff Base and Their Characterization

Suneel Sahu* and S.P.Shrivastava

Heterocyclic Research Laboratory, Department of Chemistry, Dr. H. S. Gour Central University Sagar (M.P.)

Email: sahusuneel6@gmail.com

Keywords: Triazole, Pyrazole, Schiff base

Schiff bases are the compounds which contain –C=N– functional group. The chemistry of 1,2,4-triazole and its fused heterocyclic derivatives have received considerable attention owing to their synthetic and effective biological importance. There are some microbial drugs containing a triazole moiety, for instance fluconazole, used in medical therapy. In addition vorozole, fadrozole and anastrozole are non steroidal drugs for the treatment of estrogen dependent breast cancer. In the present investigation, a series of new Schiff bases 4-{(Subsituted-phenyl)-1-phenyl-1H-pyrazol-4ylmethylene)-amino}-5-(substituted-phenyl) 4H-(1,2,4) triazole-3-thiol were synthesized by the condensation of 4-Amino-5-subsituted-4H[1,2,4]triazole-3-thiol with various substituted of 3-(4-substitutedphenyl)-1H-pyrazole-4-carbaldehyde in ethanol–dioxane mixture, using catalytic amount of sulfuric acid. The synthesized derivatives were characterized by spectral data (IR and ^{1}H NMR).

POSTER

Efficient Use of Stem, Bark, Roots and Rhizomes of Some Plants to Cure Fractured Bones

P.Gouda and V.R. Raju

Khallikote Autonomous College, Berhampur, Ganjam, Odisha, India

Email: pngouda@rediffmail.com

Medicinal plants play a dominant role in the health care of 80% of the world population and it is estimated that more than 50% of the drugs in clinical use have their origin in natural products. The state of Odisha is tribal dominant. The aboriginal tribes such as Saura, Khond, Pulian, Lodha, Dora, Godaba and Jotagu have their habitant in the forests. Lack of urban medical facilities has made them use plant parts as medicines for various diseases. As a case study it has been concluded that they successfully use stems, barks, roots and rhizomes of some plants to cure fractured bones. The bark of ***Terminalia arjuna,*** roots of ***Capparis horrida*** and ***Dumesia villioisa*** and rhizomes of ***Vitis trifolia*** have been used by the tribes for the above purposes.

Chemical investigations of these plants have revealed that the main constituents of ***Terminalia arjuna*** is Olean-3β-22β-diol-12-en-D-glucopyranoside-ioc acid. The main constituent of ***Capparis horrida*** is β-sitosteryl-glucoside-6'-heptadecanoate, and that of ***Vitis trifolia*** are Friedelan-3β-ol and trans-N-caffeoyltyramine. ***Dumesia villioisa*** is mainly constituted of Olean-3α-ol-1,6,11-tri-en-28β-glucopyvanoside-28-oic acid.

Priliminary findings towards pharmacological effect was done on frog muscle tissue. The muscle tissue showed contraction of muscle suggesting that the isolated compounds could be a contributing factor leading to the healing and growth of muscle tissues. The antimicrobial activity of the compounds was tested against various micro- organisms like *E-coli*, *Staphylococcus aureas* and *Bacillus cereus* and thus Friedelan-3β-ol and trans-N-caffeoyltyramine are found to exhibit antimicrobial activity.

POSTER

Design and Synthesis of Sugar Modified Triazole-Linked Nucleoside Dimers: Neutral Nucleic Acid Mimic

Smriti Srivastava, Sunil K. Singh and Ashok K. Prasad*

Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110 007

E-mail: ashokenzyme@yahoo.com

Antisense oligonucleotides (ASONs) have attracted considerable attention of both biologists and chemists due to their potent therapeutic activities. Successful drug development based on inhibition of gene expression by antisense oligonucleotides requires the synthesis and use of chemically modified oligonucleotides that renders stability to nucleolytic digestion, enhance cellular uptake, hybridize with high affinity and specific towards the targeted mRNA. The ongoing synthetic studies on these class of compounds have focused on chemical modification of backbone, base and sugar functionalities of the natural DNA/RNA. One such modification of the ribose moiety is locked nucleic acid (LNA) in which the furanose moiety is locked in an *N*-type (C3- *endo*) conformation by the introduction of a 2- *O*, 4- *C* methylene-linkage.

LNA has been found to be very useful for antisense applications, as incorporation of one or more LNA monomer unit(s) into an ONs shows extraordinary thermal stability when hybridised with either DNA or with RNA or LNA itself. Among various modifications of phosphate backbone, triazole linkage seems to be a lead backbone modification for further studies in antisense constructs. We have designed and synthesized triazole-linked LNA based dimers using Cu catalysed click reaction (**Fig-1**). The detailed synthetic scheme will be presented during the poster session.

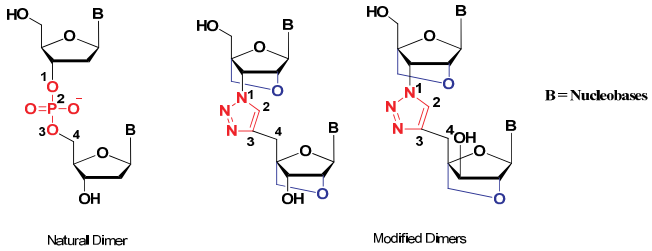

Figure- 1

Acknowledgement: We are greatful for financial assistance from DU-DST Purse grant. S. Srivastava and S. K. Singh thank CSIR, New Delhi for providing JRF/SRF.

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POSTER

Production of Chitin Nanofibers in Deep Eutectic Solvents and Its Hybrid Gel Beads with Calcium Alginate for Slow Drug Delivery

Chandrakant Mukesh and Kamalesh Prasad*

Email: kamlesh@csmcri.org

Biopolymer and synthetic polymer based nanofibers are being extensively used in various applications in the field of tissue engineering, slow drug delivery as well as for the preparation of various functional nanocomposites in nanotechnology. Chitin, the (1–4)-2-acetamido-2-deoxy- ъ-D-glucan, is the second most abundant biopolymer present on the earth after cellulose. The main sources of the biopolymer for industrial exploitation are crab, squid and shrimp. The extensive biomedical application of chitin and chitosan is driven by their mucoadhesive, antimicrobial, biodegradable and nontoxic properties. In the work reported herewith, the chitin nanofibers (CNF) were prepared in choline chloride – thiourea (DES, a deep eutectic solvent obtained by heating the two substrates at 1: 2 molar ratio) and three different ionic liquids having similar physicochemical properties that with the deep eutectic solvents. The chitin nano fibers thus obtained were characterized by ^{13}C NMR, FT-IR, powdered XRD, SEM, AFM and TEM and the quality and performance of the CNFs prepared in DES was found to be at par that prepared in the ILs. Further, the nanofibers were embedded in calcium alginate gel beads to result formation of the nanocomposite gel beads. The nanocomposite gel beads were used as sustained drug release matrix for an anticancer drug, 5-fluorouracil at pH 7.2.

POSTER

Study of Anticancer Properties of Novel Synthetic Compound(S) On Prostate Cancer Cell Lines

Guru Prasad Sharma[1], Amir Azam[2] and Neelima Mondal[1]

[1]School of Life Science, Jawaharlal Nehru University, New Delhi. [2]Jamia Milia Islamia, New Delhi.

Email: nmondal@mail.jnu.ac.in

Cancer is a group of diseases involving unregulated cell growth. Prostate cancer is the second most diagnosed cancer in men. Leading morbidity due to prostate cancer has rendered researchers to focus on advanced chemopreventive measures worldwide. Early studies indicate that hormonal ablation therapy and chemotherapies are the potential therapies but they confer side effects. Hence there is need for such compound having least side effects and high efficacy. To address this, we screened some novel synthetic hydrazone based compounds on prostate cancer cell lines (DU-145 and PC3). Since hydrazine bond is unstable in acidic pH and niche around cancerous cell is more acidic than normal healthy cells. Based on this notion we hypothesized that these compounds might affect cancerous cells over the normal cells. Out of 10 synthetic compounds, 3 compounds namely F4, F8 and F9 were found to be toxic on these cell lines. IC_{50} values for compounds F4, F8 and F9 were found to be 60µM, 80µM, 70µM in DU-145 cell line and 60µM, 80µM, 80µM in PC3 cell line respectively. To prove our hypothesis we tested cytotoxicity of the screened compounds, at their IC_{50} concentration, in fibroblast cell and found that more than 70% cells were viable. We took F4 for the further studies. Cell cycle study in fibroblast cell indicated that F4 elicited polyploidy, hence we reduced concentration and found that F4 (10 µM) was inhibitory to cancerous cells and not to the fibroblast cells. F4 arrested cells in S-phase of the cell cycle with sub-G1 population. Western blot study of compound F4 indicated that expression of cyclinA was inhibited and expression of p21 was induced in a time dependent manner in both cell lines. These results suggested that p21 might be playing an inhibitory role on the Cyclin-Cdk complex. We also checked the expression of retinoblastoma (RB) protein and found that upon F4 treatment, hyperphosphorylatd form of retinoblastoma was down regulated, while total RB level remained almost unchanged in PC3 cell line. In DU-145 cell line, compound F4 induced serine-15 phosphorylation of p53, while total p53 level remained unchanged. Here we hypothesized that, the compound F4 might be promoting tumor suppressor activity of p53 and RB in PC3 and DU-145 cell line respectively via p21 regulated pathway; though further studies are needed. The degradation of PARP [Poly (ADP-ribose) Polymerase] in western blot data, and sub-G1 population in cell cycle study indicated that compound F4-arrested cells lead to apoptosis at later time points. Present study suggests that these synthetic compounds may be promising chemopreventive candidates with tissue selective effect for Prostate cancer therapy.

POSTER

Solvation Behaviour of Tetraalkylammonium Salts In Acetonitrile and Methanol Mixture Studied by Ultrasonic Velocity and Viscosity Measurements at 298.15K

Hardeep Anand* and Renu Verma

Department of Chemistry, Kurukshetra University, Kurukshetra

Email:Vrenu16@ymail.com

Ultrasonic velocity (u), density (ρ) and viscosity (η) of tetraalkylammonium perchlorate (R_4NClO_4 where R= Bu, Pr, Et, Me) and tetrabutylammonium tetraphenylborate (Bu_4NPh_4B) solutions have been measured at different salt concentrations in the range 0.003-0.05 mol kg^{-1} in the binary mixtures of acetonitrile (AN) with methanol (MeOH) containing 0, 20, 40, 60, 80 and 100 mol % methanol. The isentropic compressibility (K_s) and apparent molal isentropic compressibility ($K_{s,}$) of different salts in the solvent mixtures have been calculated. Limiting apparent molal isentropic compressibilities ($K^o_{s,}$) for various salts have been evaluated and split into contributions of individual ions i.e. into $(K^o_{s,})_\pm$ values. The hydrophobic or solvophobic interactions, taking place between tetraalkylammonium ions and solvent molecules, can be identified by evaluation of their $(K^o_{s,})_\pm$ values. The variation of $(K^o_{s,})_\pm$ values with solvent composition shows that Bu_4N^+ and Ph_4B^- have very large positive $(K^o_{s,})_\pm$ values which show strong solvophobic interactions in AN and in AN + MeOH mixtures over the entire solvent composition range. These positive values indicate some special type of interactions with the solvent molecules which increase with increase of MeOH composition. Negative $(K^o_{s,})_\pm$ values are generally obtained due to stronger ion-solvent interactions involving electrostatic ion-dipole, or some special type of interactions. ClO_4^- shows much weaker solvation in AN + MeOH mixtures by having some interaction with AN in the AN rich region of the mixtures. The negative values of Et_4N^+ and Me_4N^+ show strong structural effects which arise due to solute-solute and solute-solvent interactions in AN rich region of mixtures. This is also supported by the viscometric studies.

POSTER

POSTER

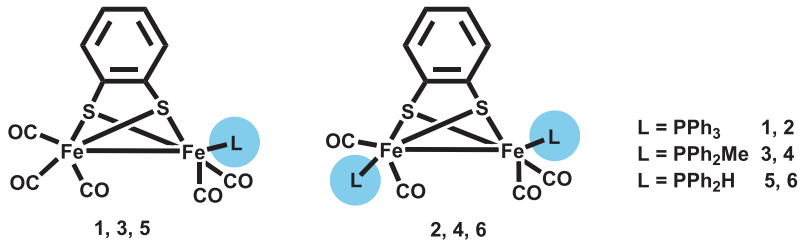
Phosphine Substituted Diiron Carbonyl Complexes as Proton Reduction Catalysts: Mimicking the [FeFe] Hydrogenase Enzyme Active Site

Indresh Kumar Pandey, M. Natarajan and Sandeep Kaur-Ghumaan*

Inorganic & Bio-Inorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110007, India

Email: skaur@chemistry.du.ac.in; 22ipandey@gmail.com

Hydrogenase (H_2ase) enzymes are known for their remarkable efficiency in dihydrogen production and activation. Therefore, special attention has been paid in recent years to molecular models of these enzymes. In nature, three types of H_2ases are known: the Fe-S cluster containing [FeFe]- and [FeNi]-H_2ases and the Fe-S cluster-free [Fe]-H_2ase.The [FeFe]- and [NiFe]-H_2ases participate in hydrogen production and/or oxidation while the [Fe]-H_2ase engages mainly in hydrogen activation. In this context, a series of diiron complexes $[Fe_2(CO)_5(\mu\text{-bdt})(PPh_3)]$ **1**, $[Fe_2(CO)_4(\mu\text{-bdt})(PPh_3)_2]$ **2**, $[Fe_2(CO)_5(\mu\text{-bdt})(PPh_2Me)]$ **3**, $[Fe_2(CO)_4(\mu\text{-bdt})(PPh_2Me)_2]$ **4**, $[Fe_2(CO)_5(\mu\text{-bdt})(PPh_2H)]$ **5**, $[Fe_2(CO)_4(\mu\text{-bdt})(PPh_2H)_2]$ **6** (bdt = benzene-1, 2-dithiolate) were synthesized which contain some of the structural features of the [FeFe]-H_2ase active site. Controllable (CO) displacement from the starting complex, $[Fe_2(CO)_6(\mu\text{-bdt})]$ with monodentate phosphine ligands lead to the formation of complexes **1-6**. All six complexes were characterized by various spectroscopic techniques. The structures for complexes **1-3** were confirmed by X- ray crystallography. The effects of the tertiary phosphane ligands on the redox properties of the complexes were investigated by electrochemical methods. Further the compounds were tested as electrocatalysts for reduction of protons to molecular hydrogen in acetonitrile. Out of the six compounds, only complexes **1** and **3** were found to be active catalysts in the presence of trifluoroacetic acid, reducing protons at -1.4 V and -1.5 V *vs* Fc/Fc^+, respectively with mild over potentials.



1, 3, 5 2, 4, 6

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Novel Synthetic Compounds with Potent Anticancer Activity in Breast Cancer Cell Line

Kunwar Somesh Vikramdeo[1], Amir Azam[2] and Neelima Mondal[1]

[1]*School of Life Sciences, Jawaharlal Nehru University, New Delhi,*
[2]*Jamia Milia Islamia, New Delhi, India*

Cancer is the manifestation of defect in cell cycle checkpoints which results in abnormal proliferation of and ultimately resulting in formation of a mass of cells called tumour. A tumour can be localized (benign) or spread to other parts of body via blood or lymph in which case it becomes difficult to treat. Breast cancer is one of the most prevalent cancer which accounts for more than 11% of all types of cancers reported worldwide and is the leading cause of death due to cancer in women. One of the methods used for treatment of cancer include chemotherapy. Chemotherapy uses various cytotoxic agents which target actively dividing cells, a prominent feature of cancer cells. Unfortunately, chemotherapy also results in damage to normal proliferating cells. One way to alleviate this problem is to design synthetic drugs which have specific and potent anticancer activity and are least harmful to normal cells. This study employs the use of hydrazone based synthetic compounds. 6 compounds were assessed for cytotoxic activity in MCF-7 cells, a breast cancer cell line. It was found that out of them 3 compounds namely F4, F7 and F9 were most effective showing IC_{50} of 25 µM, 30µM and 50µM respectively. These compounds were also found to have distinct effect on cell cycle profile of MCF-7 with F4 arresting the cells in G2/M phase while F7 and F9 causing S-phase arrest. Expression level of cyclins were also checked which showed that in response to F4 there was decrease in levels of cyclin B1, cyclin A and cyclin E levels. Extensive DNA damage was also detected at late time points in response to F4 treatment which resulted in apoptosis as was suggested by increased γ-H_2AX phosphorylation and cleavage of PARP-1. In response to F7, cyclin A and cyclin B1 levels decreased while up regulation in cyclin E levels was observed. In case of F9, there was increase in cyclin B1 and cyclin A levels while cyclin E levels remained unaffected. Low levels of DNA damage was detected in response to F9 suggested by comparatively low levels γ-H_2AX phosphorylation and cleavage of PARP-1 was seen in case of F9 treatment but not in case of F7. All the observations show that F4, F7 and F9 have very significant cytotoxic effect in MCF-7 cell line. This study therefore suggests the use of F4, F7 and F9 as potential anticancer compounds.

POSTER

Synthesis of Thioether Derivatives of Quinoxaline Prospective Antimicrobial Agents

Richa Sahu*and S. P. Shrivastava

Heterocyclic Research Laboratory, Department of Chemistry, Dr. H. S. Gour Central University Sagar (M. P.)

Email: richasahu776@gmail.com

Keywords : Quinoxaline, antimicrobial activity

Initial compound quinoxaline 2,3-dione (I),was synthesized in good yield by condensation of oxalic acid and o-phenylenediamine in 20% HCl. Reaction of compound(I) with $POCl_3$ under refluxing conditions lead to chlorination & formation of 2,3-dichloroquinoxaline(II). Compound (II), on (2+3) cyclo addition with sodium azide in DMSO at acidic pH, cyclized to 4-chloro-tetrazolo [1,5-]-quinoxaline(III). Compounds(III) on treatment with sodium sulphide in DMF gave sodium tetrazolo [1,5-a]quinxaline-4-thiolate(IV) which on treatment with various N-substituted-2-chloro-acetamide under refluxing condition furnished corresponding N-(substituted phenyl)2-tetrazolo[1,5-a] quinoxaline 4-yl thioacetamide. The structures of all the compounds were confirmed on the basis of ^{1}HNMR and FT-IR spectral data. All the newly synthesized compounds were screened for antimicrobial activity against *E.coli, S.aureus, k.pneumoniae*.

POSTER

Cloning and Homology Modeling Study of Arginase from *Leishmania Donovani*

Neha Gaur, Shashi Gandhi, J.K. Saxena and Uma Roy

Division of Biochemistry, CSIR- Central Drug Research Institute, Lucknow-226031, U.P, India

Email: gaurneha145@gmail.com

Leishmaniasis is a vector-born chronic infectious disease caused by a group of protozoan parasites of the Leishmania genus. The most severe form is visceral leishmaniasis (VL), typically fatal if untreated. The polyamine pathway of protozoan parasites has been successfully targeted in anti-parasitic therapies and is significantly different from that of the mammalian host. Despite the plethora of molecular and biochemical studies on the polyamine biosynthetic pathway of *T. brucei*, *L. donovani*, and other parasites, little is known about the metabolic avenues by which polyamine precursors are produced. To initiate an investigation into the pathways by which polyamine precursors are synthesized and to begin a validation of ARG as a potential therapeutic target, we have cloned and characterized *arginase* from *L.donovani.*

To exploit the Arginase(Arg) gene in *Leishmania donovani* an amplicon of 990 bp was cloned in pGEM-T vector. The recombinant clone contained an open reading frame of 330 amino acids giving a predicted mass of 36.3 KDa. The sequence of Arg of *L.donovani* was subjected to find out probable templates for the given protein using BlastP. Differences could be seen between two non conserved equivalent amino acids His 228 and Met 239, respectively in human and Leishmania donovani arginases, forming a differential space channel like structure. The Gly 235,in human arginase is uncharged whereas in the equivalent position Leishmania arginase presents a polar uncharged Thr 246.The difference observed in the neighbourhood of the active site i.e Arg 308,Met 239 and Thr 246 are not conserved. The crystal structure of LdArg is therefore of interest,because it will show structural rearrangements that can be explored in the design of specific Leishmania donovani arginase inhibitors .

POSTER

Arg-265: A Critical Residue of *L.donovani* cytosolic SHMT in Maintaining the Binding of THF

Shashi Gandhi[a], Neha Gaur[a], Shagun Krishna[b], Mohd. Imran Siddiqi[b],Uma Roy[a] and Jitendra Kumar Saxena[a,*]

[a] *Division of Biohemistry, Central Drug Research Institute, CSIR, Lucknow 226031, India*
[b] *Division of Molecular and Structural Biology, Central Drug Research Institute, CSIR, Lucknow 226031, India*

Serine hydroxymethyltransferase belongs to the class of pyridoxal-5-phosphate enzymes along with aspartate aminotransferase.To explore the function of residue(s) involved in binding of the carboxylate group of Tetrahydrofolic acid (THF) to *L.donovani* cytosolic serine hydroxymethyltransferase (cSHMT),the gene was cloned in pET-28(a) vector, overexpressed and purified to homogeneity. With the help of docking results of THF to the active site of protein, the key residues involved in interaction were identified.

In an attempt to understand the function of Arg265 residue involved in binding of the carboxylate group of THF, Arg-265 was mutated to Ala by site-directed mutagenesis. Neither a spectrally discernible 495-nm quinonoid intermediate (which is characteristic of the native enzyme when substrates are added) nor its enhancement by addition of THF was observed in Arg265Ala mutant enzyme. In tritium exchange studies, there was no increment in the rate of the exchange of the α-proton of glycine upon addition of THF to the Arg265Ala mutant enzyme as observed with the native enzyme. These studies support the interpretation that Arg265 residue is required for the interaction of Tetrahydrofolate in cytosolic SHMT of *L.donovani.*

POSTER

L-proline Catalysed Regioselective Synthesis of Pyranothiophene

Satya Narayan Sahu, Surjeet Singh, Pratik Yadav, Ramendra Pratap*

Department of Chemistry, University of Delhi, North campus, New Delhi 110007

Email: satyasahuiitd@gmail.com

A series of pyranothiophenes were designed and synthesized by L-proline catalyzed reaction of 6-aryl-4-methylthio-2H-pyran-2-one-3-carbonitriles and methylthioglycolate in good yields. Precursor can be synthesized by reaction of 2-cyano-3,3-bis-methylsulfanyl-acrylic acid methyl ester and various aryl methyl ketone under basic reaction condition.

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POSTER

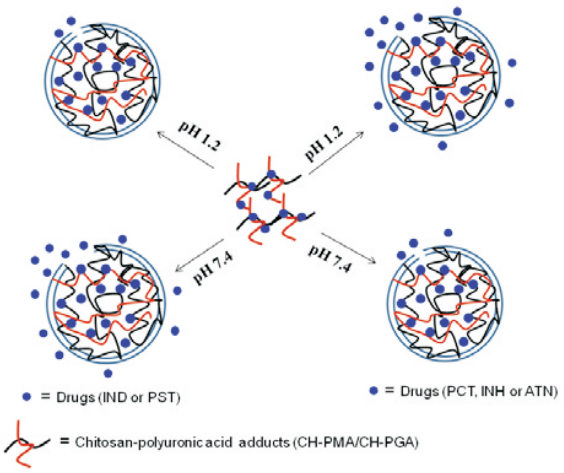
Microwave Assisted Synthesis of Chitosan-Polyuronic Acid Adducts and Their Drug Release Performance

Jai Prakash Chaudhary, A. K. Siddhanta and Ramavatar Meena*

Scale-Up & Process Engineering Unit, CSIR-Central Salt & Marine Chemicals Research Institute
G. B. Marg, Bhavnagar-364 002, Gujarat, India

Email: rmeena@csmcri.org; jpdu1@yahoo.com

Super swellable, pH responsive (pH 1-12), stable and insoluble chitosan adducts were synthesized with poly-mannuronic acid (PMA) and poly-guluronic acid (PGA), using one-pot solvent-free process under microwave irradiation conditions. Controlled-release performance of chitosan-polymannuronic (CH-PMA) acid and chitosan-polyguluronic (CH-PGA) acid adducts, using five structurally different drugs, i.e. paracetamol (PCT), indomethacine (IND), isoniazid (INH), atenolol (ATN) and pravastatin (PST) was studied. Out of these PCT, INH, and ATN having amide (-NH-CO-) functionality displayed greatest release at pH 1.2 and lowest at pH 7.4, while IND and PST without amide functionality express greatest release at pH 7.4 and the lowest at pH 1.2. This study revealed that acquired biopolymer based materials could be used in pharmaceutical and agricultural applications.



Scheme: Controlled release performance of chitosan-polyuronic acid adducts.

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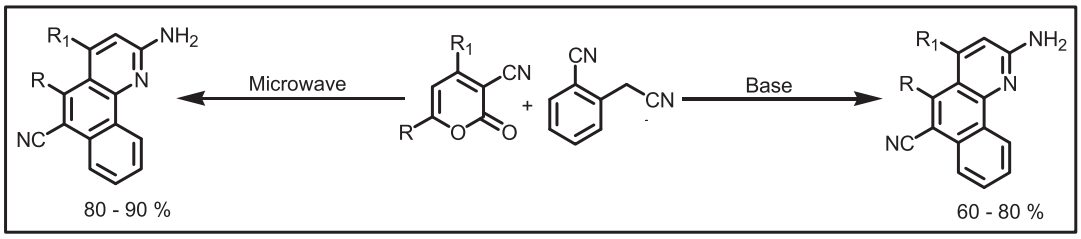
POSTER

Base Induced Cascade Synthesis of Functionalized Benzo[*H*]Quinolines By Inter and Intra Molecular C-C And C-N Bond Formation Reaction

Surjeet Singh, Pratik Yadav, Satya Narayan Sahu and Ramendra Pratap*

Department of Chemistry, University of Delhi, North campus, New Delhi 110007

Email: surjeetmalayan@gmail.com



A simple and efficient cascade synthesis of functionalized benzo[*h*]quinoline, has been delineated through reaction of suitably functionalized 2*H*-pyran-2-ones and 2-cyanomethyl-benzonitrile in presence of sodamide in good yield, which involves inter and intra molecular C-C and C-N bond formation reactions. The above reaction have been carried out under microwave irradiation, and better results were obtained. Structure was confirmed by single crystal X-ray crystallography.

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POSTER

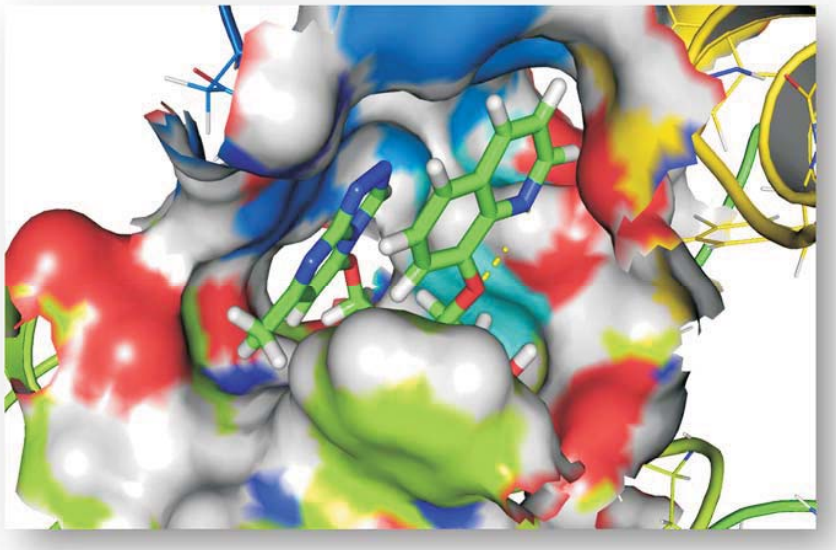
Structure Guided Design of Dual Binding Site Acetylcholinesterase Inhibitors for the Treatment of Alzheimers Disease

Jitendra kumar[1] and Nasimul Hoda[1*]

Department of chemistry ,Jamia Millia Islamia, New Delhi

Email: hodanasimul@gmail.com

Acetylcholinesterase(AChE) is a serine hydrolase enzyme which catalyzes the metabolism of the neurotrans acetylcholine and thus maintain homeostasis of this neurotransmitter in the central and peripheral ne systems. Inhibitors of this enzyme are mainstay drugs for the symptomatic treatment of Alzheimer's disea they efficiently elevate acetylcholine levels in the brain and hence protect and preserve the brain function. study Triazolopyrimidine-quinoline hybrid molecules were designed and synthesized via an easily acce convergent synthetic route. Triazolopyrimidine scaffold is connected with quinoline through a alkyne linker helps to achieve greater binding affinity through π – π interactions not only with Catalytic anionic sit Peripheral anionic site residues but also with aromatic gorge of enzyme.



Veiw of docked structure of lead molecule with Acetylcholinesterase enzyme

POSTER

Density Functional Study of the Reaction of Alloxan and Its Derivatives with Glutathione

Bharti Badhani and Rita Kakkar*

Computational Chemistry Laboratory, Department of Chemistry, University of Delhi, Delhi-110007

Email: rkakkar@chemistry.du.ac.in

The reaction of alloxan and its derivatives with glutathione (γ-glutamylcysteinylglycine, GSH), a sulphydryl (-SH) antioxidant, antitoxin, and enzyme cofactor is studied using density functional theory. The potent reducing power of GSH is responsible for its free-radical scavenging, electron-donating and sulfhydryl-donating capacity. Alloxan reacts with GSH to produce the alloxan radical, AH• and the glutathione GS• radical. AH• reacts with another GSH molecule to produce dialuric acid. The reactions involved in the alloxan-dialuric acid redox cycle with the participation of glutathione are investigated in this work. We have already characterized some of the participants, i.e. alloxan, its radical and reduction product, dialuric acid. In this work, we begin with a characterization of glutathione and its radical in three different environments. Our investigations on the structure of glutathione and its reaction with alloxan reveal that it is the anion formed by ionization of the sulfhydryl group that is responsible for its reaction. The computed orbital energies of the anion and alloxan reveal that the former can readily donate an electron to alloxan. Hence, the initial step is the loss of a proton from glutathione, yielding a sulfur-centered radical, followed by electron loss. An initial formation of a hydrogen-bonded complex with alloxan, with subsequent donation of electron density and a hydrogen to alloxan may lead to radical formation. Calculated redox potentials at the physiological pH indicate that a one electron reduction is not thermodynamically feasible; rather a two electron reduction takes place, yielding dialuric acid anion directly. Further, a systematic investigation of several alloxan-like substances that do not show diabetogenic activity has been performed in order to understand the factors responsible for the loss of diabetogenicity in these derivatives. The lipophilicity and electron affinity of alloxan derivatives are found to be inversely correlated, indicating that increasing chain length decreases the diabetogenicity on both counts, i.e. decrease in the electron affinity, and thus the ability to accept an electron, and increase in lipophilicity.

POSTER

Improved Synthesis of N -2'- substituted Ethanoic Acids of Succinimidyl Cand the Role of Substituents in Controlling the Conformation about Nsp^2-Csp^3 bond

Vandana Srivastava* and Shweta Srivastava

Department of Chemistry, Indian Institute of Technology (B H U), Varsnasi-221005 (INDIA)

Email: vsrivastava.apc@itbhu.ac.in

Microwave-Assisted Organic Synthesis of N -2'- substituted 9,10-dihydro anthracene -9, 10-diyl)succinimido -ethan-1'-oic acids has been achieved by reaction of anthracene-maleic anhydride Diels-Alder adduct with different amino acids. Synthesis by microwave irradiation gave the desired compounds in one step , in higher yields and in shorter reaction times than those obtained by conventional method. The carboxyl group in these derivatives remains in *anti* orientation and does not exhibit hydrogen bonding with the carbonyls of the succinimide. In case of a – OH group at 2'- position a six membered intramolecular hydrogen bonded cyclic structure orthogonal to the succinimidyl ring has been demonstrated by NMR spectroscopy.

POSTER

Design, Synthesis and Evaluation of Imidazo[2,1-B]Thiazoline as a Multi-Targeted Inhibitors of Insulin-Like Growth Factor Receptor (IGF1-R) and Epidermal Growth Factor (EGFR)

Ravindra Janrao[a], S. Balapadmasree[a], Nitin Gaikwad[a], Pradip K. Gadekar,[a] Ganesh Urunkar[a], Abhijit Roychowdhury,[a] Rajiv Sharma[a] and Sireesha kola[b] and Julie Bose[b].

[a]Department of Medicinal Chemistry, Piramal Enterprises Ltd, 1 Nirlon Complex, Goregaon (E), Mumbai-400063
[b]Research Technology, Piramal Enterprises Ltd, 1 Nirlon Complex, Goregaon (E), Mumbai-400063

Email: abhijit.roychowdhury@piramal.com

Insulin-like growth factor-1 receptor (IGF1-R) and epidermal growth factor (EGFR) are members of the receptor tyrosine kinases family[1]. Recently, several small molecule inhibitors targeting IGF-1R and EGFR have been synthesized and studied their enzymatic SAR[2, 3]. Recent literature suggested that a dual targeting of EGFR and IGF-1R may be a better strategy compared to single targeting of either of these two receptors. Literature also suggested the existence of an IGF-1R and EGFR axis and over expression of IGF-1R could be an important contributor in EGFR resistance. Thus in the quest of a dual inhibition of EGFR and IGF-1R we explore the design and synthesis of novel 2,3-dihydroimidazo[2,1-b]thiazol-benzamide as a dual kinases inhibitor for IGF-1R and EGFR.

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POSTER

Late-stage labeling and Characterization of Deuterated Mesalamine employing Heavy Water

Sabera Bijani[a], Pratik Ambasana[a], D. Padamnabhan[b] and Anamik Shah*[a]

[a] *National Facility for Drug Discovery Center, Department of Chemistry, Saurashtra University, Rajkot – 360005 (Gujarat)*
[b] *Board of Radiation and Isotope Technology, BARC/BRIT Vashi Complex Sector-20,Vashi, Navi Mumbai – 400703 (India)*

Email: anamik_shah@hotmail.com

Deuterated Active Pharmaceutical Ingredients (APIs) and New Chemical Entities (NCEs) are highly in demand in drug discovery and development sector. Deuterated organic substances show significant effects on mechanistic, spectroscopic, metabolic and several other miscellaneous physico-chemical and biological profiles, due to well-known kinetic isotope effect of deuterium.

In this study, we are reporting an efficient ***"late-stage"*** deuterium exchange methodology for the deuteration of anticoagulant drug, Mesalamine employing readily available D_2O (Heavy Water) as deuterium source. After exploring various acid/base chemistry, heterogeneous transition metal catalyzed pathway was discovered, which offer excellent yields and percentage labeling. The role of temperature, % catalyst loading and volume were examined. The deuterium labelled mesalamine was well characterized by ^{1}H NMR, ^{13}C NMR, LC-MS, HRMS techniques.

POSTER