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Abstracts – National conference on Ethnopharmacology and Biotechnology in Drug Development: Prospects and Challenges

Organized by: *Institute of Biomedical Sciences & Vaidya Ram Narayan Sharma Institute of Ayurved and Alternate Medical Education and Research, Bundelkhand University, Jhansi, UP, India*

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INTRODUCTION

Discovery and development of new therapeutic agents has been a continuing process. In-spite of the fact that large numbers of therapeutic molecules are available for human health care programs, the thrust for safer and effective medicines is increasing. There is an utmost need to understand the principles of traditional systems of medicine more precisely in the light of modern science. The fusion of Ethnopharmacology, Biotechnology and modern medicine may provide solutions to incurable diseases.

The organizing committee of National Conference on 'Ethnopharmacology in Drug Development: Prospects and Challenges' organized by Institute of Biomedical Sciences and Vaidya Ram Naryan Sharma Institute of Ayurved and Alternate Medical Education and Research, Bundelkhand University, Jhansi in collaboration with Society for Ethnopharmacology, India, welcome all the participitants to Jhansi. The conference is supported by Department of Science and Technology and Department of Biotechnology, Government of India and Sree Baidyanath Ayurved Bhawan Pvt. Ltd., Jhansi.

The conference focused on the recent developments in traditional medicines, herbal formulations, dietary supplements, phytoceuticals and pharmaceuticals from natural sources as well as role of biotechnology in drug development . The organizers extend thanks to the speakers for their willingness to participate in and contribute to the success of the programme.

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INVITED LECTURES

Trans resveratrol protects ischemic PC12 cells by inhibiting the hypoxia associated transcription factors and increasing the levels of antioxidant defense enzymes

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An *in vitro* model of ischemic cerebral stroke [oxygen-glucose deprivation (OGD) for 6 h followed by 24 h reoxygenation (R)] with PC12 cells, increase Ca^{2+} influx by upregulating native L-type Ca^{2+} channels and reactive oxygen species (ROS) generation. This reactive oxygen species generation and increase in intracellular Ca^{2+} triggers the expression of hypoxic homeostasis transcription factors like-hypoxia induced factor-1 alpha (HIF-1α), Cav-beta 3 (Cav β3), signal transducer and activator of transcription 3 (STAT3), heat shock protein 27 (hsp-27), and cationic channel transient receptor potential melastatin 7 (TRPM7). OGD insulted PC12 cells were subjected to biologically safe doses (5, 10 and 25 µM) of *trans* resveratrol in three different treatment groups, : 24 h prior to OGD (pre-treatment); 24 h post OGD (post-treatment) and from 24 h before OGD to end of reoxygenation period (whole treatment). Here, we demonstrated that OGD-R-induced neuronal injury/death is by reactive oxygen species generation, increase in intracellular calcium levels and decrease in antioxidant defense enzymes. *Trans*-resveratrol increases the viability of OGD-R insulted PC12 cells, which was assessed by using MTT, NRU and LDH release assay. In addition, *trans* resveratrol significantly decreases reactive oxygen species generation, intracellular Ca^{2+} levels, hypoxia associated transcription factors and also

increases the level of antioxidant defense enzymes. Our data shows that the whole treatment group of *trans* resveratrol is most efficient in decreasing hypoxia induced cell death through its antioxidant properties.

Challenges & issues related to quality of raw materials in pharmaceutical herbal drug industry

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There has been an increasing realization that the green medicine is safer and this has led to the spurt in the use of plant based medicines across the world and in India too. The global herbal market is about US$ 90 billion which is growing at the rate of 10-15% annually and is expected to cross 5 trillion US$ by 2030. In India there are more than 1000 herbal industries and in Uttar Pradesh there are approximately less than 1500 small herbal industries are registered. The traditional medicine in India functions through two streams i.e. the folk stream and the classical organized stream that includes the Ayurveda, Unani, Siddha etc. The folklore medicine is again routed either through the rural village based or the tribal based. Thus the use of medicinal plants amounts to around 8000 wild plants in these medicines. Although the global market of herbal drug is growing at a fast pace, the Indian share is only 2%. The major reason for this being the lack of proper quality, safety and efficacy of herbal drugs despite having in-depth knowledge in traditional herbal medicine. There are opportunities in 21st century for developing countries like India with traditional knowledge base to develop globally acceptable newer herbal drugs/neutraceuticals and convert their rich bioresources & associated traditional knowledge systems & for economic wealth & thereby bring prosperity to the nation.

Indian herbal drug industries generally face the problem of adulteration & substitution. It is observed that in herbal markets of the country, sometimes not only the various species of particular genus but entirely different taxa are being sold under the same vernacular name. For example in the name of 'Talispatra' an important Ayurvedic drug, different leaves of *Taxus wallichiana*, *Abies spectabilis* and *Rhododendran anthopogan* are being sold in Dehradun, Kolkatta & Amritsar market respectively. Similarly on the name of Pittapapra different plants viz. *Fumaria parviflora*, *Peristrophe bicalyculata* and *Oldenlandia corymbesa* and *Rungia* are being sold in various crude drug markets.

Therefore, there is a need to develop quality parameters of raw drugs, proper collection and processing along with HPTLC/HPLC finger printing to get desirable quality of raw material. Indian government has taken a number of initiatives including the preparation of the Ayurvedic Pharmacopoeia of India (AYUSH) and also preparation of monographs of individual plants in Quality standards of Indian medicinal plants (ICMR). Such initiatives are mainly aimed at providing the quality parameters for standardization of herbal drugs. Further under GTP; AYUSH, CSIR, ICMR are working together for validation of number of Ayurvedic formulations for global market. Apart from this state should have quality testing units under Dep of AYUSH or under Food and drug Authority where small herbal units can test their products.

In the whole process of development in herbal medicine/formulations based on traditional knowledge needs proper taxonomically identified safe raw material as well as scientific validation of the products. Further get constant supply of right raw material whether procured from wild or cultivated and their proper storage one has to follow. Good Agriculture Practices (GAP), Good Collection Practices (GCP), Good Ethical Practices (GEP), Good Procurement Practices (GPP), Good Safety Practices (GSP) *[Pesticide, heavy metal, microbial load as per WHO guidelines]* and Good Storage Practices (GSP).

Marine invertebrates with ethnomedicine potential: some glimpses

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Emerson and Taft (1945), Halstead (1957), Nigrelli (1958), and Burkholder (1963) were among the first to focus attention on marine research and it's potential for yielding ethno medicines. However, in the early sixties the idea of Drugs from the Sea gained popular acceptance, perhaps riding the crest of "**back to the nature**". In 1968 the first formal "**Drugs from the Sea**" conference was organized by the Marine Biology Committee at Washington D.C. On the 13th and 14th February, 1975 Marine Biomedical Research Committee meeting was held at Smithsonian Institute's Museum of Natural History in Washington D.C. About 125 scientists from all over the world attended the meeting. One of the major areas covered included Drugs from the Sea. This was the beginning of the new era in identifying various types of biomedically important molecules from the sea. Research in this field has now progressed to the state where we can now catalogue certain types of biomedically and physiologically active agents from the various classes of marine invertebrates. We have witnessed during the last 2 decades the re-emergence and resurgence of a few diseases such as Kala-Azar, Lymphatic filariasis, Malaria, Plague, Anthrax, HIV, Dangue, Hepatitis B, & C etc. It was claimed that these diseases were eradicated. The agents of these infectious diseases appear to have developed immunity or resistance to the conventional drugs in use today. The literature is replete with examples of antibiotics, aggregation factors and growth inhibitors from sponges; neurohumoral and anticoagulant agents from coelenterates; insecticide like PADAN from polychaetes; antiviral, neuromuscular and growth inhibiting, and hemolytic agents from mollusks; anti tumor agents from mollusks and sea cucumbers; cardio active agents

from arthropods; and sperm immobilizing, neuromuscular-blocking and neuroactive substances from echinoderms;. Marine invertebrates certainly show prominence in possessing biologically active substances, which can be exploited for developing important drugs beneficial to mankind. As mentioned above, many diseases of protozoan, helminthic, bacterial, viral, fungal and of unknown origin are showing re-emergence and/or resurgence. Hence, the identifica- tion and use of many biologically potent substances from sea sources as "tools" or "molecular probes" in basic pharmacological research will be of great significance to develop new drugs which could be a boon to the welfare of mankind.

Pharmacoproteomics of *Aspergillus fumigatus* for identification of novel targets of new antifungals

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The infections caused by pathogenic species of *Aspergillus* have emerged as a major threat to public health in past 2-3 decades, and the species *A. fumigatus* has been found to be primary causative agent responsible for more than 90% of such infections in lowlanders. Although a classified description of *A. fumigatus* induced infections in natives of high altitude has not been available, its pathophysiology and treatment regimens may not differ in low and highlanders.

The successful therapy of aspergillosis has been extremely difficult due to inefficient diagnostic methods and very limited number of effective drugs. The high toxicity, drug induced immunosuppression, development of resistance in fungal pathogens and high mortality even under treatment, have been major limitations of currently available anti-*Aspergillus* therapy. This necessitates identification of novel compounds for development of new antimycotic formulations with least toxicity and having alternate mechanisms of action different than those used by present drugs. Such formulations could be used to treat aspergillosis effectively.

Research attempt in this direction, resulted in identification of a synthetic coumarin derivative, called SCD-1, which had potential against pathogen *in vitro* as well as *in vivo*. The pharmaco-proteomic studies were carried out to identify the molecular targets of SCD-1 and to elucidate its mechanism of action. The results thus obtained revealed that the compound altered the expression of total 143 proteins in *A. fumigatus*, of which 4 were completely inhibited, 30 downregulated, 96 upregulated and 13 were newly expressed. Analysis of proteins for sub-cellular localization showed that 79.02% of them were localized in the cytoplasm where as only 2.10% belonged to the cytoplasmic membrane. The localization of 16.08% of proteins could not be established. A pathway map was prepared using 86 molecular targets. It was interesting to observe that SCD-1 targeted unique pathways of *A. fumigatus* including those which were specific to the pathogen.

Development of drugs based on medicinal plants: Translational and Regulatory Challenges

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Despite several decades of intensive research and development, few herbal drugs have been introduced into the public health programmes even while drug discovery strategies based on medicinal plants /natural products are re-emerging as major global strategies. In fact, several modern drugs used in the treatment of significant ailments have been developed from Indian medicinal plants like reserpine, from *Rauwolfia serpentina* (L.) Benth. ex Kurz, withanolide from *Withania somenifera* Dunal, curcumin from *Curcuma longa* L quinine from *Cinchona officinalis* L decades earlier. This could be due to more stringent regulatory systems put in place to ensure safety of medical interventions and increasing reports of the heavy metals and other contaminants found in herbal preparations. Unlike the allopathic drugs, the discovery-development of herbal-based drugs via., the conversion of a lead to a product (translational research) and bringing the lead molecule to the market (regulatory issues) face several new challenges in. The absence of credible evidence acceptable to the regulatory agencies often due to lack of rationally designed, carefully standardized experiments/trials to gather robust scientific evidence is a concern as also quality control Unlike pharmaceuticals based on a single chemical entity the safety of plant-based drugs in many cases is not well known and understood as the entire composition of the herbal preparation are not completely know. There are challenges like use of multi-ingredient polyherbals that are increasingly being explored for multi-target therapeutic formulations (from Ayurveda) for hard-to-cure diseases like cancers. Lack of systematic databases on the plant based drugs on taxonomy, chemistry, pharmacology, pharmacognosy etc. hampers the identification of potential leads for the development of safe and efficacious drugs. Several attempts are being made to addresses these challenges. Like the generation of adequate pharmaco-epidemiological evidence through well designed experiments to substantiate both safety and efficacy. Approaches like the reverse pharmacology for plant-based preparations used in traditional medical systems like Ayurveda, Siddha etc. are being increasingly being adapted. Generation of robust systems of quality assurance enhances the chance of regulatory approvals and improving the acceptance of botanical drug products and formulations will greatly help considerably bring down the wide spread skepticism about the safety and efficacy of herbals and improve acceptability. The Government of India has taken effective steps to promote the development of quality, safe, efficacious drugs. Agencies like the AYUSH in India and the US FDA have prescribed the same standards for safety and efficacy for marketing approval. The above will be discussed with some successful case studies.

Management of Diabetes Through Traditional Medicine

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Diabetes mellitus (DM) is a complex metabolic disorder that seriously troubled the human health and quality of life. It is an important human ailment afflicting many from various walks of life in different countries. In India it is proving to be a major health problem, especially in the urban areas. Conventional chemical/drugs are being used to control diabetes along with lifestyle management. However, they are not completely effective and no one has ever been reported to have fully recovered from diabetes. Though there are various approaches to reduce the pathological effects of diabetes and its secondary complications. Herbal formulations are preferred due to lesser side effects and low cost.[1]

Plants have always been a source of drugs for humans since time immemorial. The Indian traditional system of medicine is replete with the use of plants for the management of diabetes. Up to 90% of world population in developing countries uses plants and its products as traditional medicine for primary health care. There are about 800 plants in worldwide which have been reported to show antidiabetic property.[2]

The etiological factors responsible for diabetes in modern or *Prameha* in Ayurveda is somehow like similar but the onset of the diseased condition and diagnostic systems are different. According to Ayurveda kapha dosha undergoing increase, vitiates the medas (fat), mamsa (muscle) and kleda (body fluids), draws them to the urinary bladder due to the indulgence in sitting on soft cushions for long periods (thus avoiding physical activity), sleeping for long hours, use of curds, flesh of animals of domestic, aquatic or of marshy places, dietary products, fresh grains, pudding made of jiggery/sugar and finally produces prameha (diabetes). Out of 20 types of prameha 10 kinds produced by kapha are easily curable, 6 kinds by pitta are controllable and 4 kinds by vata are incurable. All varieties of prameha, if not treated in tine will ultimately become *madhumeha*. In madhumeha, the urine is like honey, which is sweet in taste and also incurable. Those incurable pramehas actually mean that they cannot be cured completely rather they are manageable with continuous monitoring with proper medication. The untreated madhumeha is further expressed very badly with various types of carbuncles, mainly in the lower extremities of the body.[2-3]

Numerous medicinal plants have been used for the management of diabetes mellitus in various traditional systems of medicine worldwide as they are a great source of biological constituents and many of them are known to be effective against diabetes. A record of various medicinal plants with their established antidiabetic and other health benefits has been reported. These include *Allium sativa, Eugenia jambolana, Panax ginseng, Gymnema sylvestre, Momrodica charantia, Ocimum sanctum, Phyllanthus amarus, Pterocarpus marsupium, Trigonella foenum graecum*, *Tinospora cordifolia, Withania somnifera Ficus religiosa, Gymnema sylvestre and* so on. All of them have shown a certain degree of antidiabetic activity by different mechanisms of action.[4]

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Biotransformation Using Cow Urine: A Boon for Exploring Potential of Medicinal Plants

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Biotransformation is the process in which suitable modification of substrate structure is achieved with the help of biological enzyme or catalyst. In this process, drug is suitably modified into another active form with the help of enzymes or bacteria or fungus.

Cow urine therapy is found helpful in Cancer, diabetes patient, aids, asthma, psoriasis, eczema, blood pressure, heartdisease, prostrate, piles, cough, phlegm, vericose veins, dismenorrhoea, cholesterol, chest pain, migraine, headache, tension, constipation, thyroid, ringworm, itching and other skin problems, liver disorder, kidney problems, gynaec and many such disease. As cow urine is useful in various manner, there is no doubt about various products which are obtained from cow urine, as the efficacy of the products may be the same or more than that of only cow urine. Thus, by considering this fact, it is envisaged to develop some novel medicines and novel molecules by treating the herbal drug with cow urine to get some better products and formulations.

One of the better way to use the cow urine is as "Biotransformation medium" in which herbal drugs are mixed with cow urine and resultant is then treated for curing the disease. With a backup of so many references on miraculous capabilities of Cow Urine, it was thought necessary to carry out some biotransformation study with it, so that some novel molecules can emerge out for treating various disorders. A case study of Microbial biotransformation, phytochemical studies, pharmacological evaluation of crude drug and their actives was performed and by considering all the facts it is found that indeed, the cow urine and it's different biotransformed products can be a boon for potentizing the crude drugs used for treating various diseases and overall health of human being.

Ethnopharmacology and Globalisation of Traditional Medicine through Evidence Based validation

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Drugs from medicinal plants are widely respected for their unique chemical and biological features, and are gaining global acceptance because they offer natural ways to treat diseases and promote healthcare. Natural products are the best sources of chemical diversity for finding new drugs and leads. The development of natural products requires the confluence of modern techniques and integrated approaches related to their research in various fields of science through International coordination and cooperation. The global health survey in 1970, boost up the use of ancient systems of medicine for better healthcare. Scientists around the world are searching for medicinal plants as alternative medicine and their potential in health care.

The development of traditional medicines with the perspectives of safety, efficacy and quality will help not only to preserve the traditional heritage but also to rationalize the use of herbal medicine in the human and animal health care. Nature is considered as a compendium for templates of new chemical entities (NCEs). The plant species mentioned in the ancient texts of different Indian systems of medicines may be explored with the modern scientific approaches for better leads in the health care. This development was supported by the diverse biodiversity in flora and fauna due to variations in geographical landscaping.

Evidence based validation of the ethnopharmacological claims on traditional medicine is the need of the hour for its globalisation and promotion.

Combining the unique features of identifying biomarkers that are highly conserved across species this can offer a promising approach to biomarker-driven drug discovery and development. Globalization of traditional medicine (TM) is necessary for health care with assessment of its safety, efficacy, therapeutic and clinical evidences. New technology and science has developed many techniques and systems to raise the natural compounds for global existence.

Natural Cyclooligopeptides: Potential Targets for Novel Drug Discovery & Development

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Medicinal plants are enriched with several active constituents responsible for their biopotency. Among these, peptides have received special attention due to their wide pharmacological profile including antimicrobial, anti-inflammatory, anti-AIDS, antimalarial, cytotoxicity, nematocidal, inhibitory activity against thrombin, trypsin, plasmin, tyrosinase and superoxide generation, calcium channel antagonistic activity and may prove better candidates to overcome the problem of resistance towards conventional drugs. Although linear peptides are associated with diverse bioactivities but cyclopolypeptides dominate over them due to the fact that inherent flexibility of linear peptides lead to different conformations which can bind to more than one receptor molecules, resulting in undesirable adverse effects. Furthermore, cyclization of peptides reduces the degree of freedom for each constituent within the ring and thus substantially leads to reduced flexibility, increased potency and selectivity of cyclic peptides. These cyclic congeners possess unusual or modified amino acid residues like Dhha, Adha, Ahoa, AHMP and exhibit their bioactivities through binding to corresponding enzymes. This characteristic feature can allow bioactive cyclopeptides to act as therapeutic agents in this resistant world. Present report includes complex structures, synthesis by solution phase technique, biopotential of natural cyclooligopeptides of plant origin.

Curcumin: a potent molecule for "Brain Self Repair" in Alzheimer's Disease

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Neurogenesis, a process of generation of new neurons, involved proliferation of neural stem cells (NSC) and neuronal differentiation in the hippocampus region of the brain. This process is found to be reduced in several neurodegenerative disorders including Alzheimer's disease (AD). Therefore, activation of neurogenesis by targeting endogenous NSC population in the brain could be a promising therapeutic approach to such diseases by influencing the brain self regenerative capacity. The neuroprotective role of curcumin is very well established in several neurodegenerative disorders. However, curcumin has poor brain bio-availability, therefore needs large quantity to achieve optimum therapeutic benefits in clinical conditions. We have designed a novel formulation of curcumin encapsulated PLGA nanoparticles (Cur-PLGA-NPs) and studied the effects on NSC proliferation *in vitro* and *in vivo*. Herein, we report that Cur-PLGA-NPs potently induce NSC proliferation and neuronal differentiation *in vitro* and in the hippocampus and subventricular zone of adult rats, as compared to uncoated bulk curcumin. Cur-PLGA-NPs induce neurogenesis by internalization into the hippocampal NSC. Cur-PLGA-NPs significantly increase expression of genes involved in cell proliferation (reelin, nestin and Pax6) and neuronal differentiation (neurogenin, neuroD1, neuregulin, neuroligin and Stat3). Curcumin nanoparticles increase neuronal differentiation by activating the Wnt/β-catenin pathway, involved in regulation of neurogenesis. These nanoparticles caused enhanced nuclear translocation of β-catenin, decreased GSK-3β levels, and increased promoter activity of the TCF/LEF

and cyclin-D1. Pharmacological and siRNA mediated genetic inhibition of the Wnt pathway blocked neurogenesis stimulating effects of curcumin. These nanoparticles reverse learning and memory impairments in an amyloid beta induced rat model of AD like phenotypes, by inducing neurogenesis. *In silico* molecular docking studies suggest that curcumin interacts with Wif-1, Dkk and GSK-3β. These results suggest that curcumin nanoparticles induce adult neurogenesis through activation of the canonical Wnt/β-catenin pathway, and may offer a therapeutic approach to treating neurodegenerative diseases such as AD, by enhancing a brain self repair mechanism.

Role of Smac/DIABLO in mitochondrial dependent apoptosis by 2-amino-3-hydroxypyridine under ambient UV R exposure

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The popularity of hair dyes use is increasing regularly as fashion trend in the world due to high demand in hair coloring and cosmetic products. 2-amino-3-hydroxypyridine (A132) is widely used as a hair dye ingredient all over the world. We are reporting first time the photosensitizing mechanism of A132 under ambient environmental UVB radiation. It shows maximum absorption in UVB region (317 nm) and forms photoproduct within an hour of UV-B exposure. Photocytotoxicity of A132 in human keratinocyte cell line (HaCaT) was measured as reduction in cell viability by mitochondrial (MTT), lysosomal (NRU) and LDH assays. Noteworthy, formation of Tail DNA (comet assay) and Cyclobutane pyrimidine dimers (CPDs) (immunocytochemistry) confirmed the photogenotoxic potential of dye. Cell cycle study (Sub-G1peak) and staining with EB/AO revealed the cell cycle arrest and apoptosis, respectively. Further, mitochondrial mediated apoptosis was corroborated by reduction of MMP, release of cytochrome c and upregulation of caspase-3. Release of mitochondrial Smac/DIABLO in cytoplasm demonstrated the caspase dependent apoptotic cell death by photolabile dye. In-addition, increased Bax/Bcl2 ratio again proved the apoptosis. The results of two dimensional gel electrophoresis showed upregulation of various proteins involved in oxidative stress, DNA damage and apoptotic cell death. Thus, study suggests that A132 induce photogenotoxicity, phototoxicity and apoptotic cell death through the involvement of Smac/DIABLO in mitochondrial apoptosis via caspase dependent manner. Therefore, the long term use of A132 dye and solar UVB exposure jointly increase oxidative stress which may cause premature hair loss, damage to progenitor cells of hair follicles and finally lead to various skin diseases in human beings including mutation and skin cancers.

Production of Rifamycin analogs by Genetic Manipulation of Rifamycin Polyketide Biosynthetic Gene Cluster of *Amycolatopsis mediterranei*to overcome the problem of MDR strains of*Mycobacterium tuberculosis*

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Rifamycin B, which can be called a Wonder Drug because of its widespread and indispensable clinical use, is produced by *Amycolatopsismediterranei* S699. It is imperative for the treatment of tuberculosis (TB), Leprosy and AIDS related mycobacterial infections. Despite its widespread use, there has been an omnipresent threat due to the emergence of drug resistance in the pathogens. This resistance, although is evolutionarily directed due to the amassment of propitious mutations, is made into a more severe a threat because of the inappropriate treatment and the denial of the patients to follow the complete regime. This is majorly due to the lack of awareness and amenities especially in the developing and under developed countries. India has been one such bearer of an impending tragedy, with accounting for more than 21% global cases in the world and having the highest number of MDR- TB patients and the first to report a totally drug resistant strain of *Mycobacterium tuberculosis*. Therefore is the dire need to develop novel analogs of rifamycin B to combat such MDR infections.

However, due to the chemical complexity of the molecule, only six chemical derivatives of it are available for clinical use. Also, other methods of modification are not generally applicable to this molecule or the producer organism.Even though, the collinear nature of the rifamycinpolyketidesynthse gene cluster was decrypted in 1988, still, genetically modifying it seemed to be a daunting task. However, we for the first time could manipulate the *rif*PKS gene cluster by combinatorial biosynthetic approach. The efforts led to the swapping of acyltransferase (AT) domain of the sixth module (AT6) of rifamycinpolyketide synthase (which adds propionate unit to the growing polyketide chain) with that of AT domain of the second module (AT2) of rapamycin PKS (*rap*PKS) (which adds acetate unit) in *Amycolatopsismediterranei* S699. The resulting mutant produced rifamycin derivative 24-desmethylrifamycin B which lacked a pendant methyl group at C-33 of the rifamycin skeletal structure, as predicted. It was confirmed using NMR and LC-MS studies. The novel analog was further converted to 24-desmethylrifamycin S & 24-desmethylrifampicin, that were found to have a better antibacterial activity than rifamycin B. The drug testing analysis of the novel analog also confirmed its better activity (ten times) against multi-drug resistant strain of *M. tuberculosis*. This study has been taken as a cornerstone for

further manipulations of *rif*PKS cluster by swapping other domains or inactivating modules for producing large number of rifamycin analogs for biological and pharmaceutical applications.

Intellectual Property Rights in herbal products: Some issues and concerns

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There is an enormous scope for India to emerge as a major player in the global herbal medicines. With over 6000 medicinal plant that are in traditional, folk and herbal medicine, representing about 75 per cent of the medicinal needs of the Third World countries, India can play a key role. Three of the ten most widely selling herbal medicines in the developed countries viz., preparations of *Allium sativum, Aloe barbedensis* and *Panax* sp. are available in India. A strong focus is, however, needed for the overall development of herbal industry in India in terms of market prospects through promotion of investments for the sustainable cultivation, processing, storage and quality control, creation of entrepreneurship *etc.* With appropriate support system and encouragement, Indian herbal medicine sector has the potential to turn out as a billion dollar industry with great employment generation potential. A major problem is the unfair exploitation of the Indian herbal wealth through patenting and other forms of intellectual property rights protection. This evident from the granting of patent rights by the United States Patent and Trademark Office (USPTO) on turmeric and neem by the European Patent Office (EPO). There are also several attempts by the global pharma industry to exploit the Indian heritage through illegal exporting and IP protection of Indian herbals used in Ayurveda. There have been serious debate globally and in India to formulate strategies that at once will prevent unfair exploitation of our herbal wealth and also provide opportunity for jobs and economic benefits to small farmers and entrepreneurs. Some suggestions to safeguard protection to knowledge, innovations and practices include: (i) Documentation of Traditional Knowledge; (ii) Registration; (iii) Development of contracts with companies for commercialization, transfer of technology, benefit sharing etc; (iv) Grant of Intellectual Property rights under existing IPR systems; and (v) Development of a sui generis system etc. The Convention on Biological Diversity (CBD) that provides for protection of genetic resources and benefit sharing for the people whose livelihood depends on the plant wealth. India has also taken several initiative to ensure that our natural heritage from biopiracy and other means of unfair exploitation. The presentation will discuss these and other strategies that countries like India should take to ensure that our natural herbal heritage is preserved and protected from unfair exploitation.

Chrysin prevents DEN initiated and 2-AAF promoted hepatocarcinogenesis: Probable role of Cell proliferation, angiogenesis, inflammation and apoptosis

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Hepatocarcinogenesis is a multistep process and it originates from a series of molecular and histopathological alterations. Chrysin (CH) is an important member of the flavonoid family. It has several pharmacological and biological properties such as anti-inflammatory, anti-viral, immunomodulatory and anti-cancer. In the present study, we investigated the chemopreventive potential of CH against Diethylnitrosamine (DEN) initiated and 2 Acetylaminofluorine (2-AAF) promoted hepatocarcinogenesis and its role in regulating the hyperproliferation, inflammation, angiogenesis and apoptosis in the liver of Wistar rats. We found that there was an upregulation of proliferation, inflammation and suppression of apoptosis in hepatic cancer group. It was found that CH supplementation suppressed the development of precancerous lesions.CH supplementation down regulated proliferation, angiogenesis and inflammation via expression of PCNA, VEGF, NF-kB-p65, COX-2, iNOS, TNF-α and IL6. There was also upregulation in the activity of caspase-9 and caspase-3 indicating apoptosis. Our findings suggest that CH has strong chemopreventive potential against chemically-induced hepatocarcinogenesis by suppressing proliferation, inflammation and inducing apoptosis.

Isolation of antihyperlipidemic and anticancer compounds from the indian medicinal plants and their chemical transformations

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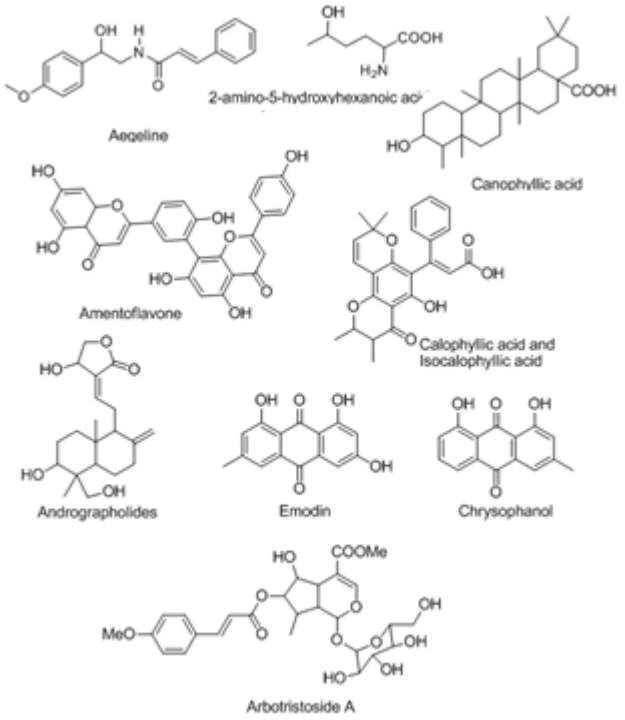
In continuation of drug discovery program on the Indian Medicinal Plants we identified several bioactive molecules for diseases such as diabetes, dyslipidemia, cancer etc. From *Aegle marmelos*[1] we identified an alkaloidal amide (aegeline), which exhibits *in vivo* antihyperglycemic activity and lipid lowering activity. A series of synthetic compounds related to aegeline have been synthesized and evaluated for their antidyslipidemic and antioxidant activity.[2,3] We isolated an unusual amino acid, i.e. 2-amino-5-hydroxyhexanoic acid from the seeds of *Crotalaria juncea,*[4] and canophyllic acid, amentoflavone and calophyllic acid and isocalophyllic acid from the leaves of *Calophyllum inophyllum*,[5] which showed lipid lowering activity in the in vivo experiments. Andrographolide has been identified

as one of the active constituents against atherosclerosis from *Andrographis paniculata*. We synthesized few novel derivatives of andrographolide to improve their antidyslipidemic, LDL-oxidation and antioxidant activity.[6] We also isolated few anticancer compounds such as anthraquinones (emodin and chrysophanol) from *Rheum emodi*[7,8] and iridoids (arbotristoside A) from *Nyctanthes arbortristis* and a large number of derivatives were synthesized and studied their activity.[9] The structure activity relationships, mechanistic aspects and improvement in their therapeutic activity will be discussed.



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Development of Diverse Glycoconjugates of Potential Chemotherapeutic Agents

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Carbohydrates are identified to play pivotal roles in various pathologically and physiologically important biological processes. The clear understanding of role of sugars in these important biological events has led to the increased demand for significant amounts of carbohydrate based molecules for their complete chemical, biological, medicinal, and pharmacological investigations. Carbohydrate-containing molecules have recognized as valuable scaffolds to an easy access of diverse library of compounds, where many of them have shown promising pharmacological activities against wide range of diseases and thus received great importance in drug discovery processes.Therefore, tremendous efforts have been made to develop novel and facile procedures to achieve the desired sugar based molecules of great biological interest; where with an increasing focus on the glycoconjugates, click reaction of an azide and an alkyne has been increasingly used in the glycoscience field including synthesis of oligosaccharides, glycodendrimers, combinatorial scaffolds, macrocycles, sialic acid-containing oligosaccharides etc. In this context along-with detailed discussions on chemoenzymatic synthesis of complex sialic acids; design and development of diverse class of sugar-based potential chemotherapeutic agents that has been executed in our lab will also be presented. The impact of carbohydrates in drug discovery and development will be presented in great detail.

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Importance, Strengths and Challenges in Packaging of Drugs & Allied Products: Quality Assurance Perspective for Research & Development

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Packaging is the vibrant technology of enclosing or protecting products for distribution, storage, sale and use. Packaging has several objectives ranging from marketing, security, information dissemination to protection from physical or environmental contamination, potion control, containment and barrier to protect from adverse effects, oxygen, water vapor, dust etc. The driving force behind packaging and product legislation is environmental concern over resource use, pollution, and waste management, coupled with the notion that businesses that manufacture and use packaging should bear some of the burden of managing packaging waste. Packaging plays a critical role in the consumer goods industry. It protects and preserves our products and raw materials as they transit through our supply chains.

The industry has a responsibility to review the packaging it uses and to ensure that any negative impact arising from its production or disposal is minimized. We must try to understand the impact of product losses that may result from the use of too little packaging materials as well the impacts of using too much. Good packaging uses only as much of the right kind of material as necessary to deliver what is required. As packaging is reduced, the range of scenarios under which product losses occur rises, until eventually a point is reached where the increase in product loss exceeds the savings from the use of less packaging material. The efficiently designed packaging will meet the requirements of the product i.e protection, promotion, convenience, unitization, handling, information dissemination etc while minimizing the economic, social and environmental impacts of both the product and its package. With e- commerce, sales using flipkart, snap deals, amazon, jabong etc to name a few and the trend toward products with short life-spans continue to develop, the volume of goods placed on the market has increased dramatically often faster than waste disposal capacity.

Packaging can be described as a coordinated system of preparing goods for transport, warehousing, logistics, sale and meet end use. Herbal medicines have a long therapeutic history and are still serving many of the health needs of a large population of the world. However, the quality control and quality assurance still remains a challenge because of the high variability of chemical components involved. Herbal drugs contain numerous compounds in complex matrices in which no single active constituent is responsible for the overall efficacy. They create a challenge in establishing quality control standards and standardization of finished herbal drugs. As per law, traditional medicine products like all medicinal products have to be registered with the Food and Drugs authority (FDA). There is a vital need of testing for safety and quality assurance before approval and registration. Recognizing that inputs could significantly contribute to improvement in the quality of life and public services, CSIR, DST, DBT institutions and well recognized universities of the world have provided R&D based solutions to mitigate the vulnerability and improve the quality of life especially for rural society. Sustainable development of rural areas can be achieved by significant technological interventions in several areas including drinking water, environment, health and food. Novelty may be through process of design, evaluation and production of specialized packages. Prominent innovations in the packaging industry were developed first for military uses and thereafter improved to meet other customer needs or demands.

Packaging designed for targeting remote areas must transport material, supplies, foods, etc. under the most severe distribution and storage conditions. Permeation is a critical factor in design. Some packages desiccants or oxygen absorbers help to extend the shelf life. Packaging may be looked for transport or distribution package can be the shipping container for transfer, store, and handle the product or inner packages. Symbols on package are important for varied purposes viz. know the type of product, direction during transportation, preventive measures. Plastic containers are extremely resistant to breakage and thus offer safety to consumers along with reduction of breakage losses at all levels of distribution and use. Organoleptic parameters, physicochemical analysis, heavy metal analysis, pesticide residue and microbial overload analysis need to be ascertained prior to usage using state of art analytical techniques viz NMR, HPTLC, GC-MS, SEM, TEM etc depending on the need. The global pharmaceutical market is undergoing rapid transformation. The pharma industry in India are witnessing trends such as acquisition activity, increasing investment, deeper penetration into the tier I to tier VI and rural markets, growth in insurance coverage and innovation in healthcare delivery. Taken together, these trends are leading to increased affordability of services to patients and access to quality medical care. We believe these trends, along with the favorable macro environment will propel the industry to the next level of growth. We must ensure for appropriate identification, assay/potency, contaminants, if any and performance as per specifications. The World Health Organization has estimated that at least 25% of all allopathic medicines contain a plant derivative. There is a growing interest of farmer for commercial plantation of medicinal and aromatic plants. The ever increasing demand for herbal products and shift in people's interest in nature has led to indiscriminate exploitation of plants and species from the forest. The investments in large-scale quality plantation are needed adopting scientific methods of cultivation. Reputable Indian and foreign companies will look to increase their market share by entering into strategic alliances, strengthening their sales forces and increasing penetration into newer markets.

The compliance with the national regulations is to improve the quality of herbal medicinal products and enhance the acceptability and efficacy for the consumers. Appropriate packaging as per international norms is important. Certification from reputable third party which is accredited internationally

reduces the regulatory burden by creating a common review and audit function in participating countries, promote public health and augment burden of revalidation from quality perspective. Thus there are great potential for packaging industry and need to adhere to the norms of National and International guidelines.

ORAL PRESENTATIONS

Boswellia serrata(L.) Extracts Down-Regulate Leukotriene C_4 Synthase mRNA Expression in HL-60 Cells & Reduces Ova Induced Inflammation In Mice.

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Ayurveda, an Indian system of traditional medicine, has described several drugs from indigenous plant sources for use in the treatment of bronchial asthma and allergic disorders. Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has risen in the recent years despite an improvement in the general health of the population (Ring et. al., 2001).[1]There are number of inflammatory diseases where increased production of leukotrienes is associated with the inflammatory process. Bronchial asthma is one such disease in which leukotrienes play a strong role and leukotriene antagonists are a potential target as far as therapy is concerned. In the present study, we briefly assess the role of *Boswellia serrata* as potential anti-asthma agents. Bronchial asthma is a chronic inflammatory condition characterized by bronchial hyper responsiveness and reversible airways obstruction. A wide range of compounds mediate these processes. Leukotrienes were identified as products of arachidonic acid metabolism and as inflammatory mediators in the late 1970. Prior to this their existence was recognized as the slow reacting substances of anaphylaxis (SRS-A). Kellaway and Trethewie[2] suggested a role of SRS-A in asthma but it was not until 40 years later that it became clear that SRS-A consisted of the leukotrienes. Hence the present study was done to investigate the in vitro and in vivo anti-inflammatory effects of *Boswellia serrata* extracts in HL-60 cells and in OVA-induced inflammation in BALB/C mice. *Boswellia serrata* (Commonly known as Guggul) barks were collected in Vidisha (M.P.), India, identified and dried. The dried plant materials were pulverized to a powder, extracted in ethanol to exhaustion, dried and fractionated. The ethanol extract and fractions were tested for their effects on leukotriene C_4-synthase, leukotriene A_4-hydrolase and Cyclooxygenase-2 in HL-60 cells. The in-vivo study was approved by the ACC at UIC prior to initiating the protocol. BALB/c mice 6-8 weeks old and ~20 g body weight were obtained from Taconic (Korideck & Peterson 2009).[3] The active dried ethanol extract of *Boswellia serrata*, was then tested in vivo in an OVA-induced asthma mouse model and inflammation was assessed using 2-D imaging. *Boswellia serrata* ethanol extracts and partitions inhibited 50% leukotriene-C_4-synthase, 22% leukotriene-A_4-hydrolase and 99% cyclooxygenase-2 (COX-2) activities in cultured HL-60 cells and down regulated the mRNA expression in HL-60 cells. The results showed significant inhibition of leukotriene-C_4-synthase, leukotriene-A_4-hydrolase and cyclooxygenase-2 (COX-2) by the ethanolic extract of *Boswellia serrata* and suggesting a possible mechanism of action for the management of asthma. Intra-gastric oral administration of the *Boswellia serrata* purified extract at the rate of 50 and 100 mg/kg body weight with HPMC in BALB mice led to a reduction of OVA-induced lung inflammation as determined by 2-D in vivo imaging using an IVIS imaging system. Extracts of *Boswellia serrata* had significant anti-inflammatory effects both in vitro and in vivo and supports the Ayurvedic use for the treatment of inflammation in asthma.

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Pharmaceutical, Nutraceutical and Bioactive compounds from cyanobacteria

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Cyanobacteria are ubiquitous in nature and are next to bacteria in their distribution. This is large group of Gram negative prokaryotes , have found many traditional applications, is being utilized and further explored for biotechnological development. Cyanobcateria are increasingly attracting the attention of the biologist in view of their importance in agriculture, environment pollution abatement , conservation , biodiversity and pharmaceutical market. The fact of that cyanobacteria is general and marine form in particular , are one richest sources of known and novel bioactive compounds including toxins with wide pharmaceutical applications. In the recent years, single cell protein has attracted the attention as a major source for increasing protein supply. The yield of protein from cyanobacterial organisms has been shown to be much higher (45% on dry weight basis) as compared to other agricultural crops. The potentiality of *Spirulina* as a food for humans is exploited in many countries. There are several reports on the amino acid liberation and accumulation in bacteria by using analogue-resistant mutants.The paper summarizwd the progress made so far in cyanobacteria , and highlights various areas of applications mainly pharmaceutical , nutraceautical and proactive potential.

Isolation and functional characterization of antibacterial and apoptosis inducing compounds from *Alstonia scholaris*

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The crude extract of leaves and bark of *Alstonia scholaris* has long been used in treatment of various disorders in Ayurvedic & Siddha medicine. We have collected leaves from this plant from various parts of India and isolated single band phytochemicals from the leaves using column chromatography followed by TLC. Subsequently, we have tested their antibacterial activity and cytotoxicity on several bacterial stains and cultured mammalian cell line respectively. Importantly, standard phytochemical assay (Harbone method) showed that alkaloids, saponins, phenolics were found maximally in the middle of solvents series in leaves obtained in summer. On the contrary, winter's leaves showed maximum alkaloids and flavonoids in methanol extract, whereas saponins and phenolics are found markedly less. All the fractions from summer leaves were screened by measuring antibacterial activity following zone of inhibition methods. We observed that 58th and 128th fractions showed antibacterial activity over all the strains *Staphylococcus epidermidis, Staphylococcus aureus, Escherichia coli, Bacillus licheniformis and Pseudomonas fluorescens*. Significant results were found using different concentration of 58th fraction on *B. lechinoformis* and 128th fraction on *S. epidermidis* and *S. aureus* which had produced bigger zone of inhibition than equivalent dose of chloramphenicol, a commercially available antibiotic. We have also screened column fractions having cytotoxicity on HeLa cells through MTT assay. Those fractions were used to measure nuclear fragmentation and observed that 30th, 57th and 58th fractions were capable of inducing apoptosis as detected by nuclear fragmentation and apoptotic body formation after treactment of 16 hr. The minimum LD_{50} for nuclear fragmentation 4.5 µg/ml was observed for 58th fraction.

Antimicrobial activity of extracts of *Sesbania grandiflora* leaf

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Sesbania grandiflora (Fabaceae) is commonly known as sesbania and agathi, used as an important dietary nutritive source and often planted for its edible flowers and pods in Southeast Asian countries. In the present study, petroleum ether, chloroform, alcoholic and aqueous extract of leaves of *S. grandiflora* were screened for antibacterial and antifungal activity against various microbial stains by disc-diffusion method. The extracts produced mild antibacterial activity against the bacterial strains (*Bacillus cereus*, *Micrococcus luteus*, *Staphylococcus epidermidis*, *Clostridium sporogens*, *Streptococcus faecalis*, *Streptococcus pyogens*, *Staphylococcus aureus*, *Bacillus subtilis*, *Agrobacterium tumifaciens*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Serratia marcesens*, *Entobacteria aerogens*, *Proteus vulgaris* and *Escherichia coli*), and only petroleum ether and alcoholic extracts exhibited mild antifungal property against the tested fungal strains (*Cryptococcus neoformans, Gibberella fugikoroi, Rhizophus oligosporus, Neurospora classa, Myrothecium verrucasia, Aspergillus niger* and *Candida albicans*) compared to standard drugs.

Nanoconjugates of natural products: pharmacological and therapeutic potential in cancer therapy

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Nanomedicine has helped in the improving the delivery of natural drug molecules many fold to the target organs and brought about tremendous possibilities for application in treating the life threatening diseases. Application of nanomedicine concepts in development of anticancer drugs with high therapeutic index is a subject of considerable interest in cancer chemotherapy. The biological activity and toxicity of low molecular weight natural product based anticancer drugs depend on their physicochemical and pharmacological properties, which contribute to the pharmacokinetics, biodistribution, cellular retention, and bioavailability in the target tissue or organ. The activity and toxicity associated with an anticancer drug can be modulated by altering the physicochemical properties, such as lipophilicity, cellular uptake, and prolonged activity through chemical conjugation. Different nanoparticles viz. gold nanoparticles, silver nanoparticles, carbon nanotubes, fullerenes have been applied as delivery system for natural products and drugs.

Doxorubicin is natural product used in treatment of cancer. A number of delivery systems have been designed for delivery of Doxorubicin by various group and reported in high impact literature, but in most of cases the anti-cancer activity of system remain very low compared to parent doxorubicin and none has reached to clinical applications. Herein, I will discuss rational of delivery systems for this important drug and further development of prodrugs by our group. We designed and evaluated molecules to find out the reason for low activity and by systematic study developed Doxorubicin prodrugs having novel pharmacological profile with many fold increased delivery to target cells. Herein, a number of lipophilic derivatives of Doxorubicin hemisuccinate will be discussed which were synthesized through conjugation of doxorubicin-14-hemisucinate with different fatty amines or tetradecanol to enhance the lipophilicity, cellular uptake, and cellular retention for sustained anticancer activity. Also doxorubicin conjugates

with cell penetrating cyclic peptides will be discussed. The synthesized conjugates inhibited the cell proliferation of human leukemia (CCRF-CEM, 69-76%), colon adenocarcinoma (HT-29, 60-77%), and breast adenocarcinoma (MDA-MB-361, 66-71%) cells at a concentration of 1 μM after 96-120 h incubation. Flow cytometry analysis showed a 3-fold more cellular uptake of lipophilic compounds when compared to that of doxorubicin alone in SK-OV-3 cells. Confocal microscopy revealed that the conjugates were distributed in cytoplasmic and perinuclear areas during the first 1 h incubation and slowly relocalized in the nucleus after 24 h. The cellular hydrolysis study showed 98% of compounds were hydrolyzed intra-cellularly within 48 h and released the parent drug. The pharmacological and cellular evaluation of these new prodrugs showed novel properties with potential for clinical application and showcased the rational for development of delivery systems for this drug.

Design and Optimisation: PLGA based Nano Lipid Carrier (NLC) of Piperine

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Development of an effective formulation involves careful optimization of a number of excipients and process variables. Sometimes the number of variables is so large that even the most efficient optimization designs require a very large number of trials which put stress on costs as well as time. A creative combination of a number of design methods leads to a smaller number of trials. This study was aimed at the development of nanostructured lipid carriers (NLCs) by using a combination of different optimization methods. A total of 11 variables were first screened using the Plackett–Burman design for their effects on formulation characteristics like size and entrapment efficiency. Four out of all variables were found to have insignificant effects on the formulation parameters and hence were screened out. Out of the remaining variables, four (concentration of tween-80, PLGA, sodium taurocholate, and total lipid) were found to have significant effects on the size of the particles while the other three (phase ratio, drug to lipid ratio, and sonication time) had a higher influence on the entrapment efficiency. The first four variables were optimized for their effect on size using the Taguchi L9 orthogonal array. The optimized values of the surfactants and lipids were kept constant for the next stage, where the sonication time, phase ratio, and drug:lipid ratio were varied using the Box–Behnken design response surface method to optimize the entrapment efficiency. Finally, 11 variables were optimized for the development of NLCs with a size of 141:53 ± 1:5 nm, zeta potential of 34:6 ± 0:53 mV, and 97:21±2:05% entrapment efficiency. In-vitro drug release studies were performed and evaluated by Koresmeyer Peppas equation, Higuchi kinetics and Coefficient of regression. Results of present study indicate that the investigated system has potential to remain at the desired site for prolonged period and is capable of maintaining a constant drug concentration, and effective targeted delivery can be achieved by surface modification of Nano Lipid Carrier.

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Natural or Semi-synthetic Biodegradable Nanoparticles in Drug Delivery and Targeting

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Nanotechnology deals with size dependent branch of science, which restrict matter generally in the 1–100nm dimension range.[1] Nano-medicine is one of the achievements in the field of ***medical sciences*** and is an important application of nanotechnology. This principally concerns the use of precisely engineered materials at this dimensions scale to develop novel therapeutic and diagnostic modalities.

Nanotechnology focuses on formulating therapeutic agents in biocompatible nano-composites such as nanoparticles nanocapsules, micellar systems, and conjugates. While these systems are often polymeric and submicron in size, they may be used with versatile advantages in drug delivery process.[2, 3]

These days, all over the world, many researchers are investigating the potential use of polymeric nanoparticles as carriers for a wide range of drugs for therapeutic applications. With special reference to biodegradable nanoparticles (NPs) which are gaining increased attention for their ability to serve as a viable carrier for site specific delivery of vaccines, genes, drugs and other bio-molecules in the body.[4] Because of their flexibility and ample range of properties, biodegradable polymeric nanoparticles are being used as novel drug delivery systems.[5] In particular, this class of transporter holds remarkable promise in the areas of cancer therapy and controlled delivery of vaccines. Besides they offer enhanced biocompatibility, superior drug/vaccine encapsulation, and convenient release profiles for a number of drugs, vaccines and

biomolecules to be used in a variety of applications in the field of medicine.

This paper will sum up and presents the good number of outstanding contributions of biodegradable polymeric nanoparticles and nanotechnology in the field of medical sciences as a drug delivery systems and targeting.

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Flavonoids & its complexes in the treatment of diabetes

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NIDDM (Non-insulin dependent diabetes mellitus), a metabolic disorder leading to chronic morbidity and increasing mortality due to changing life styles particularly in urban Indian population. Different module of drugs targeting insulin modulation are known to treat the disease as insulin sensitizer and/or stimulator of insulin secretion. However due to non-responsiveness of patients after treatment for some time, requires drugs acting with some other mechanisms. Agonists of β_3-adrenergic and PPAR receptor modulators stimulate the oxidative pathway to dissipate heat without the synthesis of ATP and thereby lower plasma sugar and lipids profiles. Oxidative stress plays a key role in diabetes for macrovascular complications.

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

The inhibition of PTP-1B is a potential target for treatment of type-2 diabetes. V & Zn complexes have insulin-enhancing activities, and while vanadium compounds inhibit PTP-1B, little is known on the mode of action about Zn compounds.[4] V is not only an important trace element for organisms but also the necessary element for human body. It has been demonstrated that many V-Compounds possess therapeutic effects as insulin mimetics.[1, 2] Many clinical trials of V-compounds have also been reported[3, 4] in which vanadium salts such as $VOSO_4$ and $NaVO_3$ were administered to diabetic patients. There are various V and Zn compounds have reported for anti-diabetic activity.

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

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Antiulcer and Antioxidant potential of *Zizyphus Jujuba Linn.* root extract in Aspirin and Ethanol induced Gastric Ulcers.

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The present study was carried out to investigate the antiulcerogenic and antioxidant potentials of *Zizyphus jujuba linn.* in experimental animals. The aqueous extract from the plant roots was subjected to acute oral toxicity studies according to OECD guidelines no 423. The two dose levels were then selected i.e. 150mg and 250 mg/kg body weight and were further evaluated for antiulcer activity in aspirin and ethanol induced gastric ulcer in wistar rats. Our finding reveals that aqueous extract exhibited significant ($p<0.05$) and dose dependent anti-ulcer activity in two of the ulcer models. The ulcer index was prepared and compared with the standard drug omeprazole. The plant extract showed significant inhibition of ulcers formation (protection) in aspirin and ethanol induced ulcer model compared to vector control. Based on ulcer index, percentage protections of 76.92% in aspirin model and 70% with a dose of 250 mg per kg body weight of extract, in ethanol induced ulcer model were observed. To rule out general mode of plant extracts for antiulcer activity due to their antioxidants potential which protect the mucosal wall from the free radical induced damage. We have evaluated *in vitro* antioxidant activity of water extract from roots of *Zizyphus jujuba linn.* using 1,1-diphenyl 2-picryl hydrazyl (DPPH), hydrogen peroxide

(H_2O_2)free radical scavenging and reducing power compared to ascorbic acid. Aqueous root extract showed free radical scavenging power comparable to ascorbic acid. To test oral toxicity and lethal dose, various doses of root extract viz. 2.5, 5.0, 10 and 20 times of effective doses were fed to rats and their gross behaviors was observed for 2, 6 and up to 24 hrs, no mortality was noted till 5000 mg/kg body weight of root extract, indicated high level of safety for consumption. To determine the chemical composition of plant extract, phyto-chemical screening of root extract was carried out, presence of tannins, alkaloids, saponins and flavonoids were confirmed chemically. Our results suggest that the aqueous extract from the roots *Zizyphus jujuba linn.* posses antiulcer and antioxidants potentials as claimed by its folkloric use. These results supported the ethnomedical use of Zizyphus *jujuba linn.* root extract of the treatment of gastric ulcer.

Generation of autophagic flux as a protective response against xenoestrogen Bisphenol-A induced neurotoxicity in the rat brain

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The widespread usage of xenoestrogen Bisphenol A (BPA) and its exposure on human health has raised concern all over worldwide. BPA is used chiefly as a monomer for the production of polycarbonate and epoxy resins. The exposure to BPA occurs mainly by consumption of contaminated foods and beverages that have contacted epoxy resins or polycarbonate plastics. BPA is released from the plastic polycarbonate drinking bottles and induces apoptotic cell death in the hippocampal neuronal cells by the generation of reactive oxygen species (ROS). However, the cellular and molecular mechanism(s) underlying the effects of BPA on autophagy, and association with oxidative stress and apoptosis are still obscure. Autophagy is a catabolic process involving in turnover of long-lived proteins and dysfunctional organelles. In our study we observed that BPA exposure during early postnatal period up-regulated the expression and the levels of autophagy genes/proteins in the hippocampus region of the rat brain. Knowingly, this increase in LC3-II levels can be either due to increased autophagosome formation or a block in autophagosome maturation. BPA treatment in the presence of bafilomycin A_1 (a lysosomal proton pump inhibitor) increased the levels of autophagy markers LC3-II and SQSTM1 (p62) and also potentiated GFP-LC3 puncta index in GFP-LC3 transfected hippocampal neural stem cells derived neurons, suggesting that autophagic flux is generated against BPA induced neurotoxicity. BPA induced oxidative stress and ATP depletion was alleviated in the presence of pharmacological activator of autophagy (rapamycin). Pharmacological (wortmannin and bafilomycin A_1), and genetic (beclin siRNA) inhibition of autophagy exacerbates BPA induced neurotoxicity. We found that silencing AMPK using AMPK siRNA even worsens BPA induced neurotoxicity, suggesting that autophagy generated against BPA is arbitrated by the activation of AMPK pathway. Moreover, silencing the mTOR enhances autophagy which further alleviate BPA induced ROS generation and apoptosis in neuronal cell. Our results suggest that autophagy is generated against BPA neurotoxicity via modulation of the AMPK and the mTOR pathways.

New chemical entities (NCE's): Concept, Synthesis and Identification

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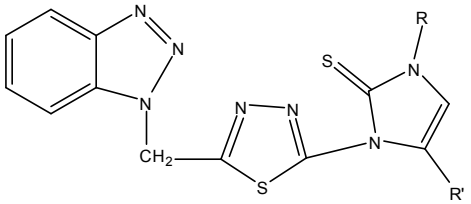
Benzotriazole, thiadiazole and imidazole nuclei showed diversified pharmacological activities. In view of potential biological activities of these nuclei it was considered worthwhile to synthesize some novel derivatives of benzotriazolo-thiadiazolyl-imidazole (X) and screen out some of the derivatives which are more potent, more efficacious and relatively safer compare to traditional one and develop some structure activity relationship (SAR).



X

The major challenges to synthesis some new chemical entities (NCEs) in today's scenario are practicing green chemistry i.e. choice of solvent is restricted to safest one for biological system and process must be economic one by selecting shortest possible route of synthesis.

Photosensitized 1, 2, 3, 4 dibenzanthracene causes MMP and DNA damage mediated apoptosis under UVR

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1, 2, 3, 4 dibenzanthracene (BNZ) is a polycyclic aromatic hydrocarbon (PAHs), produced by incomplete burning of fossil fuels and discharge of petroleum products, it tends to adsorb on atmospheric particles, incorporate into soils, sediments and produce a long-lasting contamination to ecosystem. BNZ showed strong absorption maxima (λmax) in UV-A (320-400nm) with low absorption under UV-B (280-320nm). BNZ undergoes various photochemical reactions under ultraviolet radiation (UV-R) exposure and generates free radicals and photoproducts. UV-A photoirradiated BNZ generates $^1O_2$ and induces lipid peroxidation. Photochemical analysis of BNZ showed generation of ROS & lipid peroxidation. Phototoxic effects of BNZ were assessed on HaCaT cell line. Results of MTT and Neutral red uptake assays showed significant reduction in cell viability under sunlight and UV-A (2.7J/cm^2). DCF fluorescence intensity confirmed intracellular ROS generation by BNZ ,while genotoxicity was assessed through comet assay. Formation of malondialdehyde, showed the lipid peroxidation by BNZ. AO/EB double staining suggested BNZ enhanced apoptosis in HaCaT cell line. BNZ significantly upregulates Bax and downregulates Bcl-2 gene and protein expressions. Translocation of Bax to mitochondria seen by JC-1 staining, resulted in mitochondrial membrane potential reduction. BNZ generates ROS via type II mechanism, reduction of antioxidant level and activation of apoptotic pathway, which promotes apoptotic cell death.

Ameliorative role of Ascorbic acid against *para*-nonylphenol induced toxicity in Testis of male *Mus musculus (P)*

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Present investigation aimed to study, whether *para*-nonylphenol (p-NP) induced, oxidative stress in the testis of male *Mus musculus* and co-administration of ascorbic acid can ameliorate any possible oxidative stress. For which 20 male *Mus musculus* (P) were divided in to four groups of 5 each. Group I served as control receved normal diet and water adlibitum, group II exposed with (250 mg/kg/0.2ml/day) *para*-nonylphenol orally and Group III exposed with *para*-nonylphenol along with co-administered with ascorbic acid (10ppm) and While, Group IV supplemented with ascorbic acid alone for 30 and 60 days, and histopathological, enzymological *i.e.* ACP and ALP and biochemical parameter *i.e.* cholesterol and protein levels were carried out. In histological observations, noted that *para*-nonylphenol disrupted somniferous tubules with degenerative change in spermatogenic cells and reduced number of spermatozoa in lumen, disorganized with highly atrophied in condition characterized by severe degenerative and pycknotic changes were seen in spermatozoa and leydig cells after 30 and 60 days. While, the animals supplemented with vitamin-C alongwith *para*-nonylphenol up to 30 and 60 days showed recoveries in testicular cells. In connection to this, the enzyme activities *i.e.* ACP and ALP and biochemical parameter *i.e.* cholesterol levels were significantly elevated and protein levels were significantly decreased by *para*-nonylphenol in 30 and 60 days treatment, However, there change were become lowered towards normalcy when vitamin-C supplemented along with *para*-nonylphenol.

Prenatal cypermethrin exposure restrains neuronal differentiation and maturation in the adult rat brain

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Neurogenesis is the process of generation of new neurons from the multipotent neural stem cells in the hippocampus and subventricular zone, and is associated with learning and memory regulation. Cypermethrin, a photostable synthetic type II pyrethroid is used in a wide variety of household and agricultural insecticides. Cypermethrin is known to elicit several neurochemical and neurobehavioural deficits. Here we evaluated whether oral exposure of cypermethrin during gestational day 7-21 alters postnatal hippocampal neurogenesis in the adult brain. We found that cypermethrin treatment significantly decreased pool of neural progenitor cells (NPC) and bromodeoxyuridine (BrdU) positive cell proliferation. Further co-localization of BrdU with doublecortin (DCX), Neuronal nuclei (NeuN), and GFAP (glial fibrillary acidic protein) suggested decreased neuronal differentiation and increased glial differentiation. Cypermethrin caused a significant decrease in the mRNA expression of the neurogenic genes/transcription factors such as neuregulin, neurogenin, neuroD1 and upregulation of gliogenic gene STAT3. These results suggest that early gestational exposure of cypermethrin diminishes the NSC pool, reduces generation of functional

neurons in the hippocampus and enhances neurodegeneration resulting in cognitive impairment in the adult rats.

Keywords: Neurogenesis, neural stem cells, neuronal differentiation, cypermethrin

The Biomatrix: Aggrandizes Drug Resistance and Immuno-suppressive Responses of Biofilm Cells

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In recent scenario rise in drug resistance within biofilm cells has emerged as a leading cause that has direct correlation with evolving severe clinical infections caused by biofilm. The biofilm matrix composed of hydrated extracellular polymeric substances unveiling unique properties which suppress host immune responses and limits antibiotic diffusion through its three dimensional structure. The biomatrix increases this resistive power manifold in immuno compromised individuals and in patients with implanted devices. In this article attempt has been made to review the research work carried out on different adaptive strategies performed by biomatrix to protect biofilm cells against external stresses like drugs and host immune responses. The mechanism involving in adaptive strategies such as limiting penetration of antibiotics, antiphagocytic properties of matrix, oxidation of ethanol, action of cyclic glucan, extracellular genetic material (eDNA), genetic switches and matrix microenvironment are highlighted. Studies show that mechanism of each individual strategy varies significantly with each other however collectively all these provide extensive shield to biofilm cells. A new therapeutic strategy is desperately needed to combat persistent biofilm infections. While much research has been done on the biology of biofilms, no one genetic factor has been identified by mutagenesis to effectively and uniformly control biofilm development. Identification of compounds/natural products with antibiofilm activities could be beneficial for better control of bacterial sterilization, controlling drug resistance and could potentially be used as prophylaxis.

Ameliorative role of Saffron against Zearalenone induced toxicity on morphology of female mice *mus musculus*

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The *Fusarium* species mycotoxin metabolite Zearalenone (ZEA) mimics the animal body production of estrogen and interferes with conception, ovulation, reproductive organ development and fetal development in farm animals as well as in humans. This research paper gives an overview about acute and chronic toxicity of ZEA and ameliorative role of saffron on interior and exterior morphology of female mice (*Mus musculus*). The morphological changes were seen, when six animals of each experimental group for (30, 60 and 90 days) were administrated with ZEA intraperitonially (IP) with (2.5mg/kg. bwt.) via dimethyl sulphoxide (DMSO) and oral administration of saffron (50mg/kg. bwt.). Post of each experiment, we observed that estrogenic mycotoxin reduces body weight with increased reproductive organ weight ($p < 0.01$) followed by swelled ovaries, uterus, enlarged teats, and prolapsed vagina. However, animals treated with ZEA+saffron exhibits normal morphology of mice. Besides this, animals treated with saffron alone, reveals normal architecture of teats, vagina and reproductive organs. The experimental investigation observed saffron ameliorates toxicity of zearalenone and protected the morphology of reproductive and its associate organs.

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Bioactive Electrospun Nanofibrous Scaffolds Loaded with Gentamicin and Immobilized with rhRGF to Promote Quick Diabetic Wound Healing

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The pathophysiology of diabetic ulcers is very complex due to the disturbances at proliferation or inflammation phases which ultimately lead to perturbations of the process of normal wound healing. Other complications include microbial infections at the wound bed. Tissue engineering technologies involving growth factors produce one of the most advanced generation of diabetic wound healing materials. The rationale of the present study was to design a dual nanofibrous carrier system for the release of gentamicin sulphate and recombinant human epidermal growth factor at the wound site for hastening the process of diabetic wound healing and eliminating infection. PLGA/gelatin polymer solutions containing gentamicin were electrospun into nanofibrous scaffolds using electrospinning technique and thereby immobilized with recombinant human epidermal growth factor (rhEGF) through covalent immobilization. The physicochemical characterization of the fabricated nanofibrous scaffolds was carried using Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FTIR) and X Ray Diffraction (XRD). The scaffolds exhibited *in vitro* antibacterial activity comparable to pure gentamicin powder. The *in vitro* release kinetics of rhEGF was evaluated using ELISA kit and it showed a controlled and sustained release profile with an initial burst effect and 82.4% of the immobilized rhEGF was released on the 1st day. *In vivo* wound healing efficiency was confirmed on diabetic animals with dorsal wounds and the scaffolds exhibited faster wound healing as compared to the control. This study suggested that rhEGF immobilized PLGA/gelatin nanofibrous scaffolds promoted quick wound healing in diabetes patients and could be used as a promising wound healing material. The obtained results are promising, since the benefits of delivering bioactive molecules within a dual carrier material to inactivate bacteria in diabetic wounds and simultaneously quicken wound healing by stimulating the cellular processes were clearly shown, and can enhance the applicability of delivery systems in wound healing applications.

Hepatoprotective mechanism of *Polygonum bistorta* and *Aristolochia indica* against liver failure

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The present study was carried out to observe the hepatoprotective effect and antioxidant activity of the aqueous extract of the roots of *Polygonum Bistorta* (PB) (100 mg/kg)[1] and *Aristolochia Indica* (AI) (100 mg/kg)[2] in rats treated with sub chronic exposure of carbon tetrachloride (0.15 ml/kg, *i.p.*). Extract of PB and AI at the tested doses restored the levels liver and kidney function tests with liver homogenate enzymes (glutathione peroxidase, glutathione-S-transferase, superoxide dismutase and catalase enzymes significantly)[3-4]. The activities of DNA damage by comet assay and MTT assay significantly recovered the damage towards normal[5-6]. This study suggests that *Aristolochia Indica* has a more liver protective effect in comparison of *Polygonum bistorta* and against carbon tetrachloride-induced hepatotoxicity and possess antioxidant activities and extracts exhibited moderate anticancer activity towards cell viability at higher concentration.

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Soil amendments and concerns about Public Health-an Indian perspective

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Organic amendments have been the one of the important source of plant nutrients. Their use allows better management of resources to counter changes in soils that result from essential practices for crop production. They provide macro- and micronutrients, including carbon for the restoration of soil physical and chemical properties. Challenges from the use of organic amendments arise from the presence of heavy metals, toxic organic compounds, recalcitrant compounds and the inability mineralize the organic forms of N and P into the forms available to crops, and particularly to minimize the losses of these nutrients in forms that may present a threat to human health. Animal manure, industrial sludge, discharges from hospitals and dense colonies and sewage biosolids, the organic amendments in greatest abundance, contain components that can be hazardous to human health, other animals and plants. Pathogens pose an immediate threat. Antibiotics, pharmaceuticals and hormones may be hazardous if they increase zoonotic disease organisms that are resistant to multiple antimicrobial drugs. Some approaches aimed at limiting N losses (e.g. covered liquid or slurry storage, rapid incorporation into the soil, timing applications to minimize delay before plant uptake) also tend to favor survival of pathogens. Risks to human health, through the food chain and drinking water, from the pathogens, antibiotics and hormonal substances that may be present in organic amendments can be reduced by treatment before land application, such as in the case

of sewage biosolids. A more holistic approach to management is required as intensification of agriculture increases.

Some sacred ethnomedicinal plants of Bundelkhand region

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Sacred groves are distributed across the globe, and diverse cultures recognize them in different ways encoding various rules for their protection. Many indigenous communities all over the world protect forest patches by dedicating them to local deities. Such forest pockets, referred to as sacred groves, are pieces of forests and or clusters of trees maintained on socio-religious grounds. Sacred groves occur in many parts of India. India is a land of diverse natural resources. It is also a country with the strongest traditions of nature conservation anywhere in the world. Since time immemorial, conservation of natural resources has been an integral aspect of many indigenous communities all over the world in general and India in particular. It is true that India has suffered an almost unabated devastation of its natural biological heritage, and much of what remains has been preserved through the ages because of a host of conservation-oriented socio- cultural and religious traditions. One such significant tradition of nature conservation is that of dedicating patches of forests or groves to some deities and spirits by the local people, both tribals and non-tribals. Such forest pockets, referred to as sacred groves are more or less small to large chunk of traditionally preserved near-virgin forests maintained through people's partici-pation. Sacred groves are islands of biodiversity protecting a good number of plant and animal species including some rare, threatened and endemic taxa. Folklores play a significant role in confirming the beliefs associated with the sacred groves. The sacred plants of India are actually worshipped throughout the nation owing only to its mythological significance. In India various god and goddess are worshipped in Hindu religion throughout India. Plants flowers and leaves are used during worship for pushpa-puja and patra-puja. Many sacred plants are also traditionally used as medicinal plants to cure various human ailments.

An attempt has been made to identify folklore medicinally important plants frequently used by rural communities of sacred groves of Bundelkhand region. A total of 40 medicinal plants from 38 genera under 31 families were enumerated. Most of the plants are used for curing earache, skin diseases, fever, cold, headache, cough, urinary disorder, ulcer, etc. Plants of family Poaceae were largely represented (5 species), followed by Fabaceae and Moraceae.

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Therapeutic and enthanobotanical analysis of *Terminalia arjuna* plant

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Arjuna is a 40-60 feet tall tree found in sub-himalayan, central and southern part of India. It is among the most valuable plants used in Unani, Ayurveda, Tibetian and Homopathy medicine. It bark is a rich source of flavinoids like arjunoline, ajunone, phytosterol, anti-oxidants as well as good source of minerals like copper, zinc, calcium. Its phytochemical constituents are effective in treating asthma, hypertension, ear infection, ulcer, liver problem and highly effective in LDL-cholestrol, ischemic heart diseases. A recent survey showed that 80% of world population is dependent on traditional herbal medicines especially India and China like developing countries. It is an attempt to find out the pharmacological properties of *Terminalia arjuna* which are effective for controlling various kinds of ailments.

Mast Cell De-granulation Inhibitory Effect of *Bacopa monniera* (L.) Pennell.

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The present was done to see the effect of obtained fraction of *Bacopa monniera* extract on sensitized albino rats for the inhibition of mast cell de-granulation activities. The evaluation of the mast cell de-granulation inhibitory activity were tested in Wistar albino rats, after the approval of animal research protocol from IAEC committee of CPCSEA No. 804/2003. The rats were sensitized on days 0, 7 and 14 with i.p. injections of 50 µg OVA (Grade V, Sigma-Aldrich) together with 2 g of Alum in phosphate buffered saline (PBS). Rats were injected i.p. with 50 µg Ova and 2 mg Alum of saline solution on day 0 of the experiment. This procedure was then repeated on day 7 and 14. Control rats (n=5) received i.p. injections of PBS only. On days 21 to 24, both the control and OVA sensitized rats were challenged intra-nasally daily with 100 µg of OVA in saline. For the positive treatment group, dexamethasone (Sigma-Aldrich) 100 µl was injected intra-muscularly at a dose of 10 mg/kg body weight 4 h before each daily intranasal OVA challenge on days 21 to 24 as previously described by Korideck and Peterson[1] and Soni et al.[2] In addition, on days 21-24 the rats were also treated with the *Bacopa monniera* extracts suspended in PBS by gastric lavage at a dose of 50 and 100 mg/kg b.w. All the rats were sacrificed on day 21 and lungs were taken out and kept it into ringer solution for 48 hrs. Then, put it in 70 %

alcohol till 48 hrs for fixation of the tissues. After fixation blocks were prepared using "L" pieces and trimmed section were cut using rotator microtome apparatus at 6 µ thickness. Then, mast cells were demonstrated in lungs tissues sections. Staining was carried out in metachromasia using toluidine blue, then photographs was taken at 450X magnification in the microscope**.** Both intact as well as de-granulated mast cells as well as total number of mast cells in the 5 high power fields of each section of slides were recorded on 40X magnification for calculation of Percentage of mast cells. Results were expressed as the average number of mast cells per high power field. In the present study, inhibition of mast cell de-granulation activity was evaluated using active fraction (BM-2) of *Bacopa monniera* in anaphylactic Wister albino rats. Rats of group I was served as control which was neither sensitized nor treated but sacrificed for the estimation of mast cells which were found 88.64±0.17% intact and 11.36±0.20 % de-granulated. The sensitized groups II showed 13.76±0.89% intact mast and 86.22±0.89% de-granulated mast cells. In the rats of group III which was treated with the fraction of *Bacopa monniera* extract (BM-2), by giving doses 50 mg/kg body weight orally with Acacia gum to the rats group, the de-granulation of mast cells were found 28.45±0.61% and intact mast cells were found 71.53±0.62 %. When the second dose of 100 mg/kg body weight of *Bacopa* extract was given to rats, the de-granulation of mast cells were found 23.63±0.42 % and intact mast cells were found 76.35±0.42 %. Besides this, when these doses were compared with the dose of standard/reference drug dexamethasone 10 mg/kg/body weight, it was observed that the de-granulation of mast cells was found to be 20.63±0.53 % and intact mast cells was found to be 79.35±0.53%. It appears that the de-granulation of mast cells is quite dosed dependent. It is inversely proportional to the doses, as the doses increases, the de-granulation of mast cells decreases. However, the anti-asthmatic/ anti-histaminic activity was found to be the directly proportional to the doses because the number of intact mast cells was found to be increasing simultaneously with increasing the doses. The results when compared to the control seem to be quite significant at the rate of $p < 0.001\%$.

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Effect of different storages on mycoflora of groundnut

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Groundnut (*Arachis hypogea*) is called the king of oil seeds. The groundnut is commonly known as moongphali belongs to Angiosperm family *Fabaceae.*

Storage of peanut is increasingly becoming important both among growers and user. After harvesting seeds are stored in different storage conditions and if these storage conditions are not proper various microbes interact with these seeds. Among these microbes, fungi play a dominant role in decreasing quality and longevity of the seeds. The present study deals with effect of type of storage on dynamics of storage fungi of Groundnut. The seed mycoflora of three groundnut varieties: Mainpuri, Chandra, and Rajasthani were studied by standard blotter method and Agar plate method. The dominant species isolated were *Aspergillus spp., Cercospora spp., Aspergillus flavus , Rhizopus spp. Acremonium alternata, A. niger, Aspergillus terreus, A.versicolor, Fusarium solani, Fusarium spp., Mucor spp., Penicillium spp., Penicillium citrinum, Rhizopus stolonife and Curvularia lunata etc.*

If was found that storage type in variably affected seeds in storage. The percentage incidence of storage fungi varied at different storage methods. Maximum fungi were colonized with seeds taken from plastic jars and minimum colonization was observed from seed stored jute bags.

Neuroprotection of Neurogenesis: A Lead from Phytochemicals

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Bioactive constituents from both medicinal and food plants are able to improve human health. Use of these phytochemicals, including phenylpropanoids, isoprenoids and alkaloids, through either correct dietary habits or in pharmacological preparations not only promote health benefits but also protect against the chronic degenerative disorders, such neurodegenerative diseases. In this presentation, we briefly deal mainly with Withania somnifera (WS) commonly used in traditional medicines, focusing on their neuroprotective actions. WS is one commonly prescribed Rasayana drug which is used in Indian traditional medicinal system and Ayurveda. Clinical trials and animal research supported the use of WS for treatment of anxiety, cognitive and neurological disorders icluding senile dementia, Alzheimer's (AD) and Parkinson's disease (PD). It has also been used to treat stress, dementia and insomnia. In AD links between the disease and deficiency of neurotransmitter Acetylcholine (Ach) and high Nitric oxide (NO) has been reported. High NO is deleterious to neuronal cells and contributes to disease progression. Reversal of the deficiency by alleviating the level of neurotransmitters or use of agonists are the treatments used for AD and related diseases. But these treatments are not ideal and provide only symptomatic relief. Recently, we reported that WS root extract, can increase ACh level by increasing Choline acetyltransferase (ChAT) expression, and serotonin level in hippocampus. ACh in turn inhibit NO producing enzyme NADPH-d as well. We demonstrated the correlation between distribution of cholinergic neurons and Nitergic neurons in various fore brain regions, and proposed a hypothesis that ACh inhibits NADPH-d activity. In present study we investigated the effects of fresh leaf juice of

WS on AChE and nNOS activity *in vivo* and *in vitro* to understand the potential therapeutic mechanism of the WS in AD or related diseases. Observation of histochemical colocalization of AChE and NADPH-d activity in same sections showed significant reduction in number of cells positive for both the enzymes after WS treatment as compared to cells localized AChE or NADPH-d. Biochemical study of AChE and NADPH-d levels in brain tissue also showed significant dose dependent inhibition of the activity of both the enzymes after WS treatment. These studies suggest that WS directly inhibit AChE thus increase ACh level. To check whether NO is also inhibited directly, in *vitro* study was carried out using primary hippocampal cell culture to confirm that increased acetylcholine (ACh) inhibits the nitric oxide (NO), as significantly low nitrite level was observed as compared to control. Study thus suggests that WS significantly inhibit both, AChE and NADPH-d activity but inhibition of AChE is direct, while NADPH-d is inhibited indirectly. This study might be important for therapeutic implications of WS in neurodegenerative disorders such as Alzheimer's (AD) where inhibition of both AChE and nNOS is important.

Study of Ethnomedicinal Potential of Some Plants Used by Rural Inhabitants in Villages of Datia District, Madhya Pradesh

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The work on 'study of ethnomedicinal potential of some plants used by rural inhabitants in villages of datia district, Madhya Pradesh' was done .Under present study following aspects were investigated.

- *To study diversity of traditionally used medicinal plants of studied area.*
- *To explore general health problems of the region.*
- *To document medicinal values of the plant diversity being used by rural inhabitants of area.*

The present study included 70 species of ethno-medicinal plants distributed in 67 genera belonging to 41 families. The rural communities were using these plants to treat the various ailments and diseases. The highest numbers of Ethnomedicinal plants were recorded in two families namely Fabaceae and Solanaceae, having 11 and 04 plants species, respectively. Six families were contributing 03 species. Two plant species were reported from four families namely Amaranthaceae, Asclepiadaceae, Lamiaceae and Verbenaceae. However, rest of the reported families contributes only one species each. Tree (31) was found to be the most utilized plant followed by herb (19), shrub (05), under shrub (04), grass (04) woody climbers (03) in descending order. Out 70 plant species 03 plant species namely *Capsicum annum, Datura metel, Ocimum sanctum* showed diverse habit like herb or under shrub, while 01 plant species showed habit shrub or small tree. Among the different plant parts the leaves were found to be most frequently used part for the treatment of various diseases and ailments followed by Root, Bark, Seed, Fruit, Whole plants, Flowers, Pods, Latex, Twigs, Shoot, Pulps, Gum, Thorn, Stem, Rhizome, and Tuber *etc.*

The flora of district Datia of Bundelkhand region has immense pharmaceutical and commercial potential. There are several species in this district with very rich commercial importance, but are valuable only in the wild. The knowledge of ethno-medicinal plants used is mainly restricted to local healers and it is very important to document this knowledge for future generation, otherwise it will vanish forever. Throughout the region there is an urgent need to support, safeguard and promote cultural and spiritual values of traditional medicines. Also, to test the scientific validity of the herbal preparation or drugs, clinical studies are required to be conducted. This can establish therapeutic properties of these preparations for safe and longer use. The indigenous knowledge and uses of herbal medicinal plants of a particular area have to be analyzed to develop appropriate management measures of *ex-situ* and *in-situ* conservation for best utilization of natural resources. Many developing countries have intensified their efforts in documenting the ethno-medicinal data on medicinal plants and research to find out scientific evidence for claims by tribal healers on Indian herbs has been intensified. Once these local ethno-medicinal preparations are scientifically evaluated and disseminated properly, people will be better informed regarding efficacious drug treatment and improved health status.

Evaluation of Antibacterial activity of sequentially extracted organic solvent extracts from seeds of Nigella sativa

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Present study was designed to evaluate in-vitro antibacterial activity of sequentially extracted different organic extract from seed of *Nigella sativa* with special focus on *Mycobacterium bovis*. Antibacterial activities of various solvent extract were determined by Disc agar diffusion technique using impregnated filter paper disc on inoculated LB and 7H11 agar medium. The three extracts from seed of *N. sativa* were prepared sequentially using petroleum ether, dichloromethane and methanol in soxhlet apparatus followed by complete removal of solvent in rotaevaporator. Dilutions of the extracts were prepared in DMSO in the ratio of 1:5 and antibacterial activity was assessed in *Mycobacterium bovis, Salmonella enterica, Escherichia coli* and *Mycobacterium smigmatis*. The three extract showed

pronounced dose dependent activity with maximum activity exhibited by Petroleum ether extract followed by dichloromethane and methanolic extracts. Maximum zone of inhibition against *Mycobacterium bovis, Salmonella enterica, Escherichia coli* and *Mycobacterium smigmatis* were 18mm, 20mm, 15mm and 10mm respectively. Our study indicates that petroleum ether extract shows better antibacterial property against *S. enterica* and *M. bovis* as compared to *E. coli* and *M. smigmatis*. Purification of active principle from antibacterial extracts may lead to identification of novel chemical antibacterial candidate molecule. Further studies on its mechanism of action may lead to development of new mode of antibacterial defense.

Effect of homoeopathic preparations of *Rauwolfia serpentina* on deoxycorticosterone acetate (DOCA)-salt induced hypertensive rats

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Hypertension is the main risk factor for the development of cardiovascular diseases and renal failure. *Rauwolfia serpentina* (Sarpagandha) has been used in Ayurvedic and Homoeopathic medicines for the treatment of hypertension. Homeopathically prepared *Rauwolfia serpentina* Q is the most commonly used drug for hypertension by the homoeopaths. The present study was undertaken to study the antihypertensive effect of different potencies (Q, 30c and 6c) of homoeopathically prepared *Rauwolfia serpentina* in deoxycorticosterone acetate (DOCA)-salt induced hypertensive rats. Hypertension was induced in unilaterally nephrectomized adult male Wistar rats by injecting DOCA (25 mg/kg BW) subcutaneously twice in a week and 1% NaCl in drinking water for thirty five days. The DOCA-salt hypertensive rats showed a significant increase in systolic blood pressure, diastolic blood pressure, heart rate and organ weight (kidney, heart and liver). Hypertensive rats were treated with different potencies of *Rauwolfia serpentina* orally three times a day for thirty days. Administration of homeopathic preparations of *Rauwolfia serpentina* to hypertensive rats resulted in reduction of systolic and diastolic blood pressure without any effect on the heart rate. Elevated serum sodium level in hypertensive rats were reduced in response to 30c and 6c potencies of the drug. Serum levels of AST and LDH of hypertensive rats were lowered in response to various potencies of the drug. However, serum glucose and creatinine levels of hypertensive rats decreased and increased significantly in response to 6c potency of the drug, respectively. These results suggest that *Rauwolfia serpentina* acts as an antihypertensive drug against DOCA-salt induced hypertension.

Ameliorative role of Vitamin-C against Dimethoate toxicity on Testis and Ovary of air breathing Fish *Clarias batrachus* (Linn.)

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In the present investigation we observed that the toxicity of organophosphate insecticide, Dimethoate on testis and ovary of *Clarias batrachus* and neutralizing role of vitamin-C against dimethoate induced toxicity. It is moderately toxic by ingestion, inhalation and dermal absorption, it is readily absorbed through the skin (Secaucus, 1991). Experimental fishes were divided into four groups. Group Ist served as control while, group IInd exposed with dimethoate (45µg/l), group IIIrd received dimethoate (45µg/l) and supplemented with vitamin-C (50mg/l),while, group IVth received vitamin-C (50mg/l) only for 30 and 60 days and all groups received normal diet commercially available fish food (2g/fish). After the treatment the testis and ovary was removed carefully and was quickly fixed in aqueous bouin's fluid for routine histological study. The histopathological alterations revealed a degeneration and highly diminished seminal vesicles showed hypotrophied and diminished seminiferous tubules in testis and the ovary showing significant changes on degenerated germinal vesicles (GV), stromal hemorrhage, disorinited size of GV, vacuolization in nucleus and damage of germinal epithelium cells. However, the animal's supplemented vitamin-C along with dimethoate showed recoveries towards normalcy in their histomorphological changes after 30 and 60 days in comparison to dimethoate induced group. Deka and Mahanta (2012) reported adhesion of primary follicle, cytoplasmic retraction and clumping, cytoplasmic degeneration and vitellogenic membrane in the ovary of *Heteropneustes fossilis* treated with organophosphate. Zutshi (2005) also observed that the appreciable reduction in size, with spermatids and sperms in degenerating condition, and necrosis of interstitial cells after fenthion treatment in fish, *Glossogobius giuris*. In conclusion, this study suggests that the toxicological effect of dimethoate alters morphological and physiological functions in testis of *Clarias batrachus* by modulating the histopathological changes while, these changes can be ameliorated by vitamin-C because of its antioxidant properties.

Caspase 3 dependant apoptotic cell death induced by benzophenone-1 through mitochondrial signaling pathway at environmental UVR

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Benzophenone 1 (BP-1), a commonly used UV stabilizer is an active ingredient of different cosmetic preparations. Current practices have increased its popularity with increasing solar UV radiation. A complete safety assessment for its topical application is a major concern of this study. Phototoxic potential of BP-1 was assessed using the human keratinocyte cell line under the exposure of sunlight/UVR. Photodegradation study showed that BP-1 was not stable in sunlight. Results of MTT and NRU assays showed significant decreased in cell viability under sunlight (30 min), UVA (2.7J/cm^2) and UVB (1.08J/cm^2). DCF fluorescence intensity confirmed intracellular ROS generation by BP-1. Genotoxic potential of BP-1 was measured by comet assay and it was further confirmed through CPD formation. Formation of MDA, outcome of photodynamic lipid peroxidation was estimated. AO/EB and annexin V/PI double staining suggest that BP-1 enhanced apoptosis in HaCaT cells. Flowcytometric analysis showed sub G1 population which represents apoptotic cells. BP-1 significantly increased Bax and decreased Bcl_2 protein levels, favor translocation of Bax to mitochondria and resulted in decrease of MMP, measured by JC-1 staining. It permeablised outer membrane of mitochondria triggered the release of cytochrome c and Smac/DIABLO into cytosol, as measured by immunocytochemistry. A significant increased in Apaf-1 protein was noticed, activation of caspase 3 protein was observed, suggesting apoptosis by BP-1.Thus, the study suggests, that BP-1 induces mitochondrial mediated apoptosis via caspase 3 activation. Our finding may provide new insight to understand the mechanism involved in photoxic reactions of sunscreens products for its topical application.

Keywords: phototoxicity, DNA damage, caspase 3, apoptosis and UVR

Protective role of ascorbic acid against toxicological effect of cyclophosphamide on reproductive parameters of male *rattus norvegicus*

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Cyclophosphamide (CP) is an anticancer drug, which is commonly used against malignancies, such as leukaemia, lymphoma, breast, lung, prostrate, and ovarian cancer. Considering various reports on the possible antioxidant/protective functions of ascorbic acid, the aim of this study is to evaluate the side effect of CP and ameliorative role of ascorbic acid (Vitamin-C) on male albino rat in response to body weight, sperm motility, sperm count, and testicular histological changes.

Sixty adult male albino rats (*Rattus norvegicus*) were divided into four groups of fifteen each. Group I served as control received an intraperitoneal (i.p.) injection of physiological saline as vehicle and fed with standard rodent food and water *ad libitum*. While, group II received CP dose *i.e.* 9 mg/kg. b. wt. and were introduced alternative day for period of 15, 30 and 60 days. However, group III was treated with CP dose (9 mg/kg. b.wt.) through i.p. injection and animals were also supplemented with ascorbic acid (Vitamin-C- 100 mg/kg. b.wt) via distilled water for 15, 30 and 60 days. Group IV was supplemented with only ascorbic acid. After 15, 30 and 60 days testis and cauda epididymis were dissected outweighed and semen analysis was performed.

Body weight, sperm motility and sperm count in male *Rattus norvegicus* were decreased significantly in all the experimental groups as compared to the control group; however we also found testicular histological changes in the same group. Whereas, ascorbic acid significantly ameliorates the effect of CP on the aforesaid parameters especially in 30 and 60 days treated groups. In conclusion ascorbic acid improved and protected against adverse effect of cyclophosphamide on body weight, sperm motility, sperm count and testicular histological changes. However, vitamin-C has protective effect against cyclophosphamide-induced reproductive toxicity. The mechanism is largely unknown but empirical supplementation of vitamin-C would be recommended before and during cyclophosphamide chemotherapy.

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Evaluation of food-drug interaction potential of *Aegle marmelos* through metabolism mediated cytochrome P450 inhibition assay

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The aim of present study was to evaluate the possible food drug interaction of the standardized extract of the *Aegle marmelos* fruit and their bioactive compound with cytochrome P450 isozymes. Interaction potential of the extract was evaluated by CYP450-carbonmonoxide complex (CYP450-CO) assay in combination with pooled microsome. Influence on individual isoforms of commercially available major recombinant human cytochrome P450 drug metabolizing enzymes such as CYP3A4, CYP2D6, CYP2C9 and CYP1A2 isozymes were analyzed through fluorescence screening assay and their IC_{50} values were determined. Bioactive compound was quantified through RP-HPLC, in order to standardize the sample material. The screening of toxic heavy metals in the fruits is important for protecting public health against the hazards of metal toxicity. Metals concentration in *Aegle marmelos* fruit was also determined through atomic absorption spectrometry analysis. *Aegle marmelos* extract showed higher IC_{50} value than the standard and lower than the bioactive compound imperatorin. *Aegle marmelos* extract showed significantly less ($P<0.001$, $P<0.01$) interaction potential than the standard known inhibitors. The result findings indicate that selected sample is unlikely to cause clinically relevant drug interactions involving the inhibition of major CYP isozymes. The concentrations of heavy metals were found to be within the prescribed limits and other trace metals were present in significant amount.

Oral insulin delivery by means of Solid lipid Nanoparticles

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The aim of this work was to produce and characterize cetyl-palmitate-based solid lipid nanoparticles (SLN) containing insulin, and to evaluate the potential of these colloidal carriers for oral administration. SLN were prepared by a modified solvent emulsification evaporation method based on a w/o/w double emulsion. The particle size, zeta potential and association effi- ciency of unloaded and insulin-loaded SLN were determined and were found to be around 350 nm, negatively charged and the insulin association efficiency was over 43%. After oral administration of insulin-loaded SLN to diabetic rats, a considerable hypoglycemic effect was observed during 24 hours. These results demonstrated that SLN promote the oral absorption of insulin.

Standardization of Bhuvnesvara Vati- An Ayurvedic Formulation

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Standardization of Ayurvedic formulation is essential in order to assess the quality of drugs for therapeutic value. The present work is an attempt to standardize "Bhuvnesvara Vati", an Ayurvedic formulation, used for diarrhoea in ayurvedic medicine. The various parameters performed included swelling index, foaming index, Heavy metal and Microbial analysis and high performance thin layer chromatography (HPTLC) analysis. The results obtained may be considered as tools for assistance to the regulatory authorities, scientific organizations and manufacturers for developing standard formulation of great efficacy.

Screening of Antiosteoporotic Activity in Post-menopausal Osteoporosis

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Postmenopausal osteoporosis, a silent epidemic, has become a major health hazard, afflicting about 50% of postmenopausal women worldwide, and is thought to be a disease with one of the highest incidences in senile people. It is a chronic, progressive condition associated with micro-architectural deterioration of bone tissue that results in low bone mass, decreased bone strength that predisposes to an increased risk of fracture. Women are more likely to develop osteoporosis than men due to reduction in estrogen during menopause which leads to decline in bone-formation and increase in bone-resorption activity. Estrogen is able to suppress production of proinflammatory cytokines like IL-1, IL-6, IL-7 and TNFα. This is why these cytokines are elevated in postmenopausal women. This paper deals with the various methods and parameters most frequently used for screening of antiosteoporotic activity in post-menopausal osteoporesis. The ovariectomized animal model is the most appropriate model for studying the efficacy of different drugs to prevent bone loss in postmenopausal osteoporosis. Various parameters analyzed are: Biomechanical parameters as Three point bending of tibia, Compression IV lumbar vertebra, Loading test of femoral neck, Bone mineral density measurement; Biochemical parameters viz. serum calcium and inorganic phosphorus, serum alkaline phosphatase (ALP), Tartrate resistant acid phosphatase (TRAP), protein profile, serum ACTH, corticosterone, IL-6, TNF-α, osteoprotegerin (OPG) and deoxypyridinoline crosslinks to creatinine ratio (DPD/Cr); Physical parameters like thickness

and the length of the femur, weight of femur, Femur bone volume, bone density etc; Histopathology of femur to observe histopathological changes like size, shape and bone architecture; disruptive and lytic changes and fibrocartilageneous matrix with osteodystrophy; restorative progress with mineralization along with fairly well distributed osteocytes; trabeculae and matrix, and shaft size etc; Histopathology of tibia to observe bone area, bone volume per tissue volume, bone perimeter, absolute number of active osteoblasts, the ratio of the absolute number of active cuboid osteoblasts per bone perimeter, the ratio of the absolute number of osteoclasts per osteoclast perimeter which represent part of the trabeculae that are covered with osteoclasts, trabecular thickness, trabecular separation, trabecular number, mineralized bone volume per tissue volume, the osteoid volume per bone volume, the osteoid surface per bone surface, the osteoblast surface per bone surface, the eroded surface per bone surface. Other parameters as Histopathology of uterus and mammary gland tissue, body weight, organ weight, food consumption, Estrogen receptor ligand binding assay (ER-LBA), determination of oxidative stress.

Curcumin Loaded chitosan nanoparticles ("nanocurcumin"): a novel therapy for diabetes mellitus

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Introduction and Objectives: Curcumin, a yellow polyphenol extracted from the rhizome of turmeric (*curcumin longa*) has potent antidiabetic properties, but the medicinal properties of curcumin cannot be utilized due to its low bioavailability. Therefore, numerous approaches have been undertaken, there is an extensive need for combinatorial extract "curcumin with piperine" and use of "Nanoparticle based drug delivery approaches" have the potential for rendering hydrophobic agents like curcumin dispersible in aqueous media, thus circumventing the pitfalls of poor solubility. Thus, in the present study the different formulations of curcumin was evaluated for their comparative anti-diabetic efficacy against streptozotocin induced diabetes mellitus.

Methods: A freshly prepared solution of STZ (45 mg/kg body weight) in 0.1M citrate buffer, pH 4.5 was intraperitoneally injected to overnight fasted rats to induce diabetes in the experimental animals. Animals will divided into seven groups; normal healthy group (N group), streptozotocin–induced diabetic group (STZ group), curcumin treated diabetic group (C group), Nanocurcumin treated diabetic group (NC group), curcumin+piperine treated diabetic group (C+P), Piperine treated diabetic group (P) and allopathic treated drug, glibenclamide (Gl group). Each group has six animals. Curcumin (400mg/kg body weight), nanocurcumin (100mg/kg body weight), Piperine (2mg/kg body weight) and glibenclamide (600µg/kg body weight) was administered orally as doses. Blood glucose levels and body weight of rats were measured at weekly intervals. Other biochemical parameters such as glycosylated hemoglobin, lipid profile and biomarkers of oxidative stress, degree of DNA damage, liver and kidney function markers were also measured.

Results: In 30 days of study blood glucose reduction was found in curcumin (58.6%), curcumin+piperine (50.2%) and nanocurcumin (63%). There was also a significant decreases in total cholesterol, triglycerides, HDL-Cholesterol and Very Low Density Lipoproteins . Also, the curcumin nanoparticles showed significant antioxidant activity. The kidney and liver functions remained normal. The body weights of diabetic rats were also improved after daily administration of the curcumin nanoparticles. Effect of Nanocurcumin therapy on Lipid profile, Kidney function, Liver function and antioxidant are more significant than curcumin and curcumin in combination with piperine.

Conclusion: The results indicate that the nanocurcumin is a more potent anti-diabetic than curcumin and curcumin with piperine.

Evaluation of sequentical administration of aqeous and fermented extracts of 'Diabegon' in subjects with type II diabetes mellitus

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Introduction: Phytochemical formulations appear to play a significant role in control and management of human type II diabetes mellitus. The present study investigated the effect of sequential administration of a aqueous and fermented versions of a poly herbal formulation 'Diabegon' for two months on glycemic levels, lipid metabolism and oxidative stress in human subjects with type 2 diabetes mellitus

Material and methods: A total of 15 human subjects with type 2 diabetes mellitus were recruited for the study and all anthropological and biochemical parameters were recorded at the time of registration. The subjects were given hot water extract and fermented extract obtained from 10 gm of "Diabegon" powder, "Diabegon kwath", on an empty stomach everyday in the morning for 2 months. The therapeutic functions of the "Diabegon kwath" was assessed by monitoring the blood glucose levels at 15 days intervals and glycosylated hemoglobin, lipid profile and biomarkers of oxidative stress, liver and kidney function markers at before and after therapy.

Results: Oral administration of aqueous diabegon for 30 days followed by fermented diabegon for next 30 days to same subjects resulted in significant reduction ($p \leq 0.05$) on blood glucose level. A significant increase in HDL with concamittant reductions in total cholesterol, triglycerides, LDL and VLDL were recorded. A significant improvement in glycosuria and

proteinuria, DNA damage and C-peptide levels was also observed. Also, the subjects exhibited a significant improvement in enzymatic and nonenzymatic biochemical markers of oxidative stress. The kidney and liver functions remained normal and in fact improved in many subjects.
Conclusions: The study thus revealed significant therapeutic application of 'Diabegon' in treatment of type II diabetes mellitus. Further, studies on more number of subjects are needed to further elucidate its role. Identification of target pathways and detailed phytochemical analysis are to be undertaken in order to further ascertain the role of these phytochemical extracts in addressing various metabolic derailments observed in type II diabetes mellitus.

Efficacy of *Azadirachta indica* in regulation of metabolic abnormalities induced by streptozotocin in Wistar rats

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Introduction: In traditional practice, medicinal plants are widely used in many countries for the treatment of diabetes mellitus. *Azadirachta indica* is a fast growing evergreen popular tree and is a source of bioactive compounds such as Azadirachtin, meliacin, gedunin, nimbidin, nimbolides, salanin, nimbin, valassin, meliacin. The present study evaluated the anti-hyperglycemic, anti-hyper-lipidemic and anti-oxidant potentials of *Azadirachta indica* in an experimental model.

Methodology: A freshly prepared solution of STZ (45 mg/kg body weight) in 0.1M citrate buffer, pH 4.5 was intraperitoneally injected to overnight fasted rats to induce diabetes in the experimental animals. Animals will divided into four groups of six animals each; normal healthy group (N group), streptozotocin–induced diabetic group (STZ group), Neem treated diabetic group (C group), and glybenclamide treated group (Gl group). Aqeous extract of neem leaves was administered at a dose of 500mg/kg body weight for 28 days. Group. Blood glucose levels and body weight of rats were measured at weekly intervals. Other biochemical parameters such as glycosylated hemoglobin, lipid profile and biomarkers of oxidative stress, degree of DNA damage, liver and kidney function markers were measured at the end of treatement.

Results: Streptozotocin induced diabetic rats exhibited significantly higher fasting blood glucose levels (435.4 ±11.2mg/dl) as compared to those of normal rats (89.0±2.0mg/dl). 28 days therapy of ethanolic extract of *Azardirachta indica* leaves, showed significant reductions in fasting blood glucose levels(51%), plasma triglycerides levels (15%) total cholesterol level (8.1%). A significant increase in HDL-C level (23.75%) with concomitant decrease in LDL-C level (24.08%) was recorded. A significant improvement in enzymatic and non-enzymatic biomarkers of oxidative stress was recorded following Neem therapy. The DNA damage as assessed by Comet assay showed marked improvement. Kidney and liver functions were normalized.

Conclusion: The aqueous extract of Neem proved effective in treatment of ailments associated with abnormalities of glucose and lipid metabolisms.

Efficacy of six months administration of 'Diabegon kwath', a Polyherbal formulation to subjects with type II diabetes mellitus

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Introduction: Diabetes mellitus can lead to a host of complications which may include macro and micro vascular complications and the conventional anti-diabetic therapies are reported but it shows many side-effects the goal of treatments is to prevent its acute manifestations. The study aimed to investigate the antihyperglycemic, antihyperlipidemic and antioxidant functions of a Polyherbal formulation, "Diabegon kwath", in human subjects with type 2 diabetes mellitus.

Material and methods: A total of 33 human subjects with type 2 diabetes mellitus were recruited for the study and all anthropological and biochemical parameters were recorded at the time of registration. The subjects were given hot water extract obtained from 10 gm of "Diabegon" powder, "Diabegon kwath", on an empty stomach everyday in the morning under for 6 months. The therapeutic functions of the "Diabegon kwath" was assessed by monitoring the blood glucose levels at monthly intervals and glycosylated hemoglobin, lipid profile and biomarkers of oxidative stress, liver and kidney function markers at three monthly intervals during the course of study.

Results: Daily administration of hot water extract of "Diabegon" regularly for 6 months resulted in significant reductions of blood glucose and glycosylated hemoglobin levels. There was also a significant increase in high density lipoprotein cholesterol levels with concomitant decreases in total cholesterol, triglycerides, low density lipoprotein cholesterol and very low density lipoprotein. A significant improvement in glycosuria and proteinuria was also observed. Also, the subjects exhibited a significant improvement in enzymatic and nonenzymatic biochemical markers of oxidative stress. The kidney and liver functions remained normal and in fact improved in many subjects.

Conclusions: The study which is first of its kind, advocates "Diabegon kwath" as a safe and effective Ayurvedic therapy for the treatment of human type 2 diabetes mellitus and further placebo controlled trial may substantiate the therapeutic efficacy of the formulation.