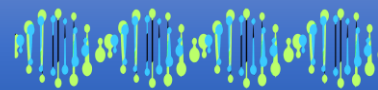
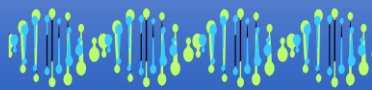


A National Conference On  
*“The Opportunities of Pharmacy in Current Scenario”*

**Supported By**



Organised By  
**Mosofiya Conference**  
(A Part of Mosofiya Group)



## Message

*It is a matter of great pleasure for me to write this message. The Mosofiya Conference, deserves appreciations for the visionary approach in bringing improvement in the quality of education in pharmaceutical sciences by organizing National Conference on “The Opportunities of Pharmacy in Current Scenario”.*

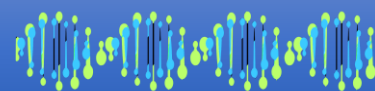
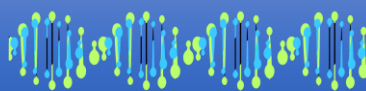
*This will be certainly be an ideal platform for the Scientists, Researchers, faculty as well as the students to have exchange of ideas on different aspects of pharmacy profession as a whole. Certainly, this Conference will provide an excellent approach towards research and development.*

*Organizing such Conference will upgrade the personal and professional mortals of individuals.*

*I wish the organizers and the core members of the Conference for the grand success.*

*Dr.A.K.S. Rawat*  
*Executive Director, Ethno-Medicine Research Centre Imphal*





सीएसआईआर-केन्द्रीय औषधि अनुसंधान संस्थान  
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वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद्  
COUNCIL OF SCIENTIFIC & INDUSTRIAL RESEARCH

March 6, 2018

It gives me immense pleasure to know that Mosofiya Conference is organizing a national conference on the topic "The Opportunities of Pharmacy in Current Scenario" which will provide a platform to share knowledge and experiences of pharmacy profession and will focus exclusively on pharmaceutical education, research & development, manufacturing, marketing and health sector.

The theme of the conference is very appropriate in the present context. I hope it will provide an opportunity for novel scientific deliberation interactive session that will be source for information and inspiration.

I carry my best wishes for the success of the conference. I hope that this conference would be beneficial to the participants & delegate for their future growth and development.



Dr. W. Haq  
Chief Scientist & Head  
Medicinal and Process Chemistry Division

सेक्टर 10, जवाहरनगर विस्तार, सीतापुर रोड, लखनऊ-226 031 (भारत)  
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### *Message*

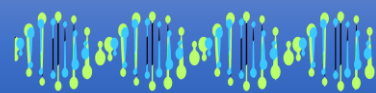
*I am glad to know that Mosofiya Conference organizes one day National Conference on the topic “ **The Opportunities of Pharmacy in Current Scenario**”. Many experts from industry, Research and Academic institutions are participating in the conference to share views, experiences , opinions’ and latest trends in the field of pharmacy which undoubtedly enrich the knowledge of participants from different parts of India.*

*I congratulate the organizers for providing the scientific platform for the interaction and wonderful scientific deliberations.*

*I am wishing all the best for successful completion of the National Conference.*

*Prof. (Dr.) Shubhini A. Saraf  
Head of Pharmaceutical Science, BBAU, Lucknow*





### *Message*

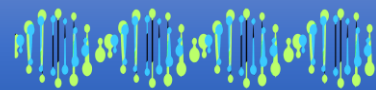
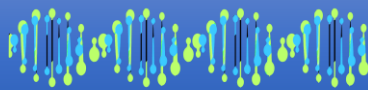
*It is a matter of great pride and pleasure that Mosofiya Conference is organizing a National Conference on the topic “ **The Opportunities of Pharmacy in Current Scenario**”. The proposed conference will certainly be an ideal platform for exchange of thought, ideas, innovations, recent advances in the field of Pharmaceutical education and its employability.*

*I convey my best wishes for the success of the conference. I hope that this conference would be beneficial to the participants and the delegates for their future research and development.*

*On this occasion, I extend my best wishes to the organizers of this Conference.*

*Prof. (Dr.) Shailendra K. Saraf*  
*Director Pharmacy, BBDNIIT, Lucknow*





### *Message*

*I am indeed glad to know that that Mosofiya Conference is organizing a National Conference on the topic “**The Opportunities of Pharmacy in current Scenario**”. Many experts from industry, Research and Academic institutions are participating in the conference to share views, experiences, opinions’ and latest trends in the field of pharmacy which undoubtedly enrich the knowledge of participants from different parts of India.*

*On this occasion, I extend my best wishes to the organizers of this National Conference with all success and fruitful outcomes.*

*Prof. (Dr.) Hefazat Husain Siddiqui  
Adjunct Professor, Integral University*





## *Message*

*I am indeed glad to inform you that Mosofiya Conference is organizing a National Conference on the topic “**The Opportunities of Pharmacy in current Scenario**”. Many experts from industry, Research and Academic institutions are participating in the conference to share views, experiences , opinions’ and latest trends in the field of pharmacy which undoubtedly enrich the knowledge of participants from different parts of India.*

*I as a chairman of Mosofiya group will be honored to welcome you and see your kind present at the National Conference on 11<sup>th</sup> March 2018 to be held at Scientific Convention Centre, KGMU, Lucknow. I particularly express my gratitude to the entire guest speakers who have come long way for the conference from their busy schedule. I hope that this conference would be beneficial to the participants and the delegates for their future research and development.*

*On this occasion, I extend my best wishes to all my team members of Mosofiya group for their kind support for making this National Conference with all success and positive outcomes.*

*Dr. Mohd. Sohrab  
Chairman, Mosofiya Group, Lucknow*





## *Message*

*I on the behalf of organizing committee welcome you all to National Conference on the topic “The Opportunities of Pharmacy in Current Scenario” at Scientific Convention Centre, Lucknow.*

*This conference is going to discuss self reliance, Sustainability & affordability of Pharmaceutical sector by improving process through innovation so that India can be more competitive and self reliant on pharmaceutical Products. Scientists across the country will participate as Keynote / Invited speakers to address the above mentioned issues.*

*This will be certainly be an ideal platform for the scientists , researchers, faculty as well as the students to have exchange of ideas on different aspects of pharmacy profession as a whole. Certainly this Conference will provide an excellent approach towards research and development.*

*I assure you a memorable experience being here in Lucknow with an excellent opportunity to enjoy conference and explore the city simultaneously.*

*Please join us in making this conference a success, which aims to promote the development and advancement of pharmacy services and research in the region.*

*Thank you and looking forward to welcome you at the conference.*

*Prof. (Dr.) Mohammad Imtiyaz Ahmad  
Organizing Secretary*







AMITY  
UNIVERSITY

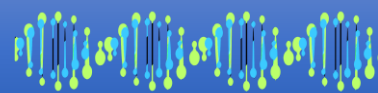
### *Message*

*I am extremely delighted to greet and welcome you all to National conference on “The Opportunities of Pharmacy in Current Scenario”. The theme of conference has much significance as it covers all the aspects on pharmaceutical profession from very fundamental issue to practical applications. The whole day of conference will be dedicated to cover a wide spectrum of themes such as pharmaceutical education, research & development, manufacturing, marketing and health sector. Now a days, the process for research and development of new medicines is growing in difficulty and length. Hence, the goal of this conference is to bring together researchers, academicians, industry persons and learners to exchange their research ideas and results. We look forward to an exciting day of insightful presentations, discussions and sharing of technical ideas with colleagues from different parts of our country.*

*I hope and expect that the theme will result in fruitful and passionate discussions.*

*Dr. Parmesh K. Dwivedi  
Joint Organizing Secretary*





## *Message*

*On my behalf as the head of the Mosofiya Group & Scientific Committee I cordially welcome all the participants who have sent abstracts and papers and all the participants who are interested in attending the seminar held on 11th March 2018 at Scientific Convention Centre, KGMU, Lucknow.*

*I assure you that we will be organizing such conferences in future as well. We will also give chances to the deserving students in every possible way to grow and flourish in their career in future. Our Mosofiya Group will organise job fairs, campus placement programs and workshops for pharmacy students. We will try to do our work with full devotion, dedication, and honesty.*

*Once again, a warm welcome and thanks to all the participants for making this program happen in such an efficient way.*

*Dr. Shashank Tiwari  
Associate Professor, Thinker & Writer*





### *Message*

*I am honored and delighted to welcome the distinguished dignitaries, intellectual speakers, Academicians, young researchers, delegates and students from all over the places to attend the National Conference on “The Opportunities of Pharmacy in current Scenario” on 11<sup>th</sup> March 2018 to be held at Scientific Convention Centre, KGMU, Lucknow.*

*This Conference will be a wonderful opportunity to discuss and share our global mission and vision, sharing best practices and learning from one another, as well as meeting or networking with guests and experts in the field of Pharmaceutical sciences. I particularly express our gratitude to the entire guest speakers who have come long way for the conference from their busy schedule.*

*I am confident that the collaborative interaction among the members will lead to build a long term partnership between our Mosofiya Group and the other teaching, research and industrial institutions all over the country.*

*Dr. Rizwan Ahmad  
Associate Professor*





# Mosofiya Conference

(A part of Mosofiya Group)



## Our Chief Guest

Dr. A.K.S. Rawat  
Executive Director, Ethno-medicine  
Research Center, Imphal.

## Our Chief Guest

Dr. Wahajul Haq  
Chief Scientist & Head, Medicinal & Process  
Chemistry Division, CSIR- CDRI, Lucknow

## Our Guest of Honors

1. Dr. Atul Kumar (Dean, NIPER, Raebareli)
2. Prof (Dr.) Shubhini A. Saraf  
(Head Deptt. of Pharm. Sciences,  
BBAU, Lucknow)
3. Prof (Dr.) Shailendra K. Saraf  
(Director, Pharmacy, BBDNIIT, Lucknow)
4. Prof (Dr.) Hefazat Husain Siddiqui  
(Adjunct Professor, Faculty of Pharmacy  
Integral University, Lucknow)

## Invited Speaker

1. Prof. (Dr.) Suneela Dhaneshwar
2. Prof. (Dr.) Alok Mukerjee
3. Prof. (Dr.) Rajiv Gupta
4. Dr. Pranay Wal
5. Dr. Syed Abid Hussain

## Scientific Committee

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4. Prof. (Dr.) Manoj kumar Mishra
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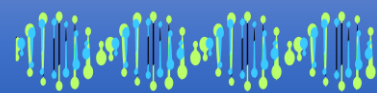
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28. Ms. Sangeeta Singh



# INVITED LECTURE



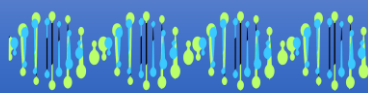


## BLENDING EIDONOMY WITH TECHNOLOGY IN MODERN DAY PHARMACOGNOSY: NEED OF HOUR

*Prof. (Dr.) Rajiv Gupta  
Head & Dean,  
School of Pharmacy, BBD University, Lucknow*

Our mother nature has a plethora of many cures and prophylaxis hidden within its traditional treatise of Indian system of medicine i.e. Ayurveda, which is yet to be fully explored. It has been observed that many traditional drugs of immense value are indiscriminately being adulterated or substituted, resulting in deviations from the expected outcome. At times it also puts a big question mark on the entire concept of traditional medicine. The problem is of serious concern when an expensive crude drug / not abundantly available crude drug are morphologically similar to an easily available & economical crude drug and hence becomes prone to adulteration/substitution. *Scindapsus officinalis* R. (H-Gajpeepal) is an important ingredient of the Ayurvedic preparations like Chandraprabha Vati, Guggul etc. Traditionally the plant is of great importance in curing *atisara* (diarrhea), *svasa* (asthma), *Krimi roga* (Anthelmintic). The marketed sample of the fruits was collected from five different districts of Uttar Pradesh and was evaluated pharmacognostically to check adulteration. CAMAG TLC Scanner with WinCATS planer chromatography manager was used for the qualitative and quantitative estimation of markers. The fruits were found to differ significantly in their Pharmacognosy. Apart from morphological variations, the vascular bundles present in the fruits were notably different. Fluorescence analysis also revealed differences in the samples which served as important parameter for comparing the samples. The quantitative estimation of markers in the samples, determined by HPTLC was found to be of varying concentration. Hence it would be pertinent to state that there is a need of estimation of benchmark parameters of microscopic characters along with specific markers in standard authenticated samples, to keep a check on rampant problem of adulteration & substitution.



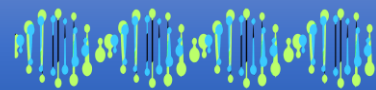
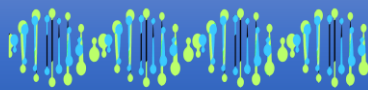


## PHARMACY EDUCATION & OPPORTUNITY FOR PUBLIC HEALTH

*Dr. Alok Mukerjee  
Professor & Principal  
United Institute of Pharmacy, Naini, Allahabad*

A pharmacist who prepare and dispense drug and medicines. Professional Pharmacists are very familiar with medication ingredients, interactions and precaution, & who cooperates, consults and sometimes advises the patient about concerning the drugs. Professional and government organizations continue to acknowledge the profound impact of pharmacists on public health, and the academy is no exception. It is necessary to recognize the importance of preparing pharmacy students to assume roles in public health. Public health means preventing diseases, prolonging life & promoting health of individual through education, promotion of healthy lifestyle & research on disease Prevention. Majority of citizens have limited access to high quality healthcare, & have poor health indicators. About 2/3<sup>rd</sup> of the population lacks access to essential medicines. Density of health care professional in the country is a little over 8 per 10,000 populations which is very low in comparison to developed countries. The practice of most community pharmacy involves work on health improvement and health and social care, but now pharmacists are also undertaking work in health protection and disease prevention and this trend is likely to continue. Pharmacists have thorough knowledge about medicines and their use and are in a better position to educate other health professionals about the rational use of medicines and have more opportunity to interact closely with the prescriber and patient and therefore, to promote the rational prescribing and use of drugs.





## PRE-SCREENING OF MICROALBUMINURIA IN A POOL OF PEOPLE IN SEMI-URBAN AREA OF KANPUR FOR SPREADING AWARENESS ABOUT NEPHROPATHY

*Pranay Wal*

*\*Dean Pharmacy PSIT Kanpur*

**OBJECTIVE:** To screen out people for micro albuminuria (urinary Albumin Excretion Rate, AER) for early diagnosis of initial stage nephropathy in Diabetic and Hypertensive patients.

**METHOD:** Micral strip test, an immunochemical strip test specific for albumin was performed in 206 individuals including 110 male and 96 female through morning sample and random sample of urine test, in five health camps of different locations in semi urban area of Kanpur.

**RESULT:** Thirty seven individuals including twenty three males and fourteen females were tested positive by immunological methods with a urinary albumin range of 35-173 mg/24 hours. The positive and negative predictive values obtained with the micral strip test for morning urine samples were 18% and 82% respectively and 21% and 79% for the random urine samples.

**CONCLUSION:** The findings suggest that the Micral strip test for morning and random urine sample is a quick, reliable, expedient and cost effective method that enables early detection of initial stage nephropathy in diabetic and cardiac patients. Moreover, the pharmacoeconomic studies have shown that these long-term benefits reflect into a significantly reduced burden on the notable resources of healthcare.







# SELECTED PAPERS





## LIQUID CRYSTALLINE DRUG DELIVERY SYSTEM FOR POORLY SOLUBLE DRUGS

*Aanchal Agrawal & Manoj Kumar Mishra*

*Department of Pharmaceutics, Shambhunath Institute of Pharmacy, Uttar Pradesh, India*

### Abstract

Poorly soluble drug molecules often have low bioavailability issues and absorption problems in the clinical setting. As the number of poorly soluble drugs increases from discovery, developing technologies to enhance their solubility, while also controlling their release is one of the many challenges facing the pharmaceutical industry today. Liquid crystalline systems, nanoparticles or macro-matrix, self-assemble in the presence of an aqueous environment and can provide a solubility enhancement, while also controlling the drug release rate. Liquid crystals are thermodynamically stable and possess long shelf life. It show bio adhesive properties and sustained release effects. The focus is on the potential of utilizing liquid crystalline systems for poorly soluble drugs followed by water soluble molecules.

**Keywords:** Drug delivery; Hexosome; Liquid crystal; poorly soluble drug; cubic crystal hexagonal crystal

### INTRODUCTION

Currently marketed compounds and most current drug development candidates remain poorly water soluble. The desire for increased potency, coupled with the realization that receptor binding is mediated, at least in part by hydrophobic interactions, further illustrates the likelihood that drug candidates will have limited aqueous solubility. The consequences of compounds with low solubility include poor absorption and bioavailability, insufficient solubility for IV dosing, artificially low activity values from bioassays, developmental challenges leading to increasing the development cost and time coupled with expensive formulations, and shifting the burden to the patient (frequent high-dose administration).

A newer technique, liquid crystalline (LC) drug delivery systems (LCDDS) have gained considerable attention in the last few decades as a multifunctional technique that may have the capability to both enhance the solubility and control the drug release rate. Lyotropic liquid crystals are mainly used as drug delivery system. Lipid-based lyotropic liquid crystals can be mainly classified into lamellar phase ( $L_\alpha$ ), cubic phase ( $V_2$ ), and hexagonal phase ( $H_2$ ) according to their different internal structures. Among them,  $V_2$  and  $H_2$  are the most important and recently have received much attention due to their highly ordered internal structures, which offers the potential as a slow release matrix for active pharmaceutical ingredients with various sizes and polarities.

Cubic and hexagonal phases provide a slow drug release matrix and protect peptides, proteins, and nucleic acids from chemical and physical degradation. The liquid crystal-forming lipids are nontoxic and biodegradable and can be used for various routes of administration. This article is not meant to provide an exhaustive review but rather to present some highlights.

### Liquid Crystal Overview

A liquid crystal is a state of matter that exhibits properties between a conventional liquid and a solid crystal, and can be subdivided into two types: lyotropic and thermotropic. Thermotropic





liquid crystals exhibit properties dependent on the applied temperature of the system, whereas lyotropic liquid crystalline systems are based upon the self-assembly of amphiphilic molecules induced by a solvent (typically aqueous) environment. The architecture of the system is based upon the amphiphilic molecule(s) structure combination of amphiphilic molecules/additives temperature, media, pH, water content, pressure, ions, and salt concentration among others. Due to the amphiphilic nature of the components used to fabricate these systems, hydrophilic, lipophilic, or amphiphilic molecules can be encapsulated into these systems.

Two main physical configurations of LLC systems for drug delivery have been explored: (1) so-called cubosomes and hexosomes, sub-micron dispersions of self-assembled reverse mesophases, where the inner structure is in thermodynamic equilibrium with the external excess aqueous environment and (2) as the bulk mesophase, gel, mesophase depot, matrix, etc, essentially describing the LC system in thermodynamic and structural equilibrium with the external environment as a single structure.

### **Cubic and Hexagonal liquid crystals**

Cubic and hexagonal crystals are binary amphiphilic systems, whereby amphiphilic molecules (e.g., lipids) are arranged in such a way as to form bulk penetrating polar solvent (e.g., water) channels, surrounded by a layer of amphiphilic molecules.

The structure of cubic crystals is unique and comprises a curved bicontinuous lipid bilayer (with an estimated thickness of 3.5 nm) extending in three dimensions and two interpenetrating, but non-contacting, aqueous nano-channels with a high interfacial area.

At present, the cubic crystals prepared by unsaturated monoglycerides or phytantriol (PT) are the most frequently investigated liquid crystal structures for drug delivery. Hydrophilic drugs will be located close to the emulsifier polar head or in the water channels, whereas lipophilic drugs will be localized within the lipid bilayer and amphiphilic drugs in the interface.

Its high viscosity makes it difficult to handle and limits its application and, furthermore, the bulk phase can cause the irritation reaction when in contact with the biological epithelia. To overcome these issues, an innovative strategy has been formulated: to disperse the bulk phase into water in the form of small particles. The dispersed cubic particles are denoted as 'cubosomes', which can stably exist in equilibrium with aqueous solution with the internal bicontinuous structure unchanged.

Hexagonal crystals are closed and extended micellar columnar structures and the long-range order is two-dimensional. It has been reported that there is no direct contact between water inside and outside the hexagonal phases. Likewise, the dispersed reversed hexagonal particles denoted as 'hexosomes' can also be obtained by dispersing the hexagonal gel into aqueous solution. To date, the hexagonal mesophases composed of glycerate-based surfactants such as oleyl glycerate (OG) and phytanyl glycerate (PG) have shown great potential in drug delivery.

### **Materials**

Lyotropic LCs, which consist of two or more components whereby one acts as a solvent to provide fluidity to the system, and the other provides an anisometric shape. The arrangement





of the LC molecules in a particular solvent depends on various factors, including temperature and concentration, as well as the shape of the LC molecule. In 1976, *Israelachvili et al.* proposed the critical packing parameter (CPP) to predict how the molecules will be arranged in an LC phase. This CPP is given by:  $p = v / (a_0 l_c)$  where  $v$  is the volume of the aliphatic chain,  $l_c$  is the length of the aliphatic chain and  $a_0$  is the polar area of the surface of the micelle.

Diverse range of components in addition to LC molecules can be added to formulate the LCFS to stabilize the LC mesophase, including phospholipids, ethanol and surfactants. Additives incorporated into the lipid bilayer may vary the curvature of the bilayer, which can result in a change of the thickness of the bilayer and/or the diameter of the water channel.

A wide variety of amphiphilic molecules form liquid crystalline phases among which first to be discovered was GMO which is thermodynamically stable in excess water, resulting in particles that can maintain their three-dimensional structure under a range of physiologically relevant conditions and at low concentrations. A more recently discovered group of amphiphiles that form a Q2 phase are oleyl glycerate OG and PG.

### Method of Preparation

Liquid crystal gels could be prepared by simply blending aqueous phase with lipid phase using vortex or ultrasonication. The manufacture of cubosomes or hexosomes is more complicated. The various process employed are:-

#### Top down approach

This approach was primarily reported by *Ljusberg-Wahren in 1996*. The extreme viscous bulk phase is prepared by mixing structure-forming lipids with stabilizers, then the resultant is dispersed into aqueous solution through the input of high energy (such as high-pressure homogenization [HPH], sonication or shearing) to form LLC nanoparticles.

Recently, a novel approach of shearing was proposed to fabricate LLC nanoparticles using a laboratory-built shearing apparatus. Compared with the well-established ultrasonication approach, the shearing treatment could effectively prepare more stable and homogeneous cubosomes or hexosomes with high content of the hydrophobic phase (oil + lipophilic additives) within a short time (less than one minute).

#### Bottom up approach

The key factor in the bottom-up approach is hydrotrope, which can dissolve water-insoluble lipids to create liquid precursors and prevent the formation of liquid crystals at high concentration. Compared with the top-down approach, this dilution-based approach can produce cubosomes without laborious fragmentation.

In other words, it needs less energy input. Moreover, this approach is far more efficient at generating small particles. The use of hydrotrope can simplify the preparation process and produce cubosomes possessing similar or even better properties than those fabricated by the top-down approach.





### Spray drying

To widen the applications of cubosomes in pharmaceutical field, dry powder precursors can be fabricated by spray drying and used for the preparation of oral solid formulations and inhalants. This approach was originally proposed and investigated by *Spicer et al.*

In his research, the powder precursor could be prepared through drying a pre dispersed aqueous solution that consisted of GMO, hydrophobically modified starch and water or contained GMO, dextran, ethanol and water, and then the colloidally stable dispersions of nano-structured cubosomes could be created by hydration of the precursors.

### Ability to sustain or controlled drug release (in case of cubic liquid crystals)

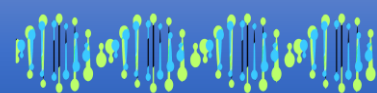
As drug carriers, cubic phase liquid crystals have the ability to provide sustained drug release. Drugs with a wide range of molecular weights and water solubilities have demonstrated sustained release in a cubic phase, such as aspirin and vitamin E propanthelene bromide and oxybutynin hydrochloride, metronidazole tetracycline, timolol maleate, chlorpheniramine maleate, propranolol hydrochloride, melatonin, pindolol, propranolol and pyrimethamine, haemoglobin, cefazolin, insulin, capsaicin, cinnarizine, and diclofenac salts. Lee et al. studied the in vitro sustained release behaviour of a number of model hydrophilic drugs with various molecular weights ( $^{14}\text{C}$ -glucose, Allura Red, and fluorescein isothiocyanate dextrans FD-4, FD-20, and FD-70) in two types of liquid crystalline matrixes, namely,  $V_{2\text{GMO}}$  (a cubic phase prepared from GMO) and  $V_{2\text{PT}}$  (a cubic phase prepared from PT). The release samples were constrained in micro beakers with a fixed surface area to ensure a constant release area between the liquid crystals and the release media. The results showed that in all cases the cumulative amount of drug diffusion through the matrix followed a linear relationship with the square root of time, which represented a Higuchi diffusion controlled release profile. The influence of phase structure and molecular weight on drug release was also investigated. It was discovered that the release rate of each drug decreased as the matrix was changed from  $V_{2\text{GMO}}$  to  $V_{2\text{PT}}$  and the diffusion coefficient of the model drugs was reduced as the molecular weight increased. The results indicated that phase type and molecular weight of drugs had an influence on their release behaviour.

### Application of OG-Based and PG-Based Hexagonal Phase

Due to the limit of materials and preparation conditions, hexagonal liquid crystals as drug carriers are less reported than those of cubic liquid crystals. Fortunately, in recent years, Boyd et al. synthesized a new class of materials with glycerate headgroups to form lyotropic liquid crystal. Among these materials, OG and PG were found to form hexagonal phase in excess water at physiological temperature. Thereafter, the OG- and PG-based hexagonal phase matrices were applied as the carriers for a series of model hydrophobic and hydrophilic drugs, such as paclitaxel, irinotecan, glucose, histidine, and octreotide, and the in vitro release studies showed that in all cases their release behaviour obeyed Higuchi kinetics. This suggested that OG- and PG-based hexagonal phases have the ability to provide sustained drug release.

In another study, Boyd et al. reported that the OG-based hexagonal phase improved the oral bioavailability of cinnarizine up to 3.5 and 3 times than that of the control suspension and GMO-based cubic phase, respectively. The in vitro lipolysis experiments showed that all of the GMO had been digested within the first 5 min. In contrast, although the hydrolysis of OG was also fast in the first 5 min, it kept steady in the following 55 min. It suggested that OG was less





susceptible to hydrolysis by pancreatic lipase than GMO and this might be responsible for increased oral bioavailability of cinnarizine when incorporated into OG formulations.

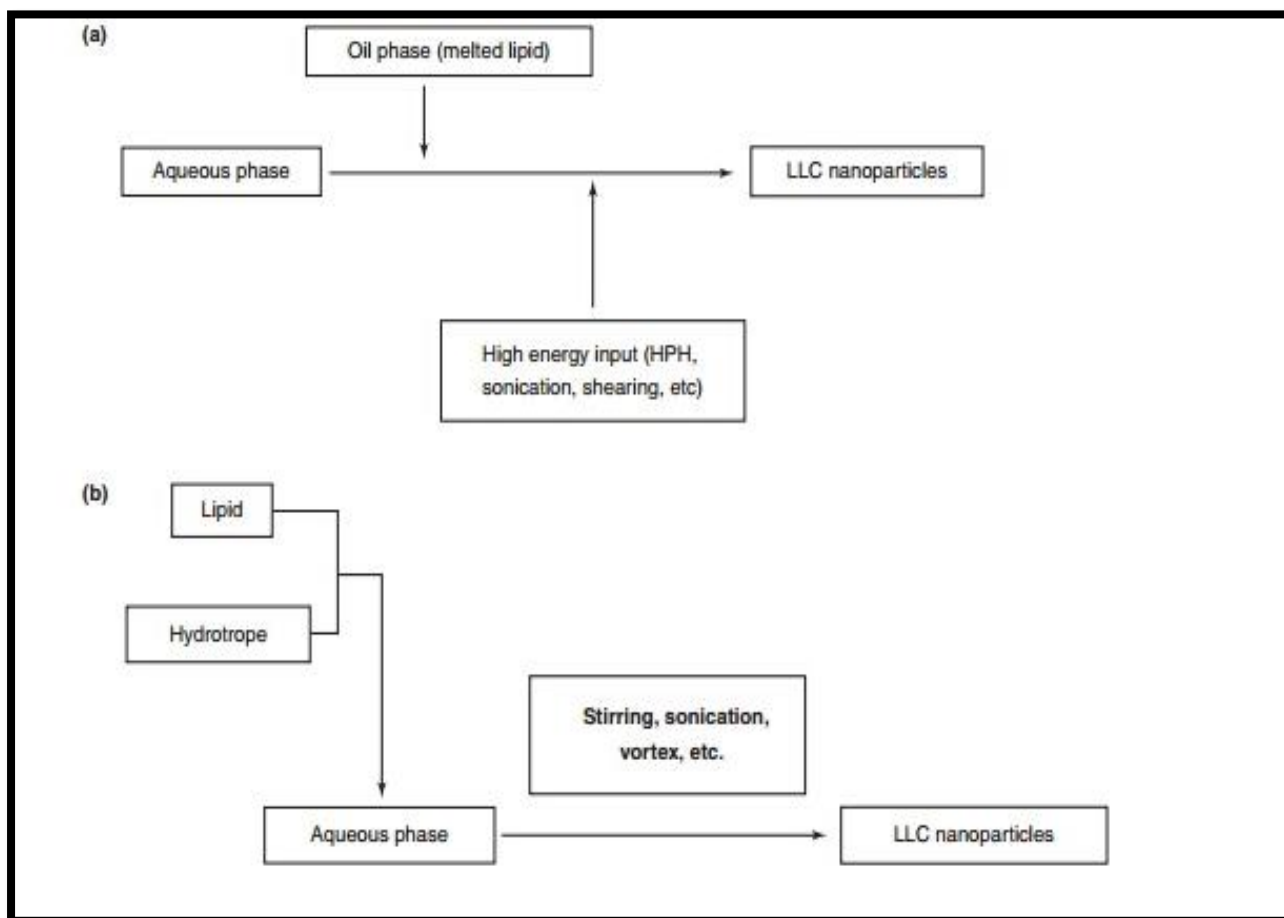
**Conclusion**

This review has attempted to explain the fundamentals of liquid crystalline systems on their potential for solubility enhancement and controlled release. Liquid crystalline systems have been investigated for both oral, IV, and subcutaneous administration of both poorly soluble and soluble drugs, in addition to topical, percutaneous, and dental.

There have been many promising results of these LLCs; however, a number of limitations need to be overcome for their clinical application. For example, with the direct administration of liquid crystal gels, problems associated with the viscosity and the frequent occurrence of burst-release must be resolved. Although mono-olein has been regarded as being generally safe, little is known about its adverse effects upon parenteral administration.

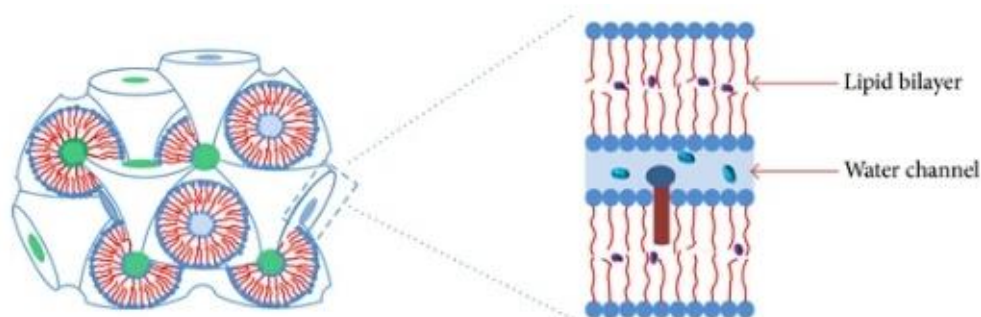
Although some new materials, such as PT, OG, PG and SMO have been shown to exhibit promising properties, questions remain regarding their safety and biological stability in vivo.

**Table 1- Method of preparations of liquid crystals**

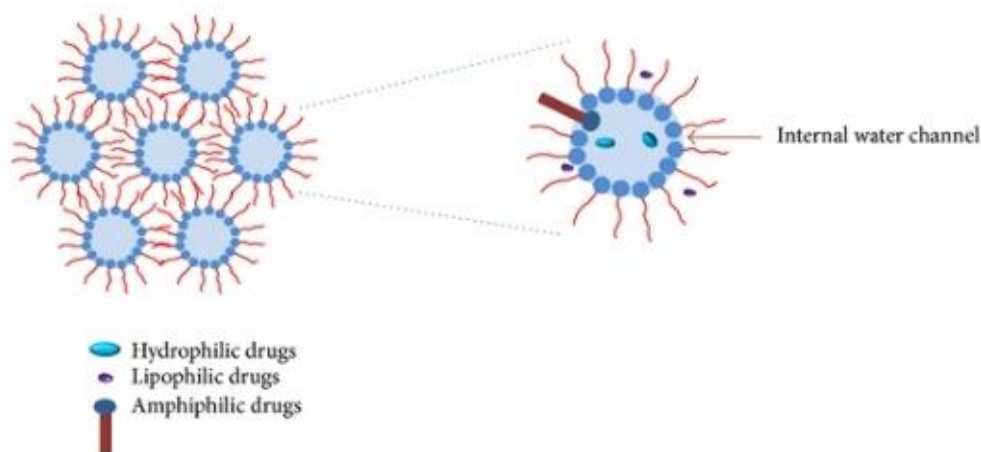


(a)Top down process (b) bottom up process





(a)



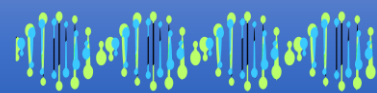
(b)

(Fig 1: Structure of (a) cubic phase (b) hexagonal phase. Possible localizations of drugs in the mesophases are also pointed out)

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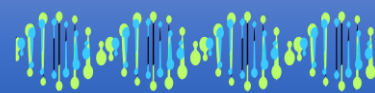




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## **‘PHARMACOGENOMICS’ REVIEW ON MEDICAL GENETIC APPROACH VIA BIOMARKERS**

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### **Abstract**

Scientifically, personalized medicine is known as pharmacogenomics (drugs combined with genes), or how genetic differences in individuals effect the way people respond to drugs. Biomarkers are biological molecules found in blood, body fluids, tissues or the tumor itself. Biomarkers can be a sign of a normal/abnormal process, or of a condition or disease. For example, blood pressure is widely accepted as a biomarker because a correlation between elevated blood pressure and adverse cardiovascular outcomes has been demonstrated. Biomarkers can be divided into categories of predictive or prognostic. Using biomarkers in recent years, significant advances in our understanding of human biology have yielded novel drug targets that may impact disease. Typically, early clinical trials test a drug target’s safety and tolerability. The efficacy of a drug is typically not tested until later stages in development. But, researchers may now be able to use pharmacogenomics to improve the efficiency of drug development. Using biomarkers, we can explore how a drug works in the body, allowing earlier decisions on whether to advance molecules in clinical trials. Biomarkers may also be used to diagnose disease and for patient selection. As research continues, our understanding to the role of biomarkers can play in the management of disease areas such as cancer, cardiology, and neurology, metabolic, autoimmune, and inflammatory diseases.

**Key words:-**Pharmacogenomics, autoimmune, drug targets, biomarker

### **Introduction**

A main focus of pharmacogenomic research is to seek the effect of original genetic differences on the pharmacokinetics, pharmacodynamics, efficacy, and safety of drug treatments . Many genetic variants have been identified that are known to alter cytochrome P450 (CYP) enzymes and drug receptors, transporters and targets. These modifications can greatly influence pharmacokinetics, dose requirements, and other factors that affect therapeutic outcomes. The clinical application of such pharmacogenetic findings holds great promise in improving drug efficacy and safety. Psychiatric disorders establish vast medical and economic burdens on patients, their families and healthcare providers worldwide. Therefore, there is a necessary need to improve early diagnosis and thus treatment scheme including prevention.

However, currently used diagnosis and disease entities in psychiatry are largely based on clinical phenomenology and lack biological validity, which is a major limitation in identifying biomarkers for psychiatric disorder. The use of biomarkers in basic and clinical research as well as in clinical practice has become so commonplace that their presence as primary endpoints in clinical trials is now accepted almost without question. In the case of specific biomarkers that have been well characterized and repeatedly shown to correctly predict relevant clinical outcomes across a variety of treatments and populations, this use is entirely





justified and appropriate. In many cases, however, the “validity” of biomarkers is assumed where, in fact, it should continue to be evaluated and reevaluated.

Biological markers (biomarkers) have been defined as “cellular, biochemical or molecular alterations that are measurable in biological media such as human tissues, cells, or fluids.” More recently, the definition has been broadened to include biological characteristics that can be objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention. In practice, biomarkers include tools and technologies that can aid in understanding the prediction, cause, diagnosis, progression, regression, or outcome of treatment of disease. For the nervous system there is a wide range of techniques used to gain information about the brain in both the healthy and diseased state.

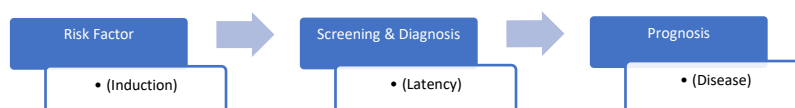
These may involve measurements directly on biological media (e.g., blood or cerebrospinal fluid) or measurements such as brain imaging which do not involve direct sampling of biological media but measure changes in the composition or function of the nervous system. Biomarkers of all types have been used by generations of epidemiologists, physicians, and scientists to study human disease. The application of biomarkers in the diagnosis and management of cardiovascular disease. The rapid growth of molecular biology and laboratory technology has expanded to the point at which the application of technically advanced biomarkers will soon become even more feasible. Molecular biomarkers will in the hands of clinical investigators, provide a dynamic and powerful approach to understanding the spectrum of neurological disease with obvious applications in analytic epidemiology, clinical trials and disease prevention, diagnosis, and disease management.

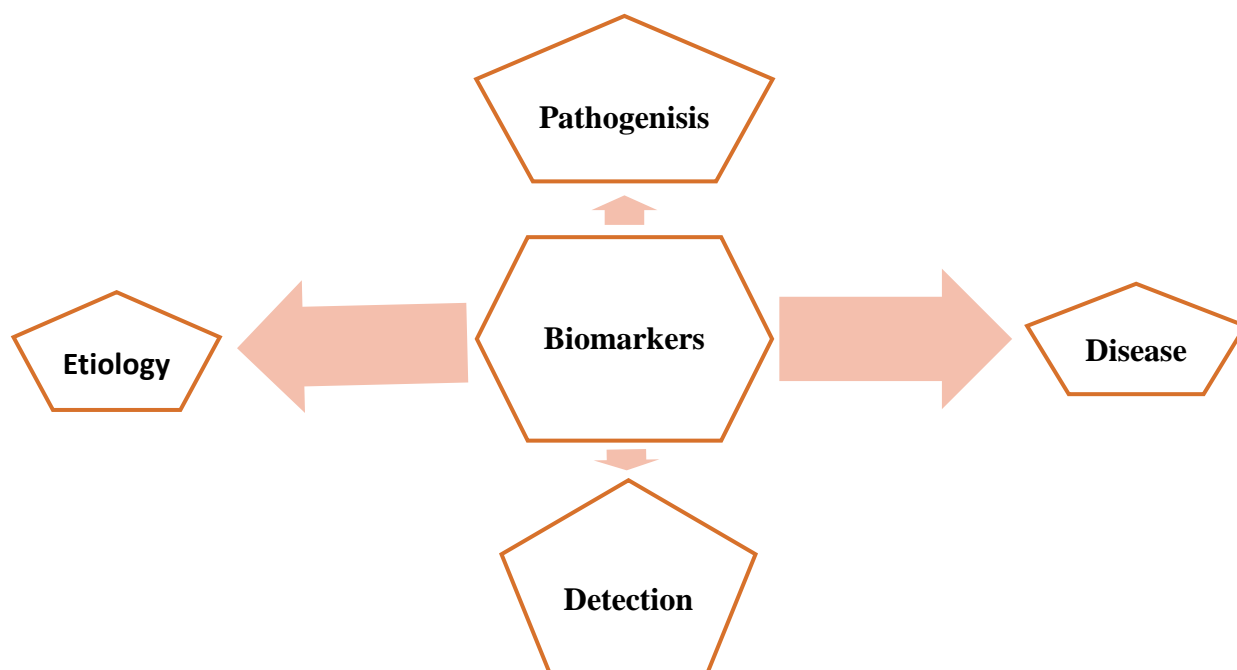
**Types of biomarkers**

In addition to delineating the events between exposure and disease, biomarkers have the potential to identify the earliest events in the natural history, reducing the degree of misclassification of both disease and exposure, opening a window to potential mechanisms related to the disease pathogenesis, accounting for some of the variability and effect modification of risk prediction. It can also provide insight into disease progression, prognosis, and response to therapy.

**Biological Pathway**

A biological pathway is a series of interactions among molecules in a cell that leads to a certain product or a change in a cell. Such a pathway can trigger the assembly of new molecules, such as a fat or protein. Pathways can also turn genes on and off, or spur a cell to move . Some of the most common biological pathways are involved in metabolism, the regulation of gene expression and the transmission of signals. Pathways play key role in advanced studies of genomics (Fig.1).





**Figure 1. Role of biomarker in Biological Pathway**

### What is a Biomarker?

The term “biomarker”, a portmanteau of “biological marker”, refers to a extensive subcategory of medical signs – that is objective indications of medical state observed from outside the patient which can be measured accurately and reproducibly. Medical signs stand in comparison to medical symptoms, which are limited to those indications of health or illness recognized by patients themselves. There are several more actual definitions of biomarkers in the research and they fortunately overlap considerably. In 1998, the National Institutes of Health Biomarkers Definitions Working Group defined a biomarker as “a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.” A joint investment on chemical safety, the International Programme on Chemical Safety, led by the World Health Organization (WHO) and in coordination with the United Nations and the International Labor Organization, has defined a biomarker as “any substance, structure, or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease”. An even broader definition takes into account not just incidence and outcome of disease, but also the effects of treatments, interventions, and even unintended environmental exposure, such as to chemicals or nutrients.

In their report on the validity of biomarkers in environment risk assessment, the WHO has stated that a true definition of biomarkers includes “almost any measurement reflecting an interaction between a biological system and a potential hazard, which may be chemical, physical, or biological. The measured response may be functional and physiological, biochemical at the cellular level, or a molecular interaction.” Examples of biomarkers include everything from pulse and blood pressure through basic chemistries to more complex





laboratory tests of blood and other tissues. Medical signs have a long history of use in clinical practice as old as medical practice itself and biomarkers are merely the most objective, quantifiable medical signs modern laboratory science allows us to measure reproducibly. The use of biomarkers, and in particular laboratory measured biomarkers, in clinical research is somewhat newer, and the best approaches to this practice are still being developed and refined. The key issue at hand is determining the relationship between any given measurable biomarker and relevant clinical endpoints.

### **Personalized medicine:**

Genetic variation contributes to both disease susceptibility and treatment response. Genome-wide association studies (GWAs) have enabled rapid discovery of genetic variants contributing to the pathogenesis of complex genetic diseases, as well as detection of many pharmacogenetic markers. The driving hope of these major advances in genetic epidemiology is that promotion of personalized medicine will improve medical decision-making. Although use of the term personalized medicine is often limited to the identification of the optimal drug and the optimal dosage for a subgroup of patients, current personalized medicine applications are far more broad, and might include situations of withholding treatment, preventive interventions, or targeted treatment options for individual patients. In prostate cancer, for example, DNA biomarker tests may be used to determine whether treatment may be safely delayed for a period of watchful waiting. If the tumor is demonstrated due to lack of genes causing an aggressive form of the cancer, it may remain stable for decades, and the need for radical surgical resection with subsequent radio or chemotherapy may be obviated. In contrast, in other instances, genetic profiles may be used to determine preventive interventions. This approach is already used for some forms of hereditary cancer, in which individual genetic testing is the basis for deciding upon specific, sometimes very radical interventions such as preventive surgery. Beyond treatment schemes that are applied identically across large subgroups of patients to which some authors have applied the distinct term stratified medicine other personalized medicine applications offer targeted treatment options for individual patients.

### **Current use of biomarkers:**

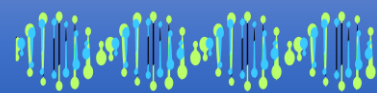
In this section, we illustrate current applications of biomarkers for diagnosis, prognosis and prediction in personalized medicine. Diagnostic biomarkers are biomarkers used to determine the diagnosis or severity of a disease. The most important within this group are screening biomarkers which are used to discriminate between healthy individuals and those in an early stage of a disease. For example, the commercially available point of care tests (POCT) test serum for antibodies to mutated citrullinated vimentin (MCV) or citrullinate peptides/proteins in order to screen for rheumatoid arthritis in non-symptomatic, healthy persons. If a diagnosis is known, prognostic biomarkers help to predict the likely course of disease in a defined clinical population under standard treatment conditions. For example, a DNA tumor biomarker for breast cancer prognosis is used following surgery to indicate whether risk of metastasis is low or high, and guide physicians to determine the best kind of treatment for the individual patient. Such therapy guidance requires the validation of the predictive capability of the biomarker. Predictive biomarkers predict the likely response of a patient to a special treatment in terms of





efficacy & safety and thus support clinical decision making. Goals of Pharmacogenomics and Pharmacogenetics Prior to the introduction of pharmacogenomics, treatment choices were traditionally made based on a patient's medical history and pathology. Possible influences on drug response that are usually considered when making treatment decisions include age, sex, disease, environmental factors, diet, and drug interactions. Dose adjustments are typically made based on a patient's age, sex, organ function, body weight, and body surface area. However, even when these factors are taken into account, drug response still often varies among patients, ranging from positive outcomes to fatal adverse reactions. These long-established clinical parameters will continue to be used to guide drug treatment. However, they don't directly consider genetic factors, which can account for 20% to 40% of inter-individual differences in drug metabolism and response. In fact, for certain drugs or drug classes, genetic factors have been shown to be the most important influence on drug treatment outcomes. Therefore, the goal of pharmacogenomic and pharmacogenetic research is to apply current knowledge about genetic variants that influence drug response to develop personalized treatment strategies that maximize therapeutic efficacy and safety. Personalized drug therapy is especially desirable when prescribing a drug with a narrow therapeutic index or when drug toxicity can be life-threatening. For example, antineoplastic, anticoagulant, and anti-HIV therapies are often administered at maximally tolerated doses that are typically chosen from population averages. However, this approach can result in toxicity in up to one-third of patients, and a significant portion of the people treated can exhibit poor or no response. Genetic factors account for 20% to 40% of inter-individual differences in metabolism and response. For certain drugs or drug classes, they are the most important influence on treatment outcomes. Severe adverse drug reactions are one of the most common reasons for hospital admissions in the U.S. Adverse drug reactions rank as the fourth leading cause of death in the U.S. and are responsible for 100,000 deaths annually. Genetic testing for drug response is expected to reduce the risk of hospitalization by as much as 30%. To this end, multidisciplinary teams of laboratory, clinical, and computational researchers are working together to personalize drug treatment by incorporating an individual's genetic information (both germline and somatic) into existing prescribing models [8]. A patient's genome needs to be identify only once in a lifetime, which makes pharmacogenetic screening a potentially very potent, cost-effective diagnostic tool Genetic testing for drug response is expected to reduce the risk of hospitalization by as much as 30%. Types of Genetic Variants That Can Influence Drug Response the number of pharmacogenetic associations known to affect drug response has steadily increased over the years. Genetic polymorphisms have been identified for many proteins that are significant in clinical pharmacology, including enzymes, drug receptors, transporters, and targets. These polymorphisms can cause alterations in the amount, structure, binding, and/or function of these proteins, affecting how drugs interact with them. Genetic variants can alter the pharmacokinetics and pharmacodynamics of a drug, potentially affecting both drug efficacy and toxicity. Evidence indicates that genetic factors can account for an estimated 20% to 95% of drug metabolism and response. The majority of observed DNA sequence variations are due to SNPs, which are single base-pair substitution mutations. These occur every 100 to 300 base pairs and account for 90% of all human genetic variations. The location of the SNPs in relation to a particular gene determines whether or not the normal function of a gene is affected. The



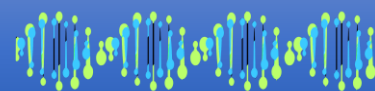
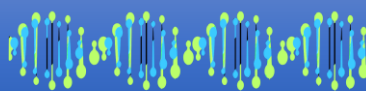


net effect of an SNP on gene function can also depend on whether one or both copies of a gene are affected by a variant; therefore, one of the aims of pharmacogenetic testing is to identify heterozygous and homozygous SNPs. Genetic variation can also occur in “non-SNP” polymorphisms, better known as structural variations (SVs). SVs consist of small (fewer than 10 base pairs) insertions or deletions (indels), copy number variations (CNVs), and inversions. These genetic modifications occur less frequently than SNPs but have greater repercussions because they encompass larger regions of genomic variation than SNPs do. For example, if an indel occurs in the coding region of a gene, this can lead to completely aberrant, nonfunctional proteins. Both SNPs and SVs are thought to play a role to varying degrees with respect to individual phenotypic drug response outcomes, such as drug sensitivity, resistance, and toxicity.

### **Characterization and Evaluation of Biomarkers**

To identify biomarkers as surrogate endpoints requires the determination of relevance and validity. Some researchers have in fact rejected the term validation as “unsuitable” to the study of biomarkers since it suggests that there can be a complete biological understanding of the relationship between a given biomarker and a clinical endpoint, an assumption they reject. Instead, an alternate term that has been offered is “evaluation” to refer to the ongoing process of studying biomarker's success at acting as surrogates for individual clinical endpoint. At the simplest level is measurement validity: is the biomarker proposed as a surrogate capable of being measured objectively and reproducibly in a given case, and does it measure an objective, quantifiable characteristic successfully? One step beyond this, the internal or study validity of the surrogate must be evaluated: within the study, can the biomarker be measured not just with precision and reproducibility, but also with accuracy? In other words, within this study population and situation, does the biomarker correlate strongly with the clinical endpoint for which it is serving as a surrogate? The next level of validation is external validity: can this surrogate be shown to have similar predictive power in other populations or in other related treatment studies? If so, the biomarker can be considered to be a useful surrogate marker in studies that are closely related to the studies establishing its conditional “validity.” The final level of surrogacy success that must be considered has not, some commentators have observed, been given enough attention. Once biomarkers become established surrogate markers for predicting the effects of a given class of treatments on one clinical endpoint, can they be safely relied upon to serve as surrogates for other related clinical endpoints? Or can they be used as surrogate markers in evaluating other classes of treatments? The assumption has frequently been made in study design that biomarkers can be used broadly, once they become established in narrow research contexts. However, this scientifically unsound approach to trial design has in past decades led to flawed research conclusions, several of which have been considered in greater depth in review articles on the topic. For years, researchers used suppression of arrhythmias as a surrogate endpoint for decreased morbidity due to cardiovascular disease, resulting in the approval of anti-arrhythmia drugs (e.g., encainide, flecainide, moricizine) that later trials actually found to increase mortality in certain patient populations. More recently, a large and well-publicized trial of the combination of two cholesterol-lowering drugs, ezetimibe





and simvastatin, highlighted the risk of relying too much on biomarkers: although the combination treatment lowered subjects' cholesterol levels more than simvastatin alone, it did not lead to any improvement in atherosclerosis or overall mortality, calling into question a great deal previous research that depended on the assumption that lowering cholesterol necessarily lowered morbidity and mortality . In both these cases, as in many others, despite the best biological and statistical evidence, biomarkers that were “validated” even in a series of previous trials were found poor predictors of clinical outcomes



**Fig.2 Discovery & development of pharmacogenomics**

**Conclusion**

Biomarkers play a critical role in improving the drug development process as well as in the larger biomedical research enterprise. Understanding the relationship between measurable biological processes and clinical outcomes is vital to expanding our arsenal of treatments for all diseases, and for deepening our understanding of normal, healthy physiology. Since at least the 1980s, the necessity of using biomarkers as surrogate outcomes in large trials of major diseases, such as cancer and heart disease, has been widely discussed. The FDA continues to promote the use of biomarkers in basic and clinical research, as well as research on potential new biomarkers to use as surrogates in future trials. However, for all their potential to do good to speed drug development, to reduce exposure to ineffective experimental treatments, and so on biomarkers present substantial risks when trial designers confuse them with clinical endpoints.

Biomarkers could only serve as true replacements for clinical relevant endpoints if we completely understood the normal physiology of a biological process, the pathophysiology of that process in the disease state, and effects of an intervention pharmacological, device, or otherwise on these processes. Since we rarely if ever have the full picture of those types of





processes, since there are always more details we don't know or understand, biomarkers as surrogate endpoints need constant reevaluation. Studies using biomarkers should always have as ultimate measures clinical outcomes. The continued erosion of sequencing costs, driven in part by increased capacity of existing technologies and improvements in chemistry, as well as the emergence of single-molecule third- and fourth-generation sequencing. We strongly encourage the systematic study of both patient and control populations wherein genomic data are systematically annotated with detailed clinical information and physiologically relevant biological assays. We propose that these activities will be necessary to gain a sufficient understanding of the genetic architecture of human pathology and to improve the validity of computational prediction algorithms to the point at which their implementation in the clinical setting can be executed with confidence.

### Future directions

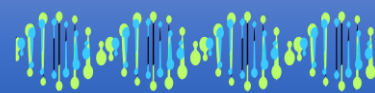
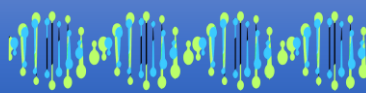
Clinicians are accustomed to making prescribing decisions based on patient characteristics such as age, renal function, liver function, drug-drug interactions, and patient preferences. Much of this prescribing, however, is taking place without optimal clinical decision support to assist in compiling those characteristics and matching them with evidenced-based choices on medications and their doses. As CDS improves and becomes more widespread, and as the evidenced supporting pharmacogenomic testing continues to grow, the momentum for clinical implementation of pharmacogenomics should accelerate. Going forward, there is a growing body of evidence that pharmacogenomics will be an expanding component of evidence-based precision medicine.

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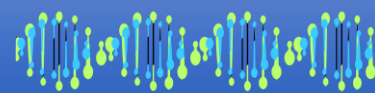






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## LEAD FINDING FROM PLANT *OCIMUM SANCTUM* WITH IMMUNOMODULATOR POTENTIALS THROUGH *IN SILICO* METHODS

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### Abstract

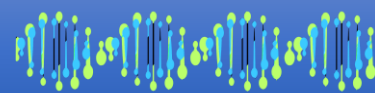
The immunity system is a host guard system compressing numerous biological structure and processes within an organism that protects in opposition to disease. Immunology is a science that examines the structure. The initial known orientation to immunity was during the plague of Athens in 430 BC. The immune system protects organism from infection with layered defenses of increasing specificity. Innate immune system and adaptive immune systems are the types of immune system. Disorders of the immune system can result in auto-immune diseases, inflammatory diseases and cancer. In humans, immunodeficiency can either be the result of a genetic disease such as harsh mutual immunodeficiency, acquired situation such as HIV/AIDS. *In silico* study in medication is deliberation to have the potential to speed the rate of discovery while reducing the need for exclusive lab work and clinical trials. In this chapter the chemdraw, molinspiration and chemspider computer softwares are applied from these working the lead constituent is finding in *ocimum sanctum* plant for immunomodulator activity.

### INTRODUCTION

#### Immunity system

Immunology is one of the most rapidly developing area of medical biotechnology research and has great promises with regard to the prevention and treatment of a wide range of disorders such as the inflammatory diseases of skin, gut, respiratory tract, joints and central organs. In addition infectious diseases are now primarily considered immunological disorders while neoplastic diseases, organ transplantation and several autoimmune diseases may involve in an immunosuppressive state. The immune system is one of our most complex biological systems in the body. The basic role of the immune system is to distinguish self from non-self (Fasano, 2012). This non-self could be an infectious organism, a transplanted organ or an endogenous cell that can be mistaken as a foreign. The immune responses of the human body against any non-self are of two types: (a) innate (or natural or non-specific) and (b) adaptive (or acquired or specific). Both these responses have two components each, viz. cellular and humoral. Innate immunity lacks specificity as there is no involvement of memory cells. Acquired immunity on other hand is specifically adapted for the inducing pathogens and response improves with subsequent exposures to the same pathogen due to the presence of memory cell line (Netea, 2013). In the innate cellular immunity there is involvement of monocytes/macrophage system, while in innate humoral immunity there is activation of component system. On the other hand the cellular component of acquired immunity consists of T-lymphocytes while the humoral component of this immunity involves the role of Blymphocytes. Normally in innate and





acquired immune responses act in concerted manner to contain or eradicate infection. In some cases innate responses are enough to neutralise the offending agent. However in many other cases, certain cells of innate immune system, such as antigen presenting cells (APC), can also process the offending agent into smaller fragments which then activate adaptive immune system to neutralise or kill these pathogens. The elements formed in the blood are erythrocytes (RBC), leukocytes (WBC) and thrombocytes (platelets) (Kondo et al., 2003). T-and B lymphocytes are involved in mediating adaptive immune responses while NK cells exert innate immune response along with mature cells originating from trilineage myeloid stem cells when exposed to specific antigens, B-lymphocytes differentiate into antibody producing plasma cells in the bone marrow. Simultaneously, T-cells, under the influence of thymic hormones, migrate to the thymus and on appropriate stimulus by antigen presenting cells (APC) acquire T-cell receptor (TCR) and get differentiated to helper T-cells (with specific protein cluster of differentiation- CD4+) and cytotoxic T-cells (with specific protein cluster of differentiation- CD8+). The CD4+ (TH cell) subtypes of T-cells differentiate further outside the thymus into several phenotypes: TH1, TH2 and TH3 which are distinguished by the different cytokines (IL-2 and IFN- $\gamma$ ) they synthesize. TH1 T-cells produce cytokines that stimulate proliferation and differentiation of T-lymphocytes and NK cells. These cytokines play an important role in cell mediated immunity (CMI). TH2 T-cells release cytokine (IL-4, IL-5, IL-10 and IL-13) that stimulate B-lymphocytes production for humoral immunity. TH3 T-cells play an important role in resting phases of immune response and in the production of anti-inflammatory immunoglobulin-A (IgA) antibodies that are important in secretory immunity (Geginat et al., 2014).

## MATERIAL AND METHODS

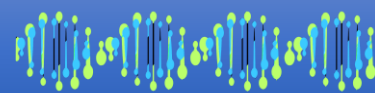
### *Ocimum sanctum*

The most important source of medicines is plant. Among them *Ocimum* species belonging to the family Lamiaceae are very important for their therapeutic potentials. *Ocimum sanctum* Linn (Tulsi), *ocimum canus* Sims (dulal Tulsi), *ocimum basilicum* Linn (Ban Tulsi), *Ocimum gratissimum* Linn (Ram Tulsi), *Ocimum micranthus* Willd and *ocimum americanum* Linn are examples of known important species (Sarkar, Srimany, & Pradeep, 2012). Among them *Ocimum sanctum* has been well documented for its therapeutic potential. Tulsi is a fragrant bushy perennial growing up to 1.5m in height with profusion of white blooms and slightly purple tinted foliage. This herb has been known from as early as the vedic period and is held by Hindus and is often planted around temples and used in roseries. It is native of India, reached western Europe in the 16th centuries. In several ancient systems of medicine including Ayurveda, Greek, Roman, Siddha and Unani. *Ocimum sanctum* has vast number of therapeutic applications such as in cardiopathy, haemopathy, leucoderma, asthma, bronchitis, catarrhal fever, vomiting, gastropathy, genitourinary disorders, ring worm, verminosis and skin disease etc. It is commonly used in cough cold, mild indigestion, diminished appetite and malaise (Pandey & Madhuri, 2010).

### ***Ocimum sanctum* has numerous pharmacological activities**

Oral administration of alcoholic extract of leaves led to marked lowering of blood sugar level in normal, glucose fed hyperglycaemic and streptozotocin induced diabetic rats. It might





potentially regulate corticosteroid-induced diabetes mellitus. Halder et al demonstrated anticataract activity in which could be related with its aldose reductase inhibitory effect. But vast et al failed to demonstrate any anti cataract effect in spite of significant antihyperglycaemic activity. It delays the process of cataractogenesis in galactosaemic cataracts. The higher doses are more effective and have no promising prophylactic role rather than curative one. In addition to the hypoglycaemic hypolipidemic effect of tulsi in diabetic rats was also indicated. Administration of fresh leaves of tulsi mixed in diet resulted in significant lowering in serum total cholesterol, triglyceride, phospholipid and HDL- cholesterol and total faecal sterol contents. Aqueous extract and aortic tissue protection from hypercholesterolemia-induced peroxidative damage. Long term feeding offers significant protection against isoproterenol-induced myocardial necrosis in wistar rats through enhancement of endogenous antioxidants (Oguanobi, Chijioke, & Ghasi, 2012).

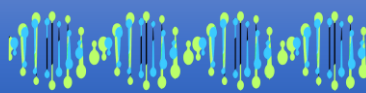
The fixed oil of tulsi was found to possess significant anti-ulcer activity against Aspirin, Indomethacin, Alcohol, histamine, reserpine and stress-induced ulceration in experimental animal models. Significant inhibition was also observed in gastric secretion and Aspirin induced gastric ulceration in pylorus ligated rats. Linolenic acid present in *Ocimum sanctum* fixed oil has the capacity to block both the cyclooxygenase and lipoxygenase pathways of arachidonate metabolism and could be responsible for the anti-inflammatory activity of the oil (Dharmani et al., 2004).

It has significant ability to scavenge highly reactive free radicals. Antioxidant bioassay-directed extraction of the fresh leaves and stems of tulsi extract yielded: cirsilin, cirsimaritin, isothymusin, isothymonin, apigenin, rosmarinic acid and appreciable quantities of eugenol. Eugenol is a major component of the volatile oil and other compounds also demonstrated good antioxidant activity. The crude aqueous extract of leaf possesses some anti bacterial and immunomodulatory active principles. The narrowest spectrum of antibacterial activity was observed in *Ocimum sanctum*. The essential oil showed potent anthelmintic activity in the *Caenorhabditis elegans* model. The ethanolic extracts from the leaves showed better activity against the B-lactamase producing methicillin-resistant *Staphylococcus aureus* strains. Alcoholic extract showed growth inhibition for *Vibrio cholerae*. Aqueous extract of the plant showed growth inhibition for *Klebsiella*, *Escherichia coli*, *Proteus* and *Staphylococcus aureus*. It possesses cognition-enhancing properties and significantly prevents hypoperfusion-induced functional and structural disturbances. It is also antithyroidic in nature (Kelm, Nair, Strasburg, & DeWitt, 2000).

### **Protection and detoxification**

Many of the physiological benefits of tulsi can be attributed to its ability to assist with the body's internal housekeeping and protection of the body from toxin-induced damage. These functions are often attributed to tulsi's high content of phenolic compounds and anti-oxidant properties, with Krishna tulsi (black/purple variety) having a higher phenolic content and anti-oxidant capacity than white Vana (wild) tulsi. Laboratory studies have shown that tulsi protects against toxic chemical-induced injury by increasing the body's levels of anti-oxidant molecules such as glutathione and enhancing the activity of anti-oxidant enzymes such as superoxide dismutase and catalase, which protect cellular organelles and membranes by mopping up damaging free radicals caused by lack of oxygen and other toxic agents. Tulsi also helps to prevent cancers caused by toxic compounds by reducing DNA damage and inducing





apoptosis in precancerous and cancerous cells, thereby reducing the growth of experimental tumors and enhancing survival. Furthermore, tulsi not only protects against the damage caused by toxic compounds, but also enables the body to more effectively transform and eliminate them by enhancing the activity of liver detoxification enzymes such as the cytochrome P450 enzymes, which deactivates toxic chemicals and enables them to be safely excreted. While these actions are vitally important for protecting against natural toxins produced within the body or by animals or plants, they are perhaps even more important in the modern age to protect against the vast range of pollutants, pesticides, pharmaceuticals, heavy metals, radiation and other industrial toxicants created from human activity(Cohen, 2014).

**Botanical classification**

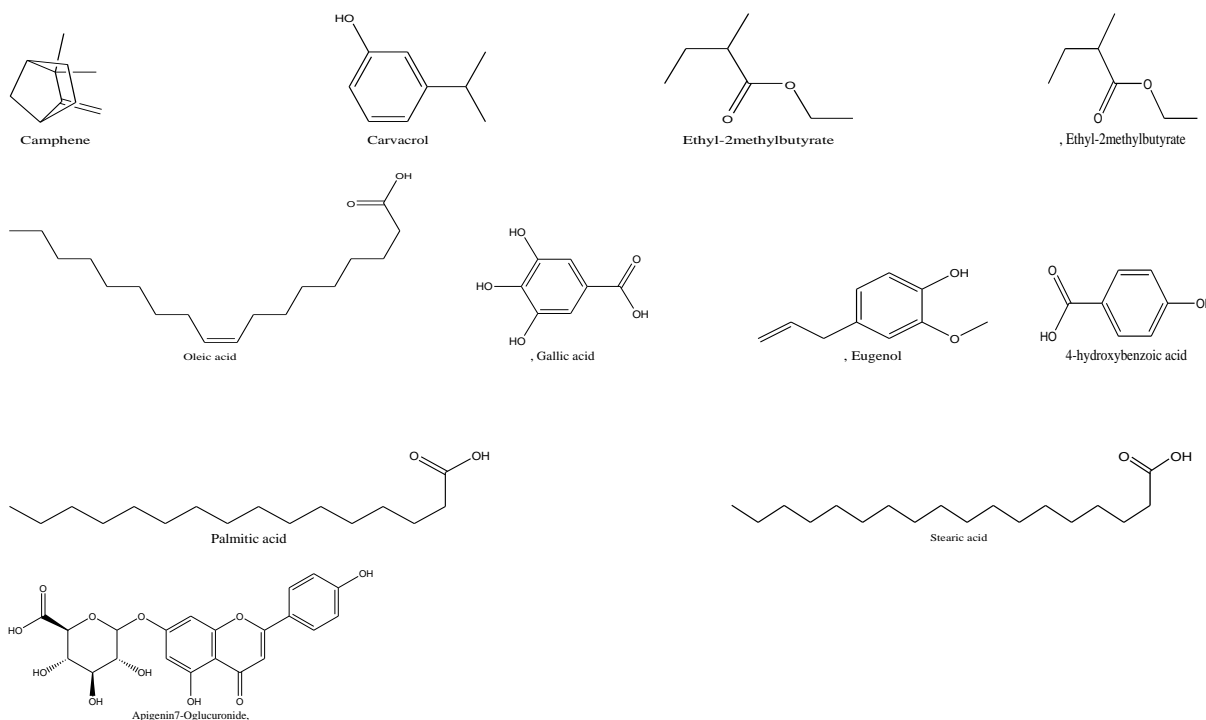
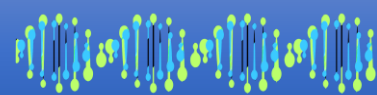
- Kingdom: Plantae
- Divison : Magnoliaphyta
- Class : Magnoliopsida
- Order : Lamiales
- Family : Lamiaceae
- Genus : Ocimum
- Species : Sanctum



**Chemical Constituents**

The different parts of *Ocimum sanctum* contain different types of constituents in varying amounts. The leaves contain a high content of essential oils which include Toluene, Camphene, Octane, Benzene, Citronellel, Sabinene, Limocene, Ledol, Dimethylbenzene, Ethyl-2methylbutyrate, Eugenol, Terpinolene,  $\beta$ -elemene, Isocaryophyllene, Iso-eugenol,  $\alpha$ -amorphene,  $\alpha$ -guaiene,  $\alpha$ -humulene,  $\alpha$ -terpeneol, Borneol, Calamine, Nerolidol, Carvacrol, Geraneol, Humulene oxide, Elemol, Tetradecanal, (EZ)-famesol, Cissesquisainenehydrate,  $\alpha$ -bisbolol, Selin-11-en-4- $\alpha$ -ol, $\alpha$ -murolene, 14-hydroxy- $\alpha$ -humulene. To separate constituents' extraction is performed in many ways. When alcoholic extraction of leaves and aerial parts of plants was done, it was found to contain Luteolin, Orientin, Urosolic acid, Apigenin7-Oglucuronide, Luteolin-7-O-glucuronide, Isorientin, Aesculin, Triacontanolferulate, Vallinin acid, Gallic acid, Circineol, Aesculetin, Triacontanolferulate, Chlogenic acid, Stigmasterol, Caffiec acid, Urosolic acid, 4-hydroxybenzoic acid, Vicenin-2, Chlorogenic acid, Procatechuic acid, Phenylpropaneglucosides,  $\beta$ -Stigmasterol. Seeds of this plant are chief source of fixed oils such as Oleic acid, Stearic acid, Hexourenic acid, Palmitic acid, Linodilinolin and Linolenic acid. The extraction of fresh leaves and stem yielded phenolic compounds like Apigenin, Circimaritin, Isothymusin, Eugenol and Rosameric acid . *O. sanctum* is also a source of monoterpenes and ssesquiterpenes like Neral, Campene. Cholesterol and stigma sterol. Vitamin A and Vitamin C are also found in this herb which stimulates antibody production up to 20% to provide protection against diseases (Vetal, Lade, & Rathod, 2012).



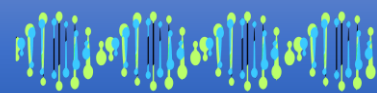
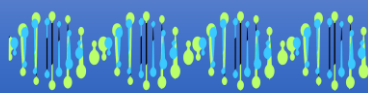


### Lipinski's rule & Druglikeness

The rule was formulated by Christopher A Lipinski in 1997. The rule describes molecular properties important for a drug's pharmacokinetics in the human body, including their absorption, distribution, metabolism and excretion (ADME). The rule is important for drug development where a pharmacologically active lead structure is optimized stepwise for increased activity and selectivity, as well as drug like properties. The modification of the molecular structure often leads to drugs with higher molecular weight, more rings, more rotatable bond and a higher lipophilicity. The rule states that poor absorption or permeation are more likely when a ligand molecule violates Lipinski rule of 5, that is, has more than five hydrogen bond donors, the molecular weight is over 500, the log P is over 5 and the sum of N and O is over 10 (Patel, Shukla, Verma, & Singh, 2016).

Druglikeness may be defined as a complex balance of various molecular properties and structure features which determine whether particular molecule is similar to the known drugs. These properties, mainly hydrophobicity, electronic distribution, hydrogen bonding characteristics, molecule size and flexibility and presence of various pharmacophoric features influence the behavior of molecule in a living organism, including bioavailability, transport properties, affinity to proteins, reactivity, toxicity, metabolic stability and many others. This screening methodology was implemented to analyze the drug likeness of the proposed ligands as it influences the behavior of molecule in a living organism, including bioavailability, transport properties, affinity to proteins, reactivity, toxicity, metabolic stability, and many more. We screened the ligands against Lipinski rule of 5 using Molinspiration.

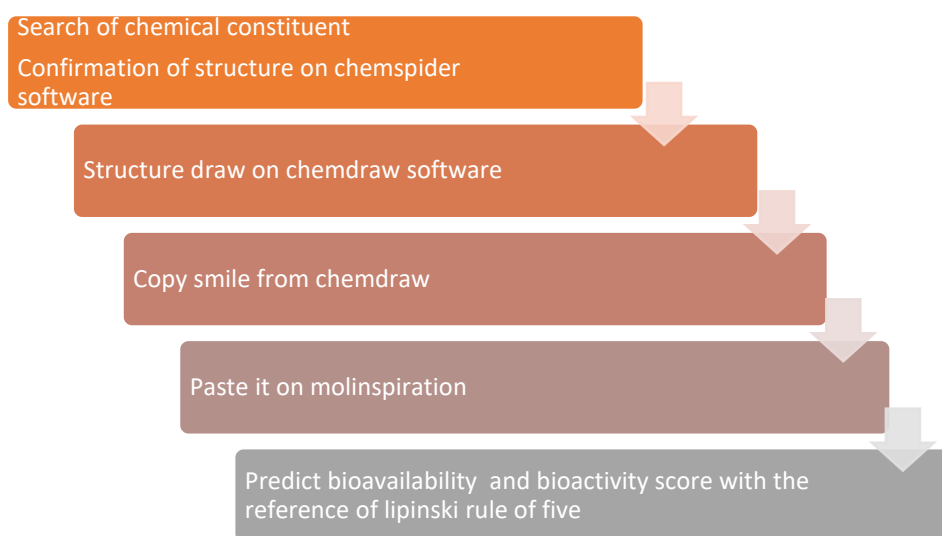




## Bioactivity Score

The drugs are also checked for the bioactivity by calculating the activity score for GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand. All the parameters were checked with the help of software Molinspiration drug-likeness score online ([www.molinspiration.com](http://www.molinspiration.com)). Calculated druglikeness score of each compounds and compared with the specific activity of each compound.

## Process of software working



## RESULT AND DISCUSSION

### Drug likeness calculation on the basis of Lipinski rule of five

The phrase "*in silico*" originally applied only to computer simulations that modeled natural or laboratory processes (in all the natural sciences), and did not refer to calculations done by computer generically (Patel et al., 2016). On the basis of literature survey we take 13 compounds from the plant and with the help of Molinspiration software we calculate different properties of these compounds. These properties are calculated on the basis of Lipinski's rule of five, which states that any compound considered as drug should have partition coefficient less than 5, its polar surface area within 140 Å<sup>2</sup>, it should have H bond acceptor less than 10, it should have H bond donor less than 5 and its molecular weight within 500 dalton. The 15 compounds showed their values for different parameter and these values recorded in Table 1.

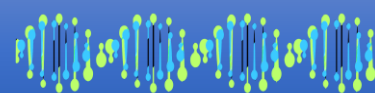
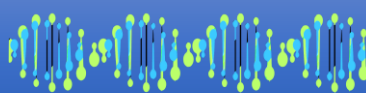



**Table 1. Drug likeness score for compounds**

S. N.	Compounds	milo g P	TPS A	n atoms	MW	n O N	N OHN H	n violatio ns	n rot b	volu me
1.	Luteolin-7-o-glucuronide	0.07	207.35	33	462.36	12	7	2	4	366.37
2.	Ethyl-2-methylbutyrate	2.18	26.30	9	130.19	2	0	0	4	140.72
3.	Eugenol	2.10	29.46	12	164.20	2	1	0	3	162.14
4.	Camphene	3.33	0.00	10	136.24	0	0	0	0	152.37
5.	4-hydroxybenzoic acid	1.37	57.53	10	138.12	3	2	0	1	119.06
6.	Triacontanolferrulate	10.24	55.77	44	615.00	4	1	2	33	676.80
7.	Gallic acid	0.59	97.98	12	170.12	5	4	0	1	135.10
8.	Apigenin-7-o-glucuronide	0.55	187.12	32	446.36	11	6	2	4	358.35
9.	Tetradecanal	6.62	17.07	15	212.38	1	0	1	12	249.80
10.	Carvacrol	3.81	20.23	11	150.22	1	1	0	1	158.57
11.	Palmitic acid	7.06	37.30	18	256.43	2	1	1	14	291.42
12.	Stearic acid	8.07	37.30	20	284.48	2	1	1	16	325.03
13.	Oleic acid	7.50	37.30	20	282.47	2	1	1	15	318.84







### Biological activity of compounds

Table.2 -Biological activity of taken compounds with the reference of receptor mechanism

S.N	Compounds	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1.	Luteolin-7-o-glucuronide	0.11	-0.03	0.01	0.40	0.01	0.42
2.	Ethyl-2-methylbutyrate	-2.38	-1.64	-3.19	-2.25	-2.16	-1.81
3.	Eugenol	-0.86	-0.36	-1.14	-0.78	-1.29	-0.41
4.	Camphene	-1.02	-0.55	-1.85	-1.15	-1.40	-0.82
5.	4-hydroxybenzoic acid	-0.98	-0.39	-1.21	-0.62	-1.19	-0.41
6.	Triacontanolferulate	-0.15	-0.68	-0.41	-0.22	-0.08/	-0.29
7.	Gallic acid	-0.77	-0.26	-0.88	-0.52	-0.94	-0.17
8.	Apigenin-7-o-glucuronide	0.12	-0.03	-0.01	0.44	0.03	0.43
9.	Tetradecanal	-0.24	0.24	-0.56	-0.34	-0.15	0.12
10.	Carvacrol	-1.02	-0.51	-1.15	-0.70	-1.25	-0.56
11.	Palmitic acid	0.02	0.06	-0.33	0.08	-0.04	0.18
12.	Stearic acid	0.11	0.05	-0.20	0.17	0.06	0.20
13.	Oleic acid	0.17	0.07	-0.22	0.23	0.07	0.27

### Potency of compounds per obtained data

#### Number of violations

In all the 13 compounds that are more important which have least number of violations. Ethyl-2-methylbutyrate, eugenol, camphene, 4-hydroxybenzoic acid, gallic acid, carvacrol are the compounds which have zero number of violation and tetradecanal, palmitic acid, stearic acid, oleic acid are the compounds have one number of violations.

#### Molecular weight

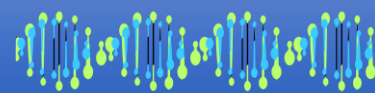
All constituents of data passes the Lipinski rule of five for molecular weight except triacontanolferulate, it crosses the value of 500 daltons.

#### Bioactivity score

#### GPCR ligand property

In the constituents of *ocimum sanctum* compounds luteolin-7-o-glucuronide, apigenin-7-o-glucuronide, palmitic acid, stearic acid, and oleic acid shows good ligand property on GPCR receptor. They also gives facilitation for the activity of immunomodulation.





### **Ion channel modulation**

In all taken constituent of table palmitic acid, stearic acid and oleic acid shows good ion channel modulation property. They helps to regulate and promote ion channels modulation activity.

### **Kinase inhibition**

Luteolin-7-o-glucuronide is the only constituent of table data which shows kinase inhibition property.

### **Nuclear receptor ligand property**

In the constituents of *ocimum sanctum* compounds luteolin-7-o-glucuronide, apigenin-7-o-glucuronide, palmitic acid, stearic acid, and oleic acid shows good nuclear receptor ligand property. They also gives facilitation for the activity of immunomodulation.

### **Protease inhibitor**

Metabolism of protein is caused by the help of protease enzyme and in above data compounds luteolin-7-o-glucuronide, apigenin-7-o-glucuronide, stearic acid, and oleic acid are the constituent which shows good protease inhibition activity.

### **Enzyme inhibitor**

Enzyme inhibition process of any compound increase the metabolism and half life of that specific compound sometimes it is used as a beneficial effect by the use of another drugs. Tetradecanal, luteolin-7-o-glucuronide, apigenin-7-o-glucuronide, palmitic acid, stearic acid and oleic acid are the constituent, shows good enzyme inhibition property.

### **CONCLUSION**


The Phytochemical screening and Pharmacognostical evaluation parameters of *ocimum sanctum* were performed and it showed the presence of many pharmacological active phytoconstituents. Effective formulations to be developed using indigenous medicinal plants, With proper pharmacological experiments and clinical trials. The manufacture of Herbal products should be governed by standards of safety and efficacy. So finally we concluded that these phytochemical screening data and phytochemical investigation of extract of *ocimum sanctum* in Ethanolic and water useful for further studies of pharmacological parameters. The different parts of *Ocimum sanctum* contain different types of constituents in varying amounts. The leaves contain a high content of essential oils which include Toluene, Camphene, Octane, Benzene, Citronellel, Sabinene, Limocene, Ledol, Dimethylbenzene, Ethyl-2methylbutyrate, Eugenol, Terpinolene,  $\beta$ -elemene, Isocaryophyllene, Iso-eugenol,  $\alpha$ -amorphenone,  $\alpha$ -guaiene,  $\alpha$ -humulene,  $\alpha$ -terpeneol, Borneol, Calamine, Nerolidol, Carvacrol, Geraneol, Humulene oxide, Elemol, Tetradecanal, (EZ)-famesol, Cissesquisainenehydrate,  $\alpha$ -bisbolol, Selin-11-en-4- $\alpha$ -ol,  $\alpha$ -murolene, 14-hydroxy- $\alpha$ -humulene. To separate constituents' extraction is performed in many ways. When alcoholic extraction of leaves and aerial parts of plants was done, it was found to contain Luteolin, Orientin, Urosolic acid, Apigenin7-Oglucuronide, Luteolin-7-O-glucuronide, Isorientin, Aesculin, Triacontanolferulate, Vallinin acid, Gallic acid, Circineol, Aesculetin, Triacontanolferulate, Chlogenic acid, Stigmasterol, Caffie acid, Urosolic acid, 4

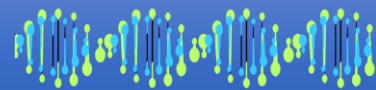
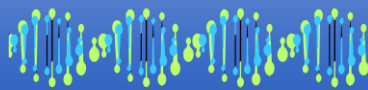




hydroxybenzoic acid, Vicenin-2, Chlorogenic acid, Procatechuic acid, Phenylpropaneglicosides,  $\beta$ -Stigmasterol. Seeds of this plant are chief source of fixed oils such as Oleic acid, Stearic acid, Hexourenic acid, Palmitic acid, Linodilinolin and Linolenic acid. The extraction of fresh leaves and stem yielded phenolic compounds like Apigenin, Circimaritin, Isothymusin, Eugenol and Rosameric acid. *O. sanctum* is also a source of monoterpenes and ssesquiterpenes like Neral, Campene. Cholesterol and stigma sterol. Vitamin A and Vitamin C are also found in this herb which stimulates antibody production up to 20% to provide protection against diseases.

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## AROMATHERAPY: THE SAFE AND EFFICIENT THERAPY

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### ABSTRACT:

The current aim of our review is to study the efficiency and safety measures of aromatherapy. Nowadays, use of alternative and complementary therapies with mainstream medicine has gained the momentum. Aromatherapy is one of the complementary therapies which use essential oils from volatile plants as the major therapeutic agents to treat several diseases. The natural oils are extracted from the of a plant like flowers, bark, stems, leaves, roots or other parts to enhance psychological and physical well-being. Aromatherapy includes mainly three modes of application: aerial diffusion, direct inhalation and topical application. It came into existence after the scientists deciphered the antiseptic and skin permeability properties of essential oils. Inhalation, local application and baths are the major methods used in aromatherapy that utilize these oils to penetrate the human skin surface with marked aura. This type of therapy utilizes various substitution and combinations to get relief from numerous complaints like depression, anxiety, indigestion, headache, fatigue, insomnia, memory loss, muscular pain, respiratory problems, skin ailments, swollen joints, urine associated complications etc. This review explores the information presented in the literature regarding therapeutic, cosmetic, psychological, olfactory, massage aromatherapy, safety issues and different plants used in aromatherapy.

### INTRODUCTION

#### History

Aromatherapy contains two words Aroma and therapy, aroma means fragrance or smell and therapy means treatment. This therapy is also known as natural way of healing of disease. In this article, just we discuss about the origin of aromatherapy, its benefits and how to perform it in own home.

In ancient civilization like Egypt, China and India have used this as a popular complementary and alternative therapy from at least 6000 years. It is said that aromatherapy was discovered by Rene-Maurice Gattefoss was working in a laboratory at his family's perfumery. A sudden explosion severely burned his hand, which he quickly plunged into a container of lavender oil. Afterward, he was surprised by how quickly his hand has been healed. The essential oils have gained their importance in therapeutic, cosmetic, aromatic, fragrant and spiritual uses. Essential oils are a mixture saturated and unsaturated hydrocarbons, alcohol, aldehydes, esters, ethers, ketones, oxides phenols and terpenes, which may produce characteristic odors. It is important to note that perfume oils also known as fragrance oils (and usually listed as "fragrance" on an ingredient label) are not the same as essential oils.





Aromatherapy uses essential oils, as the main therapeutic agents, which are said to be highly concentrated substances extracted from flowers, leaves, stalks, fruits and roots and also distilled from resins.

There are various methods by which they are administered in small quantity like inhalation, massage or simple applications on the skin surface and rarely, they are taken internally. Aromatherapy is the practice of using volatile oils, including essential oils for psychological and physical well-being.

### **The Benefit of an Aroma –**

**Inhaling Essential Oils:** Essential oils produce both psychological and physical benefits. When essential oils are inhaled into lungs it does not only stimulate the brain to trigger a reaction but natural constituents can supply the therapeutic benefits.

### **The Benefit of Physical Application:**

Essential oils also can be applied on skin for the therapeutic of skin disease. The constituent of the essential oils are absorbed into the blood stream and produce relief from the disease. Their undiluted forms are very powerful and concentrated so it should be avoided to apply undiluted aroma.

**Other Benefits:** Essential oils are also used for other purpose such as essential containing citronella candles can be use to keep mosquitoes away. Essential oils are widely believed to stimulate brain function.

### **How Aromatherapy Works:**

These aroma molecules are very potent organic plant chemicals that make the surrounding free from disease, bacteria, virus and fungus. Their versatile character of , nature along with immune booster body with hormonal, glandular, emotional, circulatory, calming effect, memory and alertness enhance, is well documented by many scientist. The stimulation properties of these oils lay in their structure,, which are closely in resemblance with actual hormones.

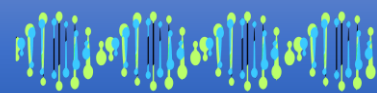
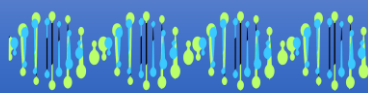
The penetration potential of these oils to reach the subcutaneous tissues is one of the important characters of this therapy. The mechanisms of their action involve integration of essential oils into a biological signal of the receptor cells in the nose when inhaled. The signal is transmitted to limbic and hypothalamus parts of the brain via olfactory bulb. These signal cause brain to release neuro- messengers like serotonin, endorphin etc. to link our nervous and other body systems assuring a desire change and to provide a feel of relief.

### **Mode of Application:**

The modes of application of aromatherapy are following:

- **Aerial diffusion:** for environmental fragancing or areal disinfection.
- **Topical applications:** for general massage, baths, compresses, therapeutic skin care.





- **Direction inhalation:** for the respiratory disinfection, decongestion, expectoration as well as psychological effects.

### **Materials-**

**Absolute:** fragrant oils extracted primarily from flowers or delicate plants tissues through solvent or supercritical fluids.

**Aroma lamps:** an electric or candles-fueled device which volatilizes essential oils, usually mixed with water.

**Essential oils:** fragrant oils extracted from plants chiefly through steam distillation (e. g., eucalyptus oil) or expression (grapefruit oil).

**Herbal distillates or hydro sols:** the aqueous by products of the distillation process (rose water). There are many herbs that make herbal distillates and they have culinary uses, medicinal distillates are chamomile, rose and lemon balm.

**Vaporizers:** typically higher oil content plant based materials dried, crushed and heated to extract and inhale the aromatic oil vapors in a direct inhalation modality.

### **Classification of Aromatherapy**

- ❖ *Cosmetic aromatherapy*
- ❖ *Massage aromatherapy*
- ❖ *Medical aromatherapy*
- ❖ *Olfactory aromatherapy*
- ❖ *Psycho-aromatherapy*

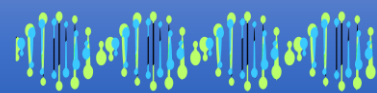
**Cosmetic aromatherapy:** This therapy utilized certain essential oils for skin, body, face and hair cosmetic products. These products are used for their various effects as cleaning, moisturizing, drying and toning. A healthy skin can be obtained by use of essential oils in facial products. On a personal level, cosmetic aromatherapy of full body or foot bath will be a simple and an effective way to have an experience. Similarly, few drops of appropriate oil give a rejuvenating and revitalizing experience.

**Massage aromatherapy:** Oils of grape seeds, almond and jojoba show the wonderful effect in body massage. This is also known as healing touch of massage.

**Medical aromatherapy:** The founder of **modern aromatherapy** Rene-Maurice Gattefosse has used essential oil to massage patient during surgery, thus utilizing the medical aromatherapy knowledge of the effect of essential oil on promoting and treating clinically diagnosed medical ailments.

**Olfactory aromatherapy:** Inhalation of essential oils has given rise to olfactory aromatherapy, where simple inhalation has resulted in enhanced emotional wellness, calmness, relaxation





rejuvenation of the human body. The release of the stress is welded with pleasurable scents which unlock odor memories. Essential oils are complemented to medical treatment can never be taken as a replacement for it.

**Psycho-aromatherapy:** The inhalation of the oils in this therapy is direct though the infusion in the room of the patient. Psych-aromatherapy and aromacology, both deals with the study and effects of aroma be it natural essential oils.

### What are the benefits?

- Nausea can be treated using aromas.
- Various emotions such as anxiety, grief and depression can be alleviated.
- It reduces muscular aches and pains.
- Blood pressure can be reduced.
- Tree essential oil is good to use for rashes, insect bite, cuts and warts.
- The treatment of acne and athletes foot can be done by Tea Tree oil.
- Lavender essential oil is a good relief to dry and inflamed skin.
- Aromatic massage reduces cortisone levels in children having juvenile rheumatoid arthritis.
- The circulation can be enhanced.
- Immune system can stimulate.
- Digestion can be improved.
- Constipation and abdominal spasm can be decrease.
- The circulation of scalp can increase and dandruff can be prevented.

### Should anyone avoid aromatherapy?

- ❖ People with high blood pressure should avoid stimulating essential oil like rosemary and spike lavender.
- ❖ People with a history of seizure should avoid hyssop oil.
- ❖ Women in the first trimesters of pregnancy should avoid all essential oils.
- ❖ People with severe asthma or a history of allergies should avoid all essential oils.

### Some plants used in aromatherapy

There are many plants which are used in aromatherapy, due to presence of essential or volatile oils. The parts of the plants (flowers, bark, stem, leaves, fruits etc.) from which the essential oils are extracted.

### Eucalyptus:

Eucalyptus [Eucalyptus globules Labill (E. globules)] belonging to the family of Myrtaceae, is a long evergreen plant with a height up to 250 feet. It is known for its constituents like cineole (70%-85%), aromadendrene limonene terpinene, cymene, phellandrene and pinene. Leucorrhoea and cystitis of genitourinary system can also be well treated with it. Throat infections, catarrh, cough, bronchitis, asthma, sinusitis associated with respiratory system have been taken care of







by oils of this plant. Eucalyptus oil has demonstrated its antioxidant, anti-inflammatory, and antibacterial activities and researcher have proved its efficacy beyond doubt in treatment of various metabolic and infectious diseases. The result are promising and can be utilized for treatment of multifactorial diseases of various origins in humans.

### **Geranium:**

Geranium (*Pelargonium graveolens* L' Herit) belong to the family Geraniaceae. A perennial hairy shrub native of South Africa, up to one meter in height, also found and cultivated in France, Italy, Central America, Japan and Congo is a plant of choice for essential oil. One of the best natural perfume, complete in itself is geranium oil, generally used in soaps and detergents because its unique nature is never challenged with alkalinity of soaps. This oil is furthered use for its sedative properties, nerve tonic, in throat infection, to rectify the blood disorder diabetes. Moreover, this oil is gaining popularity as anti-diabetic, anticancer,

### **Rosemary:**

Rosemary (*Rosemarinus officinalis* Linn.) belonging to the family of Lamiaceae bears small pale blue flowers in late spring early summer and grows up to the height of 90cm. It has 3 varieties (silver, gold and green strike); It's the green variety that is used for its medicinal properties. This plant is rich in better principle, resin, tannic acid and volatile oil. The active constituents are bornyl cetate, borneol along with other esters and special camphor similar to the possessed by the myrtle, cineol, pinene and camphene. The oil also possesses some good action on the cardiovascular system. It regularizes the blood pressure and retards the hardening of arteries. In winter, it used to relief the rheumatic pain with aggravates due to cold.

### **Tea tree:**

**Tea tree** (*Melaleuca alternifolia* cheel) belonging to the family of Myrtaceae, with yellow or purple flower and needles like leaves is a serve of marshy area. Due to its commercial value, it is cultivated on plantations. The main constituent of its oil is terpinene-4-ol, an alcoholic terpenene with a clean musty aroma. The antiviral activity is due to alpha-sabina with antibacterial and antifungal effects. It is an immune booster due to terpinene-4-ol while cineol is responsible for its antiseptic character. The oil is used in herpes, abscess, blister acne, cold sores, burns, insect bites, dandruff and oily skin. Further, in treatment of respiratory associated problems it has been used for tuberculosis, cough, bronchitis, asthma, catarrh and whooping cough; also it is used in females for vaginitis, cystitis and pruritus treatment.

### **Peppermint:**

Peppermint [*Mentha piperita* Linne. (*M. piperita*)] belongs to the family of Lamiaceae. Till date, all the 600 kinds of mints are raised from 25 well-defined species. The two most important are peppermint (*M. piperita*) and spearmint (*menthe*) *spicata*). Spearmint bears the strong aroma of sweat character with a sharp menthol undertone. Its oil constituent includes carvacrol, menthol, carvone, methyl acetate, limonene and menthone. The pharmacological action is due to menthol, a primary constituent of peppermint oil. At least 44% free menthol is present in





peppermint oil. Components are sensitive to climate, latitude and maturity of the plant. Inhalation and application of menthol on skin causes to relieve pain spasm and arthritic problems. The antispasmodic properties of oil make it a better choice during pain associated with the menstruation cycle and are also used in the treatment of irritable bowel syndrome.

Further itching due to various reasons like herpes blisters, ringworm infection, scabies, poison, oak and ivy can also be relieved. Much have been said and discussed about the menthe oil by many researchers for its various activities but its use in aroma therapy needs more efforts.

### **Ylang Ylang:**

Ylang Ylang ( *Cananga odorata* Hook. F. & Thoms) belonging to the family of Annonaceae. Native to Madagascar, Indonesia and Philippines is a small tree. Its chemical constituent includes gerany acetate, linalool, geraniol, farnesol, benzyl acetate, geranial, methyl chavicol, eugenol pinene and farnesene.

### **Pharmacological Action of Essential oils:**

Some of the pharmacological actions of essential oils are discussed below.

#### **Antiviral:**

The antiviral activity evaluated by Deans and Ritchie for the essential oils of *M. ericifolia*, *.leucadendron*, *M. armillaris* and *Melaleuca styphelioides* on kidney cells of African green monkey through plaque reduction assay on herpes simplex virus type 1, Gave the remarkable result.

#### **Antibacterial:**

Many essential oil were screened for their antibacterial activity against Gram positive and Gram negative bacteria along with antifungal properties. Much essential oil was examining one such Basil essential oil; showed a good antimicrobial potential. It has bactericidal properties against aeromanas. Many plants like *M. piperita*, black mustard (*brassica nigra*), *angelica archangelca* and *cuminum cyminum* have been tested positive for their antifungal activity. They are in the initial phase of clinical trials and if the results are per the expectation, they will be a very good alternative for existing antifungal drugs which are not frequently used for their toxic systemic effects.

#### **Anti-lice:**

Most of the preparation for head lice infestations contains the tea tree [94]. The insecticidal activity of tea tree oil is due to its anticholinesterase .

#### **Anti-tumor:**

5-Fluorouracil treatment is enhanced in human colon cancer cells if sensitized by geraniol, a component of plant essential oils. Polypharmacological anti-tumor mode of action of essential oil in cardamom has some promising results to substantiate the claims.





### **Anti- dandruff:**

In a signal blind and parallel-group study, it was observed that shampoos which contain 5% tea tree oils were effective and well tolerated by patients having mild to moderate dandruff and at least 41% improvement was observed .

### **Hormonal action:**

Geranial, neral, geraniol, nerol and trans-anethol are well established for their stimulation of estrogenic response, when compare to eugenol which has anti-estrogenic activity. Citra i.e. the combination of geraniol, nerol and eugenol were effective in replacing  $17\beta$ -estradiol from the estrogen receptors in recombination yeast cells.

### **Spasmodic action:**

Strong spasmogenic and spasmolytic activity was shown by Kunzea ericoides and leptospermum scorparium essential oils, respectively and their various extracts when tested on isolated rat ileum.

### **Conclusion:**

From the above reports and study, it has been cleared that aromatherapy is a natural and noninvasive gift of nature. This therapy is not only preventive but also can be used in the acute and chronic states of disease. There may be possibility of enhancing the rate of the reaction and bioavailability of drugs from the use of these essential oils. The immune system of the body enhanced during use of aromatherapy. Moreover, the time at which plant contains the maximum amount of volatile oil with various chemical constituents. Aromatherapy can be boon not only to patients but also to a common person. This therapy is most useful for everyone who may be done at own home.

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Figure -1: Aromatherapy



Figure -2: Eucalyptus





Figure -3: Geranium



Figure -4: Peppermint





Figure -5: Ylang ylang



Figure -6: Tea tree

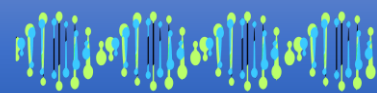




Figure -7: Rosemary







## REVIEW ON THE PHARMACOLOGICAL PROPERTIES OF THE PLANT *ZINGIBER OFFICINALE*

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### Abstract

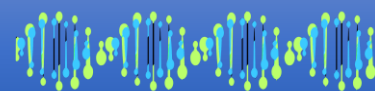
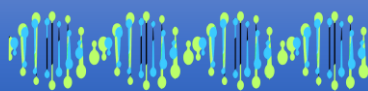
Ginger is a flowering plant whose rhizomes, ginger root or simply ginger, is widely used as a spice or a folk medicine. The English origin of the word, "ginger", is from the mid 14 century, from old *English gingifer*, from medieval *latin gingiber*, from *greek zingiberis* from prakrit. Ginger likely originated as ground flora of tropical lowland forests in region from the Indian sub continental to southern Asia. It produces clusture of white and pink flower buds that bloom into yellow flowers. The fragrant perisperm of the zingiberaceae is used as sweetmeats by Bantu and also condiment and sialogoue. In ginger the whole B complex vitamins C, E, various minerals and other phytochemicals are found which shows their relative activity. It has a sialogouge action, stimulating the production of saliva, which makes swallowing easier. Zingerone is produced from gingerols during drying, having lower pungency and spicy-sweet aroma. Studies have found no clear evidence of harm from taking ginger during pregnancy, though its safety has not been established and it is a suspected risk for mutagenicity.

### INTRODUCTION

Medicinal plants have a long history of use for the beneficial of mankind. According to the report of the World Health Organization (W.H.O.) about 80% of the world's populations rely mainly on traditional therapies which involve the use of plant extracts or their active substances (Martínez & Luján, 2011). Ginger (*Zingiber officinale*) is commonly called 'Ale' or 'Adrak' which is an important commercially grown crop for its aromatic rhizomes which are used as a spice, condiment and as a medicine. It has been used as a spice for over 2000 years. It is cultivated in many tropical and subtropical countries including China, India, Nigeria, Australia, Jamaica and Haiti. Among which, China and India are the world's leading producers of ginger (Wohlmuth, 2008).

**Biological Source-** Ginger is the underground rhizome of the ginger plant with a firm, striated texture. *Zingiber officinale* Roscoe, commonly known as ginger belongs to family Zingiberaceae (Shakya, 2015).





**MORPHOLOGY**

The plant is an aromatic herb and its taxonomic position is given in table 1.

Kingdom	Plantae
Division	Magnoliophy
Class	Liliopsida
Order	Zingiberales
Family	Zingiberaceae
Genus	<i>Zingiber</i>
Species	<i>Z.officinale</i>



**Table1-** taxonomic position of ginger.

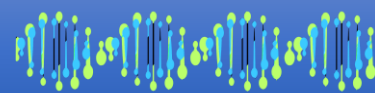
**Figure1-** ginger root

The ginger plant has a perennial, tuberous root or rhizome; the stems are erect, oblique, round, annual, and invested by the smooth sheaths of the leaves, 2 or 3 feet in height, yellow green flowers and thick tuberous rhizome. Laterally compressed rhizomes are 7-15 cm long and 1-1.5 cm broad (Gupta & Sharma, 2014). About 1-3 cm long branches arise and terminate in depress scars or in undeveloped buds. The flesh of the ginger rhizome can be yellow, white or red in color, depending upon the variety. It is covered with a brownish skin that may either be thick or thin, depending upon whether the plant was harvested when it was mature or young.

**CHEMICAL COMPOSITION**

In the fresh ginger rhizome, the gingerols were identified as the major active components. *Z. officinale* is reported to possess essential oils, phenolic compounds, flavonoids, carbohydrates, proteins, alkaloids, glycosides, saponins, steroids, Phenylalkylketones or vanillyl ketones of ginger include 6-gingerol 8-gingerol and 10-gingerol, 6-shogaol, 8-shogaol, 10-shogaol and zingerone. 6-paradol,6- and 10- dehydrogingerdione and 6- and 10- gingerdione have also been identified. terpenoids and tannin as the major phytochemical groups (Townsend et al., 2013). The volatile oil consists mainly of the mono- and sesquiterpenes; camphene,  $\beta$ -phellandrene, curcumene, cineole, geranyl acetate, terphineol, terpenes, borneol, geraniol, limonene,  $\beta$ -elemene, zingiberol, linalool,  $\alpha$ -zingiberene,  $\beta$ -sesquiphellandrene,  $\beta$ -bisabolene, zingiberenol and  $\alpha$ -farnesene. Non-volatile pungent compounds include gingerols, shogaols, paradols and zingerone that produce a ‘hot’ sensation in the mouth (Semwal, Semwal, Combrinck, & Viljoen, 2015). Zingiberol is the principal aroma contributing component of ginger rhizome . The primary pungent agents of ginger are gingerol, with other gingerol analogues such as the shogaols, paradol and zingerone also found in high levels in rhizome extracts (R & Prakash, 2010).





## PHARMACOLOGY

The *in vitro* study have shown gingerols to act as agonists of the vanilloid receptor This receptor is also activated by capsaicin, the major pungent principle in cayenne and chilli pepper, which shares structural features with the gingerols (Ludy, Moore, & Mattes, 2012).

### Anti-cancer effects:

Recent studies have shown that zingerone contains anticancer potential. Ginger has been found to be anti-carcinogenic via multiple pathways (Srinivasan, 2017). Galanals A and B have been found to be potent apoptosis inducers of human T lymphoma Jurkat cells (Wohlmuth, 2008).

### Anti-Inflammatory Effects

Ginger contains potent anti-inflammatory compounds called *gingerols*. Ginger has been found to inhibit prostaglandin biosynthesis and interfere with the inflammatory cascade and the vanilloid nociceptor (Qin & Xu, 2008).

### Anticoagulant Effects

Ginger has been shown to inhibit platelet aggregation and to decrease platelet thromboxane production *in vitro* 8-Gingerol (Qin & Xu, 2008).

### Antiemetic Effects

Ginger is the herb most commonly used to treat nausea and vomiting in pregnancy, either recommended by providers or used as self-treatment by women. It would be even more effective than vitamin B6 for relieving the severity of nausea. Ginger extract possesses antiserotonergic and 5-HT<sub>3</sub> receptor antagonism (Dhanik, Arya, & Nand, 2017) .

### Antioxidant Effects

Antioxidants are compounds or systems that can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. 6-gingerol appears to be the antioxidant constituent present in ginger (Mishra, Kumar, Kumar, College, & Pradesh, 2012).

### Cardiovascular Effects

Including in Ayurvedic science, ginger has been described as great heart tonic. *In vitro* research indicates that gingerols and the related shogaols exhibit cardio depressant activity at low doses and cardio tonic properties at higher doses (Kundu, Na, & Surh, 2009). Ginger also may help to lower high cholesterol making the heart healthy (Qin & Xu, 2008).

### Gastrointestinal Effects

Modern scientific research has revealed that ginger possesses numerous therapeutic properties including antioxidant effects, an ability to inhibit the formation of inflammatory compounds (Ali, Blunden, Tanira, & Nemmar, 2008). There is evidence that ginger rhizome (root) increases stomach acid production(Mishra et al., 2012) .

### Antimicrobial Activities

Ginger has been traditionally exploited for having broad range of antimicrobial activity against both gram positive and gram negative bacteria and fungi (Chao, Young, & Oberg, 2000) Ingenol and 6-shogaol, isolated from ginger rhizome, demonstrated antiviral activity. 40





gingerol has been reported as active inhibitor of *M. avium* and *M. tuberculosis in vitro* (Qin & Xu, 2008).

#### **Antitussive Effects**

6-shogaol, generally more potent than 6- gingerol, has exhibited antitussive effects. Ginger is often used to soothe sore throats and reduce coughing, especially those caused by the common cold. In fact, ginger lozenges and other medicinal products are commercially available, designed with the express purposed of treating coughs (Mishra et al., 2012).

#### **Immunomodulatory Effects**

*In vitro* evidence indicates that ginger has immunomodulatory effects and is an effective antimicrobial and antiviral agent. The beneficial effects of ginger in treating coughs, colds and flu is probably linked to immune-boosting properties of the Plant (Dhanik et al., 2017). The beneficial effects of ginger in treating coughs, colds and flu is probably linked to immune-boosting properties of the plant. Few studies have examined the potential immunomodulatory activity of ginger (Mishra et al., 2012).

#### **Antigenotoxic Activity**

Norethandrolone and oxandrolone were investigated for their genotoxic effect on human lymphocyte chromosomes (Beg, Siddique, Ara, Gupta, & Afzal, 2008) using chromosomal aberrations and sister chromatid exchanges as parameters and subsequently Genistein and 6-gingerol were used as antigenotoxic agents to ameliorate the genotoxicity induced by the steroids (Mishra et al., 2012).

#### **Weight Loss Effects**

Spiced foods or herbal drinks, such as those that contain ginger, have the potential to produce significant effects on metabolic targets, such as satiety, thermogenesis, and fat oxidation (Mishra et al., 2012) .

#### **Breast cancer**

The effects of chronic treatment with hot water extract of ginger rhizome on spontaneous mammary tumorigenesis have been examined in mice(Katiyar, Agarwal, & Mukhtar, 1996). In mice given free access to extract of ginger in drinking water, the development of mammary tumors was significantly inhibited (Gupta & Sharma, 2014) .

#### **CONCLUSION**

It can be concluded that ginger is a good source of antioxidant and most of the antioxidant components exhibit higher activities in alcohol media as determined by different assays. Hence, apart from its medicinal properties, ginger can also be used as an antioxidant supplement(R & Prakash, 2010)(R & Prakash, 2010)(R & Prakash, 2010)(R & Prakash, 2010)(R & Prakash, 2010)(R & Prakash, 2010)(R & Prakash, 2010)(R & Prakash, 2010). The present study clearly demonstrated that aqueous extract of ginger was able to protect the gastric mucosa from stress-induced mucosal lesions and inhibits gastric acid secretion probably by blocking H<sup>+</sup>, K<sup>+</sup>-ATPase action, inhibiting growth of *H. pylori* and offering anti-oxidant protection against oxidative stress-induced gastric damage. Finally it is studied that ginger show various pharmacological effect such as Antigenotoxic Activity, Weight Loss Effects,



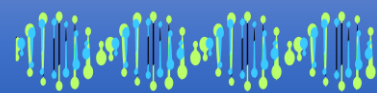


Immunomodulatory Effects, Cardiovascular Effects, Anti-Inflammatory Effects, Antiemetic Effects etc.

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## ROLE OF NATURAL PRODUCTS IN THE HEPATIC DISEASES AND PROTECTIVE ACTION

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### Abstract

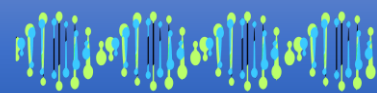
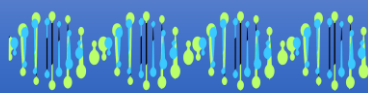
In the human body the liver is one of the most important organs in the body. It performs a very important role in the regulation of various processes, they are metabolism, secretion, storage and detoxification of endogenous and exogenous substances are major. Due to the all work liver can be infected by any type of disorders, and till now a day various types of medicine not treating properly. Liver have the self-healing ability to one third part of itself. Liver is a very major organ of body due to the improper work of it, can cause severe types of some other disease. Hepatic cells can be regenerate if the liver is affected half of their part. But in severe hepatic conditions Allopathic medicines not treating properly and in place of these drugs natural agents gives a very good response with their low toxicity and very reduced adverse effect. In all the hepatoprotective natural products the phytochemicals are present which shows their action against the disease and by nature they are very less toxic. Some natural products which improves the functioning and regulation of liver (grapefruit, cranberries, and grapes) and plants [cactus pear (nopal) and cactus pear] fruit, chamomile, silymarin and spirulina.

### INTRODUCTION

The liver is the most important organ in the body. It plays a pivotal role in regulating various physiological processes. . It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction. In addition, it aids metabolism of carbohydrate, protein and fat, detoxification, secretion of bile and storage of vitamins (Schneider, 2004). The role played by this organ in the removal of substances from the portal circulation makes it susceptible to first and persistent attack by offending foreign compounds, culminating in liver dysfunction. Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages (Abou Seif, 2016).

Medicinal plants play a key role in human health care. About 80% of the world population relies on the use of traditional medicine, which is predominantly based on plant material. Scientific studies available on medicinal plants indicate that promising phytochemicals can be developed for many health problems. For example, the vinca alkaloids (vincristine, vinblastine and vindesine), derived from *Catharanthus roseus*, *Vinca rosea*, *Lochnera rosea*, and *Ammocallis rosea* have been employed for their anticancer properties (Negi, 2011). Modern pharmaceuticals still contain at least 25% drugs derived from plants. Medicinal plants have various effects on living systems. Some are sedatives, analgesics, antipyretics, cardioprotectives, antibacterial, antiviral and antiprotozoal. The use of natural remedies for the treatment of liver diseases has a long history and medicinal plants and their derivatives are still





used all over the world in one form or another for this purpose. Liver protective plants contain a variety of chemical constituents like phenols, coumarins, monoterpenes, glycosides, alkaloids and xanthenes (O.v, 2009). In this work, we review the literature related to natural products (crude plant extracts and chemically defined molecules) with hepatoprotective activity. These findings provide greater chances and flexibility in helping researchers identify compounds with good hepatoprotective potential (Adewusi & Afolayan, 2010).

## **Liver**

Liver is the largest internal organ in the human body and is very much essential for survival. It is the biggest reticulo-endothelial organ in the body which maintains the survival of individual (Bogdanos, Gao & Gershwin, 2013).

## **Anatomy**

It is the largest gland of the body enclosed within the right lower rib cage beneath the diaphragm. The liver is a soft, pinkish brown triangular organ that normally weighs between 1.4 – 1.6 kg. Liver is divided in two principle lobes, a large right lobe and a smaller left lobe separated by falciform ligament. The right lobe is considered by many anatomists to include an inferior quadrangle lobe and a posterior caudate lobe (Abdalla, Vauthey & Couinaud, 2002).

## **Structure**

The lobes of liver are made up of many functional units called lobules. A lobule consists of specialized epithelial cells called hepatic cells or hepatocytes arranged in irregular, branching, interconnected plates around the central vein. Rather than capillaries liver has larger space lined by endothelium called sinusoids through which blood passes. The sinusoids are also partly lined with stellate reticuloendothelial (Kupffer's) cells. These phagocytes destroy worn out white and red blood cells, bacteria and toxic substances (Rogers & Dintzis, 2012).

## **FUNCTIONS OF LIVER**

### **Secretion and excretion of bile**

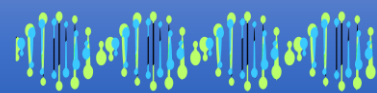
The hepatic cells secrete 800-1000 ml of bile, a yellow, brownish or olive green liquid of pH 7.6-8.6. Bile is partially an excretory product and partially a digestive secretion. The principle bile pigment is bilirubin. Bile mainly consists of water, bile salts, cholesterol, lecithin, bile pigments, and several ions (Jordan, 1964).

### **Metabolic functions**

Carbohydrate metabolism:

Liver maintains the normal blood glucose level. It can convert glucose to glycogen (glycogenesis) when blood sugar level is high and breakdown of glycogen to glucose





(glycogenolysis) when blood sugar level is low. Also liver can convert amino acid and lactic acid to glucose (gluconeogenesis) when sugar level is low (Roden & Bernroider, 2003).

Lipid metabolism:

Liver stores some triglycerides (neutral fat) and breaks down fatty acids into acetyl coenzyme-A. This process is called as  $\beta$ -oxidation and converts excess acetyl coenzyme A into ketone bodies (ketogenesis). It synthesizes lipoproteins, cholesterol and uses cholesterol to make bile salts (Yamashita, Kaneyuki & Tagawa, 2001).

Protein metabolism:

The liver deaminates (remove the amino group,  $\text{NH}_2$ ) amino acids so that they can be used for ATP production. It converts the resulting toxic ammonia ( $\text{NH}_3$ ) into much less toxic urea for excretion in urine. Hepatic cells synthesize plasma proteins such as alpha and beta globulins, albumin, prothrombin, and fibrinogen (Owen, Felig, Morgan, Wahren & Cahill, 1969).

Drug metabolism:

Liver plays a vital role in biotransformation of drugs. It converts drug molecules from non-polar to polar. These non-polar drugs can be conjugated with more polar compounds, which make them water soluble for the urinary excretion.

## LIVER DISEASES

Hepatic failure:

The most severe clinical consequence of liver disease is hepatic failure. It forms into three main categories:

Massive hepatic necrosis:

Acetaminophen, anti-tubercular drugs, anti-depressant, and industrial chemicals such as carbon tetrachloride and poisoning drugs collectively tend to cause massive hepatic necrosis. The mechanism may be direct toxic damage to hepatocytes but more often is a variable combination of toxicity and inflammation with immune mediated hepatocytes destruction.

Chronic liver disease:

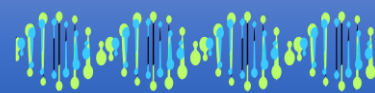
This is the most common route to hepatic failure and is the end point of relentless chronic hepatitis ending in cirrhosis.

Hepatic dysfunction without overt necrosis:

It causes Reye's syndrome, tetracycline toxicity, and acute fatty liver of pregnancy.







#### Clinical features:

The clinical signs of hepatic failure include jaundice, hypoalbuminemia, hyperammonemia, fetor hepaticas, impaired estrogenic metabolism and consequent hyperestrogenemia leading to palmar erythema and spider angioma. In males, hyperestrogenemia may lead to hypogonadism and gynaecomastia. Hepatic failure is life threatening and cause multiple organ damages. Respiratory failure with pneumonia and sepsis combine with renal failure to claim the lives of many patients with hepatic failure.

#### Cirrhosis:

Cirrhosis is the serious condition, causes death in top countries with the ranking of 10. It is mainly due to alcohol and viral hepatitis. Cirrhosis as the end-stage of chronic liver disease is defined by three characteristics.

#### Portal hypertension:

Increased resistance to portal blood flow may develop in a variety of circumstances, which can be divided into prehepatic, intrahepatic and posthepatic causes. The major prehepatic conditions are obstructive thrombosis and narrowing of the portal vein before it ramifies within the liver. The major post hepatic causes are severe right sided heart failure, constrictive pericarditis and hepatic vein outflow obstruction. The dominant intrahepatic cause is cirrhosis, accounting for most cases of hypertension.

#### Jaundice:

Jaundice is characterized by the yellow coloration of the skin and sclerae due to the retention of pigmented bilirubin, and as cholestasis characterized by systemic retention of not only bilirubin but also other solutes eliminated in bile.

#### Cholestasis:

Cholestatic conditions which result from hepatocellular dysfunction or intrahepatic or extrahepatic biliary obstruction also may present with jaundice. Pruritis is a presenting symptom related to the elevation in plasma bile acids and their deposition in peripheral tissues particularly skin. Skin xanthomas sometimes vitamins A, D or K improve the results (Center, 2009).

#### **Infectious disorders:**

##### Viral hepatitis:

Appear as the result of hyperlipidemia and impaired excretion of cholesterol. Vitamin supplements like viral hepatitis caused by group of virus having a particular affinity to the liver. These include Infectious mononucleosis, Cytomegalovirus and Yellow fever





Autoimmune hepatitis:

Autoimmune hepatitis is a chronic hepatitis that produce Female predominance particularly in young and postmenopausal problems in women, absence of viral serological marker, Elevated serum IgG and  $\gamma$ -globulin levels, High serum titers of autoantibodies including antinuclear (ANA), antismooth muscle (SMA) and anti-liver/kidney microsome antibodies (anti-LKMI)b and Negative antimitochondrial antibody.

Alcoholic liver disease:

Excessive alcohol consumption is the major cause of liver diseases in most developing and developed countries (Rehm, 2011).

### HEPATOPROTECTIVE PLANTS:

Herbal based therapeutics for liver disorders has been in use in India for a long time and has been popularized world over by leading pharmaceuticals. Despite the significant popularity of several herbal medicines in general, and for liver diseases in particular, they are still unacceptable treatment modalities for liver diseases (Stickel & Schuppan, 2007). The limiting factors that contribute to this eventuality are (i) Lack of standardization of the herbal drugs; (ii) Lack of identification of active ingredient(s)/principle(s); (iii) Lack of randomized controlled clinical trials (RCTs) and (iv) Lack of toxicological evaluation 13. The use of natural remedies for the treatment of liver diseases has a long history, starting with the Ayurvedic treatment, and extending to the Chinese, European and other systems of traditional medicines. A large number of plants and formulations have been claimed to have hepatoprotective activity (Patwardhan, Vaidya & Chorghade, 2004). Nearly 160 phytoconstituents from 101 plants have been claimed to possess liver protecting activity. In India, more than 87 plants are used in 33 patented and proprietary multi-ingredient plant formulations<sup>14</sup>. In of the tremendous advances made, no significant and safe hepatoprotective agents are available in modern therapeutics. Therefore, due importance has been given globally to develop plant based hepatoprotective drugs effective against a variety of liver disorders The various hepatoprotective agents are *Andrographis paniculata*, *Anoectochilus formosanus*, *Azadirachta indica*, *Cassia roxburghii*, *Coccinia grandis*, *Colchicum autumnale*, *Flacourtia indica*, *Foeniculum vulgare*, *Indigofera tinctoria*, *Lepidium sativum*, *Orthosiphon stamineus*, *Prostechea michuacana*, *Rubia cordifolia*, *Scutellaria rivularis*, *Solanum nigrum*, *Terminalia catappa*. *Solanum nigrum*, *Curcuma longa*, *Phyllanthus emblica*, *Foeniculum vulgare*, *Swertia Chirata*, *Picrorhiza kurroa*, *Azadirachta indica*, *Andrographis paniculata*, *Flacourtia indica*, *Wedelia calendulacea*, *Aegle marmelos* and *Prostechea michuacana* (Kumar, 2012).

**Hepatoprotective activity of crude plant extracts** (D'Elía, Jayat, Ortiz, Salazar-Bravo, & Pardiñas, 2011)

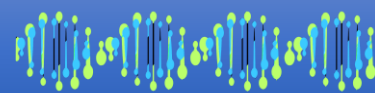




Table-1

Sl. No.	Family and botanical name	Origin	Part used	Extract
1.	Acanthaceae <i>Acanthus ilicifolius</i> L.	India	Leaves	Alcohol
2.	<i>Andrographis lineata</i> Nees	India	Leaves	Aqueous, methanol
3.	<i>Andrographis paniculata</i> (Burm.f.) Nees	India	Leaves	Alcohol
4.	<i>Anisotes trisulcus</i> (Forssk.)	Yemen	Aerial plants	Ethanol
5.	<i>Asteracantha longifolia</i> L.	Sri Lanka	Whole plant	Aqueous
6.	<i>Hygrophila auriculata</i> (K.Schum.) Heine	India	Seeds	Methanol
7.	<i>Hypoestes triflora</i> (Forssk.) Roem. and Schult	Rwanda	Leaves	Aqueous
8.	<i>Rhinacanthus nasuta</i> (L.) Kurz	India	Root	Methanol
9.	Adoxaceae <i>Viburnum tinus</i> L.	Southern Europe	Leaves	Aqueous-methanol
10.	Aizoaceae <i>Trianthema portulacastrum</i> L.	India	Leaves	Ethanol
11.	Apiaceae <i>Apium graveolens</i> L.	india	Seeds	Methanol
12.	Apocynaceae <i>Apocynum venetum</i> L.	China, Japan	Leaf	Aqueous
13.	Araliaceae <i>Acanthopanax senticosus</i> (Rupr. and Maxim.) Harms	Taiwan	Aerial plant	aqueous
14.	Asclepiadaceae <i>Sarcostemma brevistigma</i> Wight	India	Stem bark	Ethyl acetate
15.	Asteraceae <i>Achyrocline satureioides</i> (Lam.) DC.	Argentina	Aerial parts	Aqueous




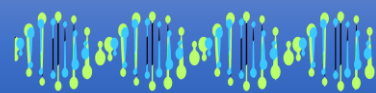


## CONCLUSION

Liver plays a most important role in detoxification and discharge of many endogenous and exogenous compounds, any injury or destruction of its function may lead to quite a lot of implications on one's health. In treating the hepatoprotective activity many momentous medicinal plant extracts are enormously cure the liver diseases. With the medicinal plant treatment we can reduce the adverse effects of the drugs, as these drugs are naturally available, these may not cause toxicity. Longer use of medicinal plants may causes some toxicity, but we can cure or minimize the side effects. The drugs Tetracycline, Salicylates, ethanolic agents may causes hepatotoxicity and a range of adverse effects, reasonably by using medicinal plants may not cause any injury to tissues and further organs.

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## PREVENTIVE EFFECT OF FLAX SEED OIL ON CATARACT INDUCED BY NAPHTHALENE AND STREPTOZOTOCIN IN EXPERIMENTAL RATS

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### ABSTRACT

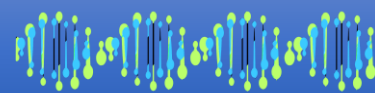
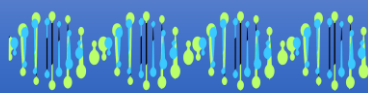
Cataract is an eye disease in which the lens of the eye becomes cloudy opaque, causing decrease in vision. Antioxidants terminate that chain reaction which causes damage or death to the cell by removing free radical intermediates, and inhibit other oxidation reactions. Flax seed oil contains omega 3 and omega-6 fatty acids having antioxidant properties. Flax seeds and its oil, contains a group of chemicals called lignans, Alpha linolenic acid (ALA), as well as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), belong to a group of substances called omega-3 fatty acids. EPA and DHA are found primarily in fish while ALA is mostly found in flax seed oil. Our research study concluded that diet containing flax seed and flax seed oil can reduce the risk of age related and diabetic cataract. In case of naphthalene induced cataract the enzymatic parameters catalase and LPO (Lipid Peroxidase) were observed. Flax seed oil treated groups (group VI (0.421) and group V (0.479) has been shown with respect to control group. The standard treatments were found that (0.254). The treatment significantly ( $p < 0.001$ ) lowered the elevated level of group II (0.685). In case of model 2<sup>nd</sup> streptozotocin induced cataract the enzymatic parameters (Catalase & LPO) were decreased with respect to control group. In this model the enzymatic parameters like LPO the flax seed oil treated group IV (1.56) & V (1.60) has been shown the treatments significantly lowered ( $p < 0.001$ ) the elevated level of group II (2.82). Finally we concluded that flax seed oil and their seeds are rich source of different fatty acids, like omega 3 and omega 6 fatty acids they can reduce the risk factor of cataract and the person who takes antioxidants rich food in their daily routine they will away from this type of risk factor of disease like cataract.

### INTRODUCTION-

Ageing is a mysterious physiological process and leads to gradual decline antioxidant enzymes. Endogenous anti-oxidative enzymes constitute a tissue defense system against ageing and stress, likely to be caused by free radicals. These enzymes like glutathione reductase and peroxidase and super oxide dismutase are necessary for removing the free radicals from the system and the lens also. Senile cataract is a major cause of blindness. There are about 12 million blind people due to cataract in India alone. A number of risk factors are associated with cataract like diabetes, hypertension and central obesity, older age, race, smoking, alcohol use and low socioeconomic status, or educational attainment. Among the various complications of diabetes mellitus in the eyes, diabetic retinopathy has been regarded as the most common cause of visual loss.. Also, the risk of post-operative surgical complications includes inflammatory response, loss of vitreous humor and posterior capsule opacification.

Naphthalene – induced cataractogenesis is a suitable model for human age related cataract. Naphthalene was converted into 1, 2 naphthaquinone and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in the





liver. This 1, 2 naphthaquinone is highly reactive and generates free radicals, alkylates proteins, glutathione and amino acids. Antioxidants delay the onset and progression of cataract. Hence the objective of the present study was Preventive Effect of Flax Seed oil on cataract induced by Naphthalene and Streptozotocin in experimental rat. India has a special position in area of herbal medicine. Since it is one of the countries which are capable of cultivating most of the important plants used both in modern and traditional system of medicine. Omega-3 fatty acids, found in Flax seed and flax seed oil, have been shown to reduce inflammation and help prevent certain chronic diseases such as heart disease and arthritis and reduce the risk factor of cataract. These essential fatty acids appear to be particularly important for cognitive and behavioral function as well as normal growth and development.

## **MATERIALS AND METHODS-**

### **Seed collection and Authentication-**

The seeds of Flax seed was collected from the local market of Azamgarh, district (UP) and authenticated by Head of Department of botany, Dr. Zia ul Hasan, with voucher Specimen No.349/Bot/Safia/2012. Professor of Saifia Science College, Bhopal.

**Procurement of animals-** Albino male rats (100-150) gm and Swiss albino mice (20-25) gm were provided from Truba institute of pharmacy, Bhopal.

### **Pharmacognostical Analysis-**

#### **Identification of fixed oil-**

1. Fixed oil completely mixes with half volume of light petroleum ether.
2. Fixed Oil mixes with Equal volume of alcohol to get Clear liquid which is Cool at 0°C for three hours to obtain clear liquid.

#### **Standard-**

Saponification value- 188-195, Iodine value- 160-200, Acid value- not more than 4

#### **Acute toxicity study-**

Oral acute toxicity studies were performed according to the OECD guidelines(423). The doses selected for the study were 3 ml/kg, 6 ml/ kg, 12 ml/ kg, 16 ml/kg, 20 ml/kg p.o., for one day. Animals were observed for any alteration in their behavior. The animals were observed for 3 hours after dose administration and also after 24 and 48 hours. The all doses of flax seed oil did not show any signs of toxicity up to the dose of 20ml/ kg p.o. After completion of acute toxicity test we selected two doses (1.5ml/kg and 3 ml/ kg) for further experimental studies.





## EXPERIMENTAL METHADODOLOGY-

### 1. Naphthalene induced cataract in rats-

Animals- Albino male rats (100-150) gm.

Chemicals- 10% Naphthalene solution, 1% Tropicamide

### Grouping & treatment of experimental animals-

The male albino rats were divided in to five groups, each group containing six animals.

**Group I-** Considered as normal control.

**GroupII-** Negative control received 10% naphthalene solution 0.5 ml/kg/day ( p.o.) for 3days & 1ml/kg/day thereafter.

**GroupIII-** Received naphthalene 1ml/kg + standard drug (vit. E 5ml/ kg p.o.)

**Group IV-** Naphthalene + (Flax seed oil 1.5ml/kg p.o.)

**Group-V-** Naphthalene + (Flax seed oil 3ml/kg p.o.)

All the drugs were administered for period of 28 days.

### Scoring of naphthalene cataract is as fallows-

**Stage 0-** Clear lens

**Stage 1-** Water clefts and spoke like opacities

**Stage 2-** More water clefts and spoke like opacities

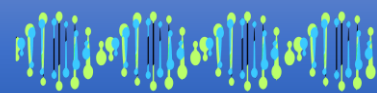
**Stage 3-** Opacities more to form a shell

**Stage 4-** Shell partly quick and white

**Stage 5 -** Shell fully thick and white. (Agrawal SS, M Paridhavi, Herbal drug technology)







### Procedure-

- The rats were dosed with 10% naphthalene solution using 18 gauge needles at 0.5gm/kg/day for three days and 1gm/kg/day thereafter.
- All drug treatment given orally.
- Morphological changes in the eyes of the rat were observed through slit lamp examination after dilating the pupil with 1% tropicamide.
- Lenses were examined twice in a week during the first two weeks and thereafter at weekly intervals.
- One week after the administration, spoke like opacities in the cortex were seen.
- By the third week, an opaque shell is visible in the deep cortex region which becomes denser and slightly deeper with time.

### 2-Streptozotocin induced diabetic cataract-Requirements-

Animal used- Albino rat (100-150) gm.

Chemicals- Streptozotacin , 1% Tropicamide

### Grouping and treatment of experimental animals-

The male albino rats were divided in to five groups, each group containing six animals.

**Group I** - Normal control (Received sodium citrate buffer)

**Group II** - Negative control received streptozotacin 7.5 mg/kg i.p.

**Group III**-Received standard treatment STZ + vit. E (5 ml/kg p.o.)

**Group IV**-STZ + Flax seed oil (1.5ml/kg p.o.)

**Group V**- STZ + Flax seed oil (3ml/kg p.o.)

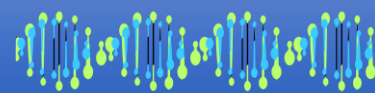
### Stages of Streptozotocin induced cataract are following-

**Stage 1** - Lenses were similar to normal lens.

**Stage 2** – Small vacuoles appearing in the periphery or central suture or cloudiness.

**Stage 3 a**- Large vacuoles spreading to the centre. **b**- Increase radial opacities fused vacuoles and cloudiness.





**Stage 4-** Disappearance of vacuoles and the radical opacities become more prominent.

**Stage 4-** Full opacity.

#### **Preparation of sodium citrate buffer-**

- Dissolve 10.0g of sodium citrate & 5.90g sodium chloride in 900ml of water. Adjust the pH by addition of HCL and dilute to 1000 ml with water.

#### **Procedure-**

- Streptozotocin were dissolved in 0.02 M sodium citrate buffer was filtered through 0.22millipore filter in to sterilized container kept in to ice for 10 min.
- The control group rats were injected sterilized buffer alone.
- After three days blood glucose level were estimated.
- STZ injected rats having blood glucose level less than 150mg/dl re- injected with a fresh solution of STZ and tested again for blood glucose.
- Progression of cataract and stages were observed.
- The initial stages of cataract 15 days after STZ injection.
- The fully mature cataract appears in nearly 110 depending on the age of rat at time of injection.
- After 30 days blood glucose level were estimated and the tissue enzymatic parameters were estimated.

### **RESULTS & DISCUSSION**

At present, the only treatment for cataract is surgery. Any antioxidant that prevents or slows the progression of cataract has a significant health impact. Oxygen radicals play an important role in

the origin of a wide range of diseases . Diabetes mellitus in 2nd experimental animal models and humans is associated with marked reductions in the levels of plasma antioxidants such as  $\alpha$ -tocopherol, ascorbic acid, uric acid, and glutathione causing lowered plasma antioxidative capacity. (M.A.EMAN, S.M. EMAN, Biophysics and laser science unit, Research institute of ophthalmology).

Cataract is a major cause of blindness all over the world. It is an age related phenomenon, over and above oxidative stress also plays its role. Surgical treatment has remained the only remedy till now. Hence, if a drug is sought which can either reverse or prevent lenticular opacity, it will be a great advance in the treatment of this disorder. A number of drugs have been shown to interfere with the process of cataract formation like aldose reductase inhibitors, resatain.





sulindac, aspirin, quercetin. The potential role of vitamins and antioxidants in preventing various diseases and in human cataract formation is reported. The free radicals are the main causative factors in cataract. The toxic species of oxygen formed in lens milieu include superoxide anion, lipid hydro peroxides, OH radicals and hydrogen peroxide. Endogenous antioxidant like reduced glutathione is present in high concentration in lens; super-oxide dismutase and catalase keep the level of free radicals below toxic levels. In cataractous lenses its concentration is decreased'. Hence, with the use of antioxidants cataract formation can be prevented. (P.Sharma, S. Kulshrestha, *et al* 1997).

Ascorbic acid, glutathione, linolenic acid, uric acid , vitt. E these are important antioxidants which are reduced risk factor of cataract.

In naphthalene induced cataract, it is a suitable model for human age related cataract. The injected naphthalene is oxidized in liver and then converted in to naphthalene dihydrodiol.

This stable compound on reaching the eyes gets converted enzymatically to dihydroxy naphthalene. Being unstable at physiological pH 1,2 dihydroxy naphthalene. Spontaneously auto oxidizes to 1,2 naphthoquinone and hydrogen peroxide . 1,2 dihydronaphthalene is also a highly reactive compound which can alkylate , proteins , glutathione , amino acids. It can also generate free radicals.

In other model streptozotacin induced cataract is also a age related cataract. In this model the dose of streptozotacin was injected and the blood glucose level was elevated to normal blood glucose. The elevated sugar level in the aqueous humor induces lens fibre swelling by osmosis and increases the lens fibre permeability resulting in disruption of the fibre. Cataractogenic sugars entering the lens converted in to their respective sugar alcohol in the presence of enzyme aldolase reductase. These alcohols accumulation in the fibres creating hypertonicity, which is corrected by an influx of water. Initially the activity of a cation pump compensate for the increased water content of the fibre and leads to an electrolyte imbalance. (Sharma P., Kulshrestha *et al*, 1998).

In case of naphthalene induced cataract the enzymatic parameters catalase and LPO were observed flax seed oil treated groups (group VI (0.421) and group V (0.479) has been shown with respect to control group. The standard treatments were found that (0.254). The treatment significantly ( $p < 0.001$ ) lowered the elevated level of group II (0.685).

In case of model 2<sup>nd</sup> streptozotocin induced cataract the enzymatic parameters (Catalase &LPO) were decreased with respect to control group. In this model the enzymatic parameters like LPO the flax seed oil treated group IV (1.56) &V (1.60) has been shown the treatments significantly lowered ( $p < 0.001$ ) the elevated level of group II( 2.82).

The person who takes healthy diet included antioxidant rich food in their daily routine they away from this type of risk factor of disease like cataract.

Flax seed oil and their seeds are rich source of different fatty acids, like omega 3 and omega 6 fatty acids they can reduce the risk factor of cataract.





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**Table : 1 Acute toxicity study**

Sr.no.	Dose in ml	No. of animal	Observation
1-	3 ml/kg	3	All animals were survived
2-	6 ml/kg	3	All animals were survived
3	12ml/kg	3	1 animal has dead rest 2 were survived
4-	16 ml/kg	3	All animals were survived
5-	20 ml/kg	3	All animals were survived



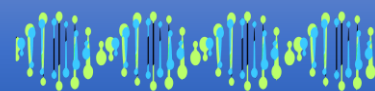
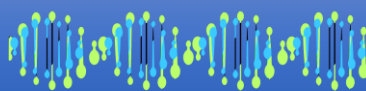
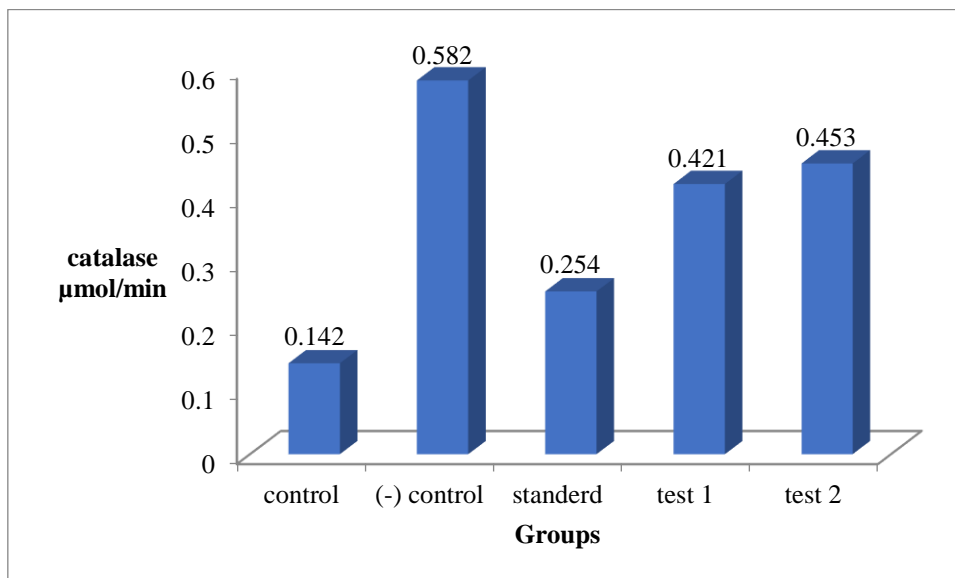


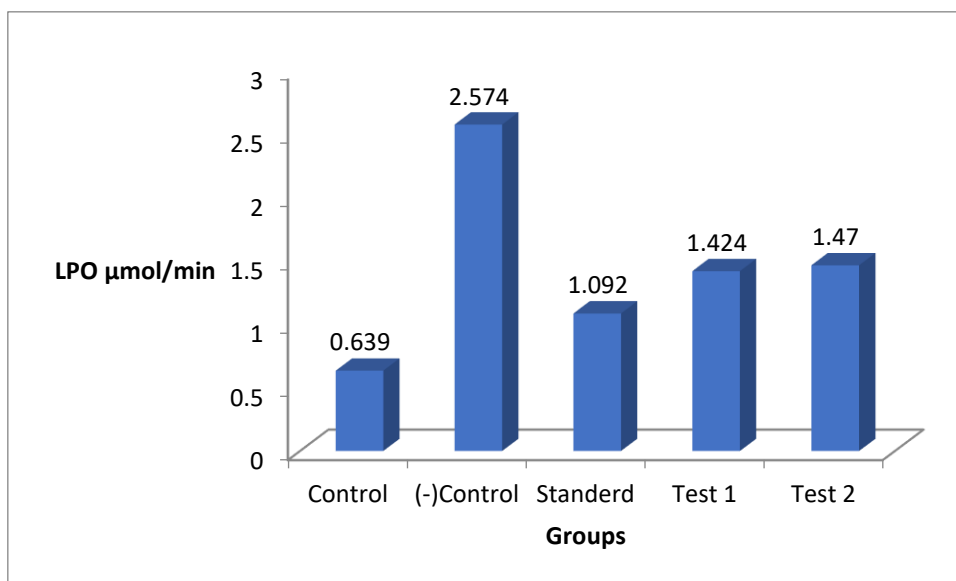
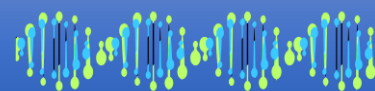
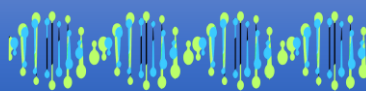
Table 2- Effect of fraction of flax seed oil on tissue enzymatic parameters in naphthalene induced cataract

S.No.	GROUP	Mean ± SEM	
		CATALASE	LIPID PEROXIDASE
1	Normal control	0.142 ± 0.008	0.639± 0.05
2	Negative control	0.685 ± 0.021 a***	2.574 ± 0.1.2 a***
3	Standard	0.254 ± 0.002 a***,b***	1.09 ± 0.08 a**,b***
4	Test-1	0.421 ± 0.003 a***,b***,c***	1.42 ± 0.02 a***, b*** c*
5	Test-2	0.479 ± 0.002 a***, b***,c*** ,d*	1.47 ± 0.04 a***, b***,c**



Graph: 1 Catalase estimation in naphthalene induced cataract



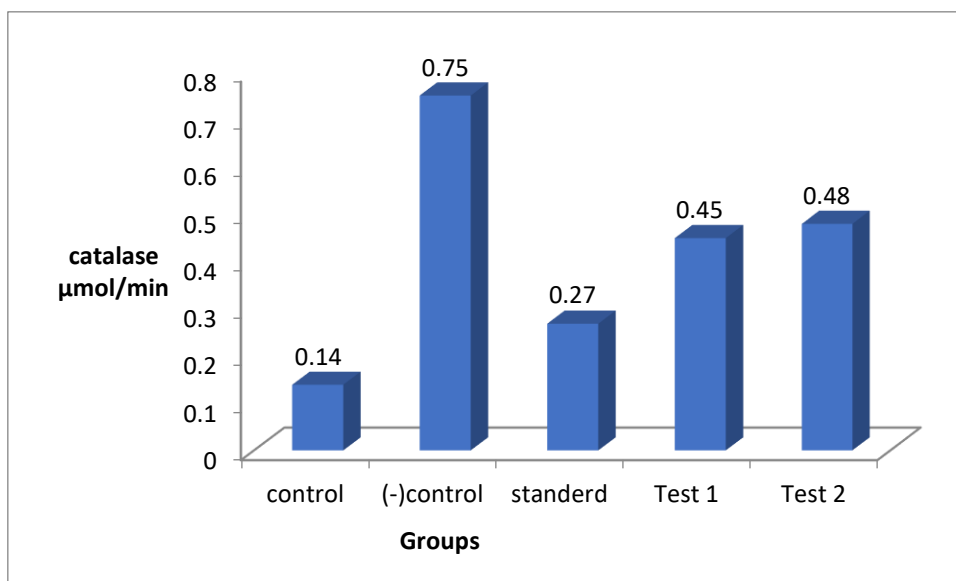
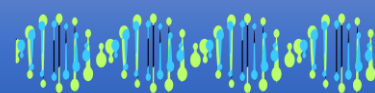
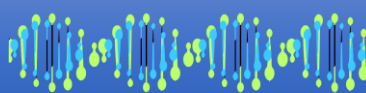


**Graph 2: Lipid per oxidation in naphthalene induced cataract**

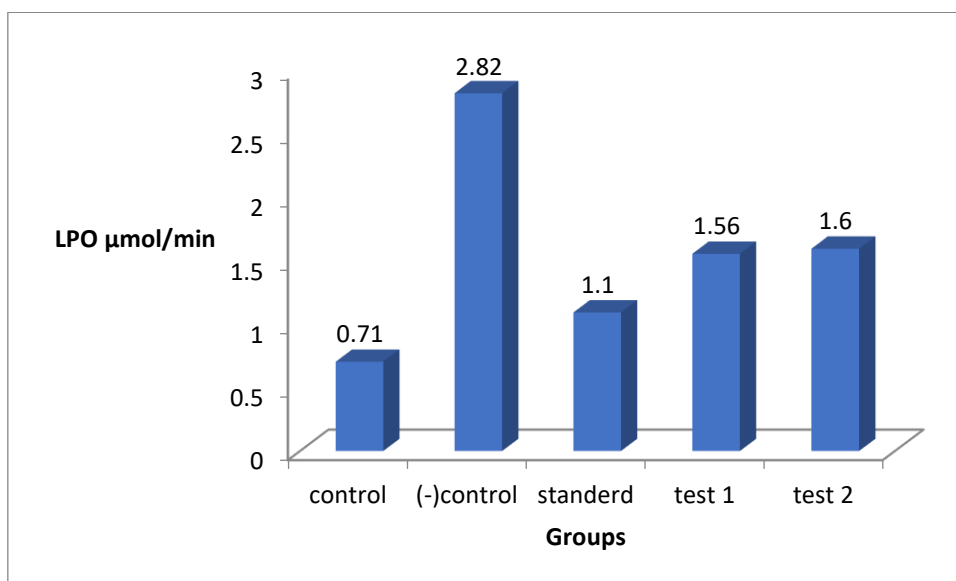
**Table 3- Effect of fraction of flax seed oil in tissue enzymatic parameters in streptozotocin induced cataract**

S.No.	GROUP	Mean $\pm$ SEM	
		CATALASE	LIPID PEROXIDASE
1	Normal control	0.140 $\pm$ 0.008	0.710 $\pm$ 0.05
2	Negative control	0.752 $\pm$ 0.021 a***	2.82 $\pm$ 0.1.2 a***
3	Standard	0.272 $\pm$ 0.002 a**,b***	1.10 $\pm$ 0.08 a**,b**
4	Test-1	0.451 $\pm$ 0.003 a***,b***,c**	1.56 $\pm$ 0.02 a***, b***,c*
5	Test-2	0.482 $\pm$ 0.002 a**, b**,c*	1.60 $\pm$ 0.04 a***, b**



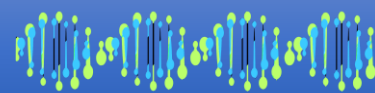


**Graph-3 Estimation of catalase in streptozotocin induced cataract**



**Graph-4 Estimation of lipid peroxidation in streptozotacin induced cataract**





## REVIEW ON BIOINFORMATICS AND SOME COMPUTER AIDED DRUG DESIGN SOFTWARE

Avadh biharee, Arpita yadav, Anoop tiwarii, Ranjeet yadav, Parjanya kumar shukla, Akanksha Gupta.

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### Abstract:

Computer aided or *in silico* drug, designing is required to detect hits and leads, optimize/ alter the absorption, distribution, metabolism, excretion and toxicity profile and prevent safety issues. Drug designing software has potential role in biotechnology and pharmaceutical field. In this review, we discuss the main principles that underpin bioinformatics analyses, look at the types of biological information and databases that are commonly used. Bioinformatics, the application of computational techniques to analyses the information associated with biomolecules on a large-scale, has now firmly established itself as a discipline in molecular biology, and encompasses a wide range of subject areas from structural biology, genomics to gene expression studies. Computer software makes our work simpler and faster. Various companies such as Accelrys, Schrodinger, Auto Dock and Argus Lab offering drug designing software. In this review, we provide an introduction and overview of the current state of the field. The main purpose of this review article is to give a brief glance about the Computer Aided Drug Design that play important role in modern medical science and its scope carries in the near future, in the service of designing newer drugs along with lesser expenditure of time and money.

### INTRODUCTION

#### History and origin of bioinformatics

This discipline represents the convergence of genomics, biotechnology and information technology, and encompasses analysis and interpretation of data, modeling of biological phenomenon, and development of algorithms and statistics. Bioinformatics is by nature a cross-disciplinary field that began in the 1960s with the efforts of Margaret O. Dayhoff, Walter M. Fitch, Russell F. Doolittle and others (Lapidus & Ph, n.d.).

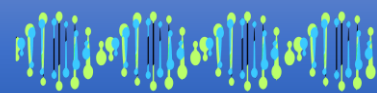
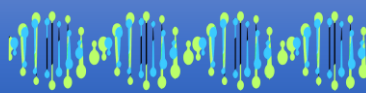
Bioinformatics started over a century ago when Gregor Mendel, an Australian monk cross-fertilized different colour of the same species of flower. Mendel illustrated that the inheritance of traits could be more easily explained if it was controlled by factors passed down from generation to generation. Since Mendel, bioinformatics and genetics record keeping have come a long way (Liu, Mendel, & Wu, 2012).

**Term bioinformatics** was invented by Paulien Hogeweg and Ben Hesper in 1970 as "the study of informatics processes in biotic systems". Paulien Hogeweg is a Dutch theoretical biologist and complex systems researcher studying biological systems as dynamic information processing systems at many interconnected levels (Lapidus & Ph, n.d.).

The term bioinformatics is used to encompass almost all computer applications in biological sciences, but was originally coined in the mid-1980s for the analysis of biological sequence data (Risler, 2002).







## Chronological History of Bioinformatics

- ❖ **1953** - Watson & Crick proposed the double helix model for DNA based x-ray data obtained by Franklin & Wilkins.
- ❖ **1954** - Perutz's group develop heavy atom methods to solve the phase problem in protein crystallography.
- ❖ **1955** - The sequence of the first protein to be analysed, bovine insulin is announced by F. Sanger.
- ❖ **1972** - The first recombinant DNA molecule is created by Paul Berg and his group.
- ❖ **1974** - Vint Cerf and Robert Khan develop the concept of connecting networks of computers into an "internet" and develop the Transmission Control Protocol (TCP).
- ❖ **1975** - Microsoft Corporation is founded by Bill Gates and Paul Allen. Two-dimensional electrophoresis, where separation of proteins on SDS polyacrylamide gel is combined with separation according to isoelectric points,
- ❖ **1988** - The National Centre for Biotechnology Information (NCBI) is established at the National Cancer Institute.
- ❖ **1988** - The human genome organization (HUGO) was founded.
- ❖ **1991** - The research institute in Geneva (CERN) announces the creation of the protocols which make up the World Wide Web.
- ❖ **1995** - The Haemophilus influenzae genome is sequenced.
- ❖ **1997** - The genome for E.coli is published.
- ❖ **2000** - The genome for Pseudomonas aeruginosa is published.
- ❖ **2001** - The human genome is published.

## Definition of Bioinformatics

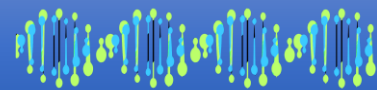
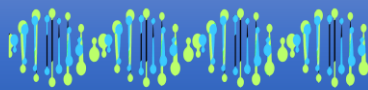
Roughly, bioinformatics describes any use of computers to handle biological information. In practice, the definition used by most people is narrower; bioinformatics to them is a synonym for "computational molecular biology"- the use of computers to characterize the molecular components of living things. Bioinformatics is the unified discipline formed from the combination of biology, computer sciences, and informational technology. It is the use of computer for the acquisition, management, and analysis of biological information (Martin-Sanchez & Hermosilla-Gimeno, 2010).

**Classical bioinformatics:** The mathematical, statistical and computing methods that aim to solve biological problems using DNA and amino acid sequences and related information.

Generally three terms: bioinformatics, computational biology and bioinformation infrastructure are often times used interchangeably; these three may be defined as follows:

- a. *Bioinformatics* refers to database-like activities, involving persistent sets of data that are maintained in a consistent state over essentially indefinite periods of time;
- b. *Computational biology* encompasses the use of algorithmic tools to facilitate biological analyses (Fickett, 2000).
- c. *Bioinformation infrastructure* comprises the entire collective of information management systems, analysis tools and communication networks supporting biology (Singh, Malik, & Sharma, 2007).





The National Center for Biotechnology Information (NCBI 2001) defines "*Bioinformatics is the field of science in which biology, computer science, and information technology merge into a single discipline.*"

### **Aims of bioinformatics**

The aims of bioinformatics are three fold.

- First, at its simplest bioinformatics organizes data in a way that allows researchers to access existing information and to submit new entries as they are produced, e.g. the Protein Data Bank for 3D macromolecular structures.
- The second aim is to develop tools and resources that aid in the analysis of data. The analysis and interpretation of various types of data including nucleotide and amino acid sequences, protein domains, and protein structures.
- The third aim is to use these tools to analyse the data and interpret the results in a biologically meaningful manner or development and implementation of tools that enable efficient access and management of different types of information.

### **Definitions Related to Bioinformatics**

**Bioinformaticist** is an expert who not only knows how to use bioinformatics tools, but also knows how to write interfaces for effective use of the tools .

**Bioinformatician** is a trained individual who only knows to use bioinformatics tools without a deeper understanding.

**Computational biology** is the science of using biological data to develop algorithm and relation among various biological systems.

**Genomics** is a field, which existed before the completion of the sequences of genomes, but in the crudest of forms, Genomics is any attempt to analyze or compare the entire genetic complement of a species.

It is, of course possible to compare genomes by comparing more-or-less representative subsets of genes within genomes.

**Proteomics** the "proteome" as "the Protein complement of the genome" and proteomics to be concerned with Qualitative and quantitative studies of gene expression at the level of the functional proteins themselves .

**Pharmacogenomics** is the application of genomic approaches and technologies to the identification of drug targets.

**Pharmacogenetics** is a subset of pharmacogenomics, which uses genomic bioinformatic methods to identify genomic correlates.

**Cheminformatics** is the combination of chemical synthesis, biological screening, and data-mining approaches used to guide drug discovery and development.





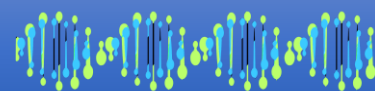
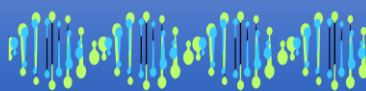
**Medical Informatics** "Biomedical Informatics is an emerging discipline that has been defined as the study, invention, and implementation of structures and algorithms to improve communication, understanding and management of medical information." Medical informatics is more concerned with structures and algorithms for the manipulation of medical data, rather than with the data itself.

### BIOINFORMATICS SOFTWARE

Computer software makes our work simpler and faster. Brief description various software use in bioinformatics given in table1. Some bioinformatics software are discussed below-

- 1- **AMPHORA** ("AutoMated Phylogenomic inference Application") is an open source bioinformatics workflow. AMPHORA2 uses 31 bacterial and 104 archaeal phylogenetic marker genes for inferring phylogenetic information from metagenomic datasets (Kerepesi, Bánky, & Grolmusz, 2014).
- 2- **Anduril**- Anduril is designed to enable systematic, flexible and efficient data analysis, particularly in the field of high-throughput experiments in biomedical research. Anduril is an open source component-based workflow framework for scientific data analysis (Stocker et al., 2009).
- 3- **Auto Dock**- Auto Dock is a molecular modeling simulation software. It is especially effective for protein-ligand docking. Auto Dock consists of two main programs:
  - I. Auto Dock for docking of the ligand to a set of grids describing the target protein;
  - II. Auto Grid for pre-calculating these grids.
- 4- **EMBOSS**- EMBOSS is an acronym for European Molecular Biology Open Software Suite. EMBOSS is a free open source software analysis package specially developed for the needs of the molecular biology and bioinformatics user community (Rice, Longden, & Bleasby, 2000). The EMBOSS package contains a variety of applications for sequence alignment, rapid database searching with sequence patterns, protein motif identification (including domain analysis), and much more.
- 5- **Galaxy**- Galaxy is also a data integration platform for biological data. Galaxy is now also used for gene expression, genome assembly, proteomics, epigenomics, transcriptomics and host of other disciplines in the life sciences (Goecks et al., 2010)(Goecks, Li, Clements, & Taylor, 2011).
- 6- **Gene Pattern**- is a freely available computational biology open-source software package originally created and developed at the Broad Institute for the analysis of genomic data (Robinson, McCarthy, & Smyth, 2010). GenePattern is a powerful scientific workflow system that provides access to hundreds of genomic analysis tools.





- 7- **Mothur**- is an open source software package for bioinformatics data processing. The package is frequently used in the analysis of DNA from uncultured microbes (Bujnicki & Tiurnyn, 2013). The first release of mothur occurred in 2009.
- 8- **UGENE**- is computer software for bioinformatics (Okonechnikov et al., 2012). It works on desktop computer operating systems such as Windows, macOS, or Linux. It is released as free and open-source software; UGENE integrates dozens of well-known biological tools, algorithms, and original tools in the context of genomics, evolutionary biology, virology, and other branches of life science (Gilbert, 2004).
- 9- **Staden Package**- The Staden Package is computer software, a set of tools for DNA sequence assembly, editing, and sequence analysis (Staden, 1996). It is open-source software, released under a BSD 3-clause license. The Staden Package was developed by Rodger Staden's group at the Medical Research Council (MRC) Laboratory of Molecular Biology, Cambridge, England, since 1977 (Staden, 1996).

**Table-1** Description of some bioinformatics software

Name of software	Description						
	Developer	Stable release	Operating system	Available in	Type	License	Website
<b>AMPHORA</b>	Martin Wu, Jonathan Eisen et al.	2.0 / 2013	Linux	English	Bioinformatics		<a href="http://wolbachia.biology.virginia.edu/WuLab/Software.html">http://wolbachia.biology.virginia.edu/WuLab/Software.html</a>
<b>Anduril</b>	Systems Biology Laboratory University of Helsinki	June 24, 2014	Linux, Microsoft Windows,	English	Bioinformatics	GPL (v.1.x), BSD (v.2.x)	<a href="http://www.anduril.org">www.anduril.org</a>
<b>Gene pattern</b>	Broad Institute, University of California, San Diego	May 2017	Windows XP and later OS X 10.7 and later Ubuntu, SuSE, CentOS	English	genomic analysis	BSD	<a href="http://www.genepattern.org">www.genepattern.org</a>
<b>Staden Package</b>	James Bonfield, et al.	24 January 2012	Unix, Linux, macOS, Windows	English	Bioinformatics	BSD 3-clause	<a href="http://staden.sourceforge.net">staden.sourceforge.net</a>
<b>UGENE</b>	Unipro	29 December 2017	Cross-platform: Windows, macOS, Linux	English, Russian,	Bioinformatics toolkit	GPLv2	<a href="http://ugene.net">ugene.net</a>
<b>Galaxy</b>		23 February 2017	Unix-like	English	Scientific workflow, data integration, analysis and data publishing		<a href="http://GalaxyProject.org">GalaxyProject.org</a>

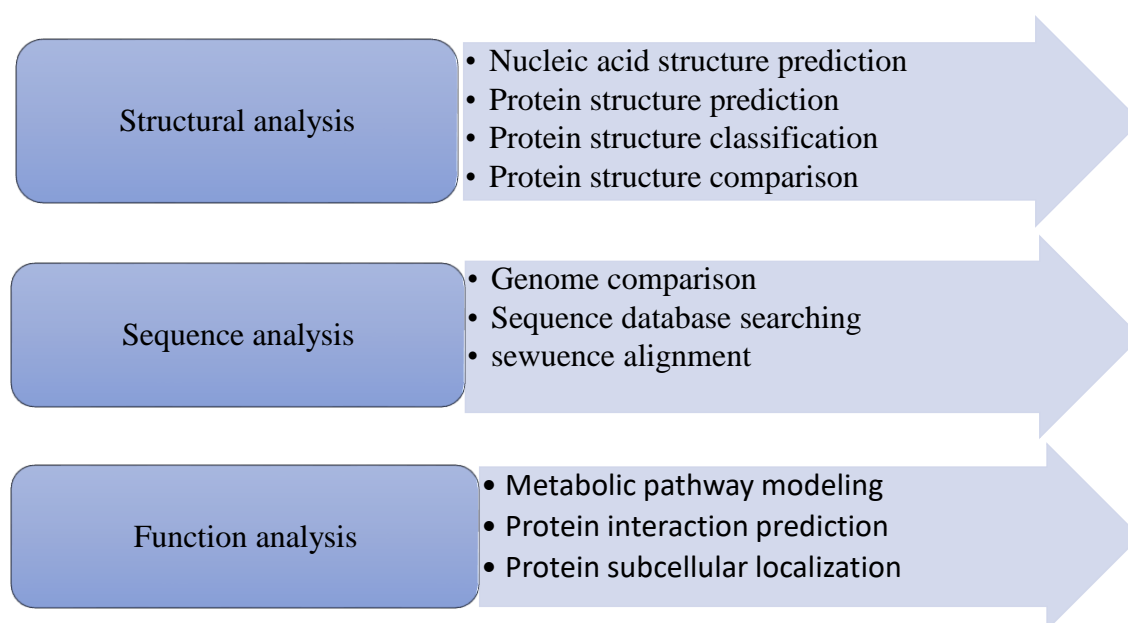




## APPLICATION OF BIOINFORMATICS

Bioinformatics has not only become essential for basic genomic and molecular biology research, but is having a major impact on many areas of biotechnology and biomedical sciences. There are wide application of bioinformatics in different field such as Molecular medicine, Gene therapy, Drug development, Microbial genome applications, Climate change Studies, Biotechnology, Antibiotic resistance, Forensic analysis of microbes, Evolutionary studies, Crop improvement, Veterinary Science, Comparative Studies etc (Lapidus & Ph, n.d.).

Various significant applications of bioinformatics are given in **figure-1**.



**Figure 1-** application of bioinformatics

## COMPUTER AIDED DRUG DESIGNING SOFTWARE

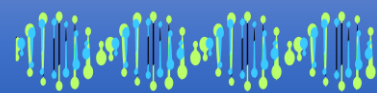
### What is drug design?

Drug is a substance or products that is used or intended to be used to modify or explore physiological system or pathological state for the benefit of the recipient (ICH Expert Working Group, 2003). In general drug is defined composition with a pharmacological effect, Approved by the Food and Drug Administration (FDA). Drug design is the inventive process of finding new medications based on the knowledge of a biological target. Drug design aims to developing a drug with high degree chemo-therapeutics index and specific action.

### What is computer aided drug design?

Drug discovery and designing is an expensive process due to the high costs of R&D and human clinical tests. Clinical testing is the most extensive and expensive phase in drug development and is done in order to obtain the necessary governmental approvals. Computer-aided drug design uses computational approaches to discover, develop, and analyze drugs and similar





biologically active molecules. Computer-aided drug design, often called structure based drug design (Song, Lim, & Tong, 2009).

Computer aided drug designing process consists of three stages:

**Stage 1:** Involves identification of therapeutic target and building a heterogenous small molecule library to be tested against it. There is development of virtual screening protocol initialised by docking of small molecules

**Stage 2:** The selected hits are checked for specificity by docking at binding sites of other known drug targets.

**Stage 3:** The selected hits are subjected to computational ADME profiling studies and those who pass these studies are called leads.

CADD shows various benefits in drug design such as, *Cost savings:* Many biopharmaceutical companies use CADD in order to reduce cost burden. *Time saving:* traditional experimentation requiring animal and human models are now replaced by CADD, which saves both time and cost. In *drug resistance:* it is hoped that in case of certain diseases like Influenza, Computational Drug Designing will play an important role in reducing the chances of drug resistance and thus would lead to production of lead compounds which would target the causative factor (Kapetanovic, 2008).

**Drug designing software-** Computer software makes our work simpler and faster (Sisodiya, 2012). Various companies such as Accelrys, Schrodinger, Auto Dock and Argus Lab offering drug designing software. List of various software is given in table2.

The different software produced by **Accelrys** are:

1. Insight II
2. Pipeline Pilot
3. Discovery Studio
4. Materials Studio
5. Accord

The various products of **Schrodinger** are:

1. Glide
2. Prime
3. Jaguar
4. Macro Model

### Auto Dock

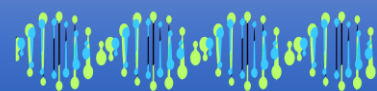
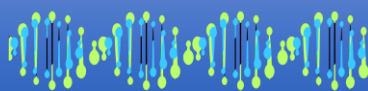
Auto Dock is a pack of automated docking tools which is designed to dock small molecules, like how substrates or drug candidate binds to the receptor of a known 3D structure (Dhanik, McMurray, & Kavradi, 2012). Auto Dock has several applications in X-ray crystallography, Structure based drug design, Lead Optimization, Virtual Screening, Combinational library design, Protein-Protein docking, Chemical mechanism studies.

It consists of two programs: 1. *Auto Dock* – it performs docking of the ligand with the target molecule which is a protein. 2. *Auto Grid* pre calculates this binding of the ligand with the target molecule (Sisodiya, 2012).

**The ligand-based computer-aided drug discovery (LBDD)** approach involves the analysis of ligand known to interact with a target of interest.

**The structure-based computer-aided drug design (SBDD)** relies on the ability to determine and analyse 3D structures of biological molecules. The core hypothesis of this approach is that a molecule's ability to interact with a specific protein and exert a desired biological effect depends on its ability to favourably interact with a particular binding site on that protein.





## GOLD

GOLD uses genetic algorithm to provide docking of exible ligand and a protein with exible hydroxyl groups. Otherwise, the protein is considered to be rigid. This makes it a good choice when the binding pocket contains amino acids that form hydrogen bonds with the ligand(Sisodiya, 2012).

## Argus lab

Argus lab is molecular modeling software that runs on windows. It is free software and can be easily accessed by the public (Pirhadi, Sunseri, & Koes, 2016) (Sisodiya, 2012).

Table2: List of Drug designing softwares and their application

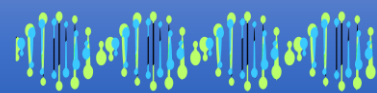
Drug Designing	Software Types	Company	Application	Website
<b>Insight II</b>	Structure based	Accelrys	Graphical molecular modeling	www.insight.com
<b>Pipeline Pilot</b>	Structure based	Accelrys	Gene sequence analysis	www.accelrys.com/products/collaborative-science/biovia-pipeline-pilot
<b>Discovery Studio</b>	Structure based	Accelrys	Protein modeling	Dassault Systèmes BIOVIA
<b>Materials studio</b>	Structure based	Accelrys	Modeling crystal structures	www.accelrys.com/products/collaborative-science/biovia-materials-studio
<b>Accord</b>	Structure based	Accelrys	Cheminformatics	--
<b>Glide</b>	Ligand based	Schrodinger	High Throughput Virtual Screening	www.Schrodinger.com/product.
<b>Prime</b>	Structure based	Schrodinger	Protein structure prediction	--
<b>Jaguar</b>	Structure based	Schrodinger	Gas and solution phase reaction	--
<b>Macro Model</b>	Ligand based	Schrodinger	Docking of ligand and target molecule	www.Schrodinger.com
<b>Argus lab</b>	Ligand based		Build molecules using templates	--
<b>Bio-suite</b>	Structure based	Tata consultancy service	Genomics, Protein modeling	www.atc.tcs.com

## INSIGHT II

Insight II is a user-friendly graphical molecular modelling program developed by Accelrys, that incorporates a variety of useful molecular modelling codes specifically designed for biological systems (Sisodiya, 2012). Insight II is a comprehensive graphic molecular modeling program. Used in conjunction with the molecular mechanics/dynamics program Discover, InsightII can be used to build and manipulate virtually any class of molecule or molecule system. This software is available on all the SGI-Irix workstations housed in the computational bays at SERC (Supercomputer education & research centre).

## Pipeline Pilot





Pipeline Pilot is the authoring tool for the Accelrys Enterprise Platform (Sisodiya, 2012). It is a scientific visual and dataflow programming language, used in various scientific domains, such as cheminformatics and QSAR, Next Generation Sequencing, image analysis, text analytics (Warr, 2012). Pipeline Pilot, a program that aggregates and provides immediate access to the volumes of disparate research data locked in silos, automates the scientific analysis of that data, and enables researchers to rapidly explore, visualize and report research results (Anson, 2009).

### **Materials Studio**

Materials Studio is a client–server model software package with Microsoft Windows-based PC clients and Windows and Linux-based servers running on PCs, Linux IA-64 workstations (including Silicon Graphics (SGI) Altix) and HP XC clusters. Materials Studio is software for simulating and modeling materials (Shacklette, 2011). It is developed and distributed by BIOVIA (formerly Accelrys), a firm specializing in research software for computational chemistry, bioinformatics, cheminformatics, molecular dynamics simulation, and quantum mechanics (Peach, Liu, Pugliese, Wallqvist, & Nicklaus, 1997).

### **Discovery Studio**

Discovery Studio is a set of software for simulating small molecule and macromolecule systems. It is developed and distributed by Accelrys (2002, 2002). The product suite has a strong academic collaboration programme, supporting scientific research and makes use of a number of software algorithms developed originally in the scientific community (Sahu & Pradesh, 2013). Discovery Studio provides software applications covering the various areas such as, Molecular Mechanics, Molecular Dynamics, Quantum Mechanics, Ligand Design, Pharmacophore modeling, QSAR, ADME etc.

### **ArgusLab**

ArgusLab is a program to build graphic representations of molecular models. Using this program, you will be able to show molecular models (Tanguenyongwatana & Jongkon, 2016) (Sisodiya, 2012).

### **BioSuite**

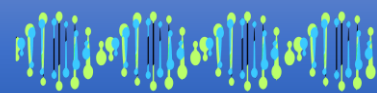
BioSuite integrates the functions of macromolecular sequence and structural analysis, cheminformatics and algorithms for aiding drug discovery (Xu & Hagler, 2002). The suite organized into four major modules, (a) Genome and Proteome Sequence analysis, (b) 3D modeling and structural analysis, (c) Molecular dynamics simulations and (d) Drug design (Bunin, Siesel, Morales, & Bajorath, 2007).

### **Prime**

Prime is a package used for protein structure predictions. It is user friendly. Prime provides users complete control over calculational settings to increase the accuracy of the result, they provide accurate receptor models for structure based drug design (Richard & Charbonneau,







2009). Comparative modeling is used to generate accurate homology models for further structure-based studies (Roy, Xu, Poisson, & Zhang, 2011).

### Accord

Accord is software specially designed for cheminformatics (Xu & Hagler, 2002). They can capture, manage, analyze, and mine chemical data. Accord is oracle based software used for storage, retrieval, analysis of chemical structures and related biological, chemical and inventory data.

### Glide

Glide offers the full spectrum of speed and accuracy from high-throughput virtual screening of millions of compounds to extremely accurate binding mode predictions, providing consistently high enrichment at every level. Accurate binding mode prediction, Glide reliably finds the correct binding modes for a large set of test cases (Sisodiya, 2012).

### CONCLUSION

With the current torrent of data, computational methods have become crucial to biological investigations. Originally developed for the analysis of biological sequences, bioinformatics now encompasses a wide range of subject areas including structural biology, genomics and gene expression studies. Bioinformatics consists of two subfields: the development of computational tools and databases and the application of these tools and databases in generating biological knowledge to better understand living systems. These two subfields are complementary to each other. It is concluded that software that are discussed in this review play important role in bioinformatic study and computer aided drug design. These softwares make research works easier and more interested also save time and cost of researchers.

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## HERBAL FORMULATIONS: NOVEL DRUG DEVELOPMENT AND DESIGN

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### Abstract

Herbal drug is growing fast but somewhere due to its unconventional drug dosage it's not widely used by people. The drug of herbal origin can be utilize in better advanced formed with enhance efficacy by incorporating in modern dosage form. With the use of these advance techniques it gives us protection from toxicity, enhancement in stability improved bioavailability of herbal formulations. Protection from physical and chemical degradation can be achieved. Prove beneficial to combat with life threatening disease more rapidly. The importance of these herbal development industries has immensely gained momentum due to the underlying side effects associated with allopathic medicines ranging from minor problems such as ulcerations to major life threatening problems such as growth retardation. In the present research study the aim was to develop oral herbal tablets from *Polyalthia longifolia* (PL), *Tabernaemontana alternifolia* (TA), *Benincasa hispida* (BH) plant extracts and perform its evaluation as per ICH guidelines. Thus, article discusses and encompasses the readers vision that in future local plants developed formulations could be probable prove to be equipotent with medicinal plants formulations useful for various therapeutic purposes.

### INTRODUCTION

Ayurveda is ancient science of Indian system of medicine. Traditional formulation contain plant material as its core ingredient. In Ayurveda *Swarasa* (Juice), *Kalka* (Paste), *Kwath* (Decoction), *Sheeta kashyay*, *Phanta* are considered as drug delivery devices. All of them had very low shelf life hence the introductions of rolled, Plants have been the basis of many traditional medicinal systems for thousands of years and continue to provide mankind with new remedies for each and every disease. Use of plants as a source of medicine has been inherited and regarded as an important component of the health care system in agricultural like India. Local plants are equipotent to medicinal plants and useful in the management of various diseases comprising microbial infections and immune system related disorders pills, e.g. Gutika, Vatika, Fermented syrups e.g. *Asasva* and *Arishtas*, Medicated oil such as *Siddha tailas*, *Koopipakva rasayana* comes in place. As it exhibit better preservation quality and enhance therapeutic effect. But all of them has their own restriction. Where all constituent may or may not be come in formulation as some of them are water soluble or lipid soluble in nature. Herbal drug itself is complex structure of many active constituents; as all of them provide synergistic action and enhance the therapeutic value. Constituents like Flavanoides, Tannins, Terpenoides when incorporate into novel techniques show enhance bio available activity and targeted action at low therapeutic dose. Traditional herbal formulations show efficacy but drug delivery device has lack of scientific justification, standardization, and identification of single chemical constituent in complex poly herbal formulation.

### Advantage of novel drug delivery system

- Help to increase the efficacy and reduce the side effect of various herbal compounds.
- Quantity of component becomes less with improving quality of drug effect.





- Fewer raw material are required to achieve the desire effect and control drug delivery to provide exact specification regarding drug dose form.
- Ready to use devices are acceptable in today's fast life style where time is important.
- Carry maximum amount of drug to the site of action by passing all barriers. Such as acidic pH of stomach increase prolong circulation of drug into blood due to their small particle size.
- Reduce repeat dose administration.
- The main aim for adaptation of novel drug delivery devices in herbal formulations are to develop better system for proper drug delivery in terms of
- Target oriented
- Sustain and Controlled release of drug at the site which help to increase the efficacy and reduces side effects at the site of formulation.
- This administration not only reduces repeat administration but also helps to increase the therapeutic value by reducing toxicity and increase the bioavailability.
- Nowadays supercritical CO<sub>2</sub> extracts of herbs are use in many formulation as it contain most of active constituents hence new drug delivery system is perfect for such extract for better therapeutic effect.

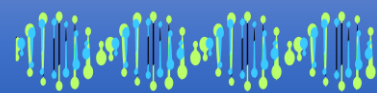
### Material and Methods

The aim of this article is to present an overall view of the current strategies to adapt for the formulation and application of herbal remedies, as well as help to conserve the environment by taking least amount of medicine to show its desire effect. Traditional way of medication depends on supply of active compound. Most of the active compounds are highly soluble in water but less get absorb during circulation which in term less bioavailable to use. In modern technology effective chloroform alcohol extract are available which is not suitable for oral consumption. this present article is to summarize the different types of novel drug delivery device which can used in herbal formulation as they can improve drug efficiency, increase patient compliance, comfort and reduced total cost. Herbal drug technology has entered into a novel approach of developing various devices for herbal drug delivery. Thus, the present review focuses on novel drug delivering devices development.

#### 1. Phytosome

This dose drug form is useful in case of water soluble phyto-constituents (like tannins, terpenoids) which are poorly absorb either due to their large molecular size which is difficult to absorb in passive diffusion or which has poor lipid solubility result in poor bioavailability of drug. It is able to permeate the hydrophilic botanical extract to better absorption in intestinal lumen. Phytosomes are prepared by complexing the polyphenolic phyto constituents in the ratio of 1:2 or 1:1 with phosphatidyl choline. The chemical bonds are formed in between phosphatidylcholine molecules, so it shows good stability. A novel hesperetin was developed by combining and complexing hesperetin with hydrogenated phosphatidyl choline. Its antioxidant activity and pharmacokinetic studies in CC<sub>14</sub> intoxicated rats along. The results of the study showed the phytosome has shown high antioxidant activity. Pharmacokinetic studies have revealed the improved bioavailability of phytosome than the parent molecule at the same dosage .





## 2. Liposomes

Liposomes are constructed with polar lipid which are made up of lipophilic and hydrophilic group of same molecule. Vesicle which are colloidal and spherical in shape entrapped an aqueous core which contains medicine in it to enhance product performance by enhancing its solubility, improving bio availability, targeting at the site of action and prolonged release of drug. Multiple herbal formulation now a day's are based on liposomal technology, but still it need improvement as major limitations of these techniques are like low encapsulation, efficiency, rapid leakage of water soluble drug in the presence of blood component and poor storage facility. Liposomes with Green Tea and *Gaultheria procumbens* extract were prepared using lipid film hydration method and the optimum ratios of the component were determined. Herbal liposomes were characterized for their vesicle size, shape, encapsulation efficiency, drug content and in-vitro drug release study. Highest encapsulation efficiency (70.0%) and *in-vitro* drug release (95.2%) was achieved with formulation. Liposomal formulations have been incorporated into carbopol gel base and found to be more superior against *Micrococcus luteus*.

## 3. Emulsion

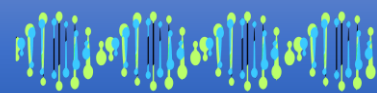
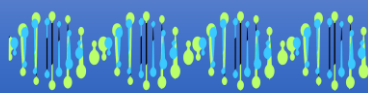
Emulsion are biphasic system in which one phase is immediately dispersed in other phase one phase is always water another phase is liquid/ oil. They have higher surface area hence they can penetrate through skin, non toxic and non irritant in nature. High solubility in skin hence high bio availability. The palatability of the non-emulsion compound and compatibility with other excipients are two major limited factors in this drug delivery device. The micro-emulsion is called as nanoemulsion and sub-micro emulsion is called as lipid emulsion. The nanoemulsion formulation containing Neem oil (*Azadirachta indica*), Tween 20 and deionized water was successfully optimized by the high-energy method. A smallest droplet size of 31.03nm was obtained. Neem oil nanoemulsion with the smallest droplet size was found to be more effective in controlling mosquito larvae compared with larger droplet sizes. Neem oil nanoemulsion may be a good alternative to other pesticides for the control of vector-borne diseases. Droplet size of 31.03 nm has been reported.

The reduced size and uniform spreading of these fine particles increased the efficacy. The nano emulsion is easily affordable, economically feasible and moreover less toxic than synthetic pesticides, and may be used as an alternative for control of vector-borne disease.

## 4. Microsphere

It is also called as micro particle. microsphere consists of spherical particle diameter range from 1-1000  $\mu\text{m}$ . Each particle of drug is dispersed in particle. It is manufactured by various kind of material. A series of plant active ingredient i.e. Rutin, Zedoras extract has been used to make micro particle. According to current reports on non-biodegradable microsphere; polylactic acid is only polymer approved to be used by people. Solid and heavy microsphere is used for different application while hollow is used as additives to lower the density of material. They can be used for ingested or injected purpose. It can be used as site specific delivery of drug. Curcumin (isolated from *Curcuma longa*) is the active ingredient of the Herb, turmeric, Curcumin floating microspheres were successfully developed using emulsion solvent diffusion method. The microspheres had good yield and showed high, drug entrapment efficiency. The flow properties of microspheres were within the acceptable range and therefore would be easily filled into capsules. Release properties were satisfactory and the formulations hold promise for





further development into drug delivery systems for oral administration of curcumin. And development and evaluation of floating microspheres of Curcumin.

### 5. Ethosomes

Ethosomes are developed by mixture of phospholipids and high concentration of ethanol. This carrier can penetrate through the skin deeply lead to improve drug delivery into deeper layer of skin and in blood circulation. These formulation are useful for topical delivery of alkaloids in form of gel and cream for patients comfort. They show increase in their permeability through the skin by fluidizing the lipid domain of the skin. Unstable nature and poor skin penetration are limits for Ethosomes topical delivery. The Ethosomes was developed and examined for their ability the topical absorption of Tetradrine through dermal delivery, and the relation of formulations to the pharmacological activity of Tetradrine loaded in the formulation was also accessed. Result of the drug levels in rat plasma showed that when Tetradrine loaded Ethosomes were topically administered in rats the drug level was low to be detected in rat plasma. By providing fewer delivery of Tetradrine into bloodstream, topical administration might offer favorable efficacy with reduced side effects, thus leading to improve patient's compliances. In conclusion, Ethosomes were demonstrated to be promising carrier for improving topical delivery of Tentradrine via skin.

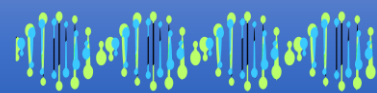
### 6. Transdermal drug delivery

Tran dermal drug delivery is carry out by a patch that is attached to the body surface. This patch is a medicated adhesive pad that is design to release the active ingredient at a constant rate over a constant period of several hours to days after application to the skin. The drug present in transdermal patch permeates into systemic circulation by diffusion through various layer of skin which lead further to effected organ. This system provides drug delivery at control rate, high bio availability, easy application, sustainable action. Limitations are hepatic first pass metabolism, maintenance of steady plasma level of drug. *Momordica charantia* is traditionally used as a medicine for Diabetes. The Transdermal film contain the fractionated component from Ethanolic extract of *M. chirantia* fruits were prepared by using hydroxy propyl methyl cellulose as a polymer. The films were evaluated for folding endurance, thickness, weight variation, drug contents and in vitro diffusion studies and in vivo parameters like acute and subacute anti hyperglycemic activity in diabetic rats, the percentage release of active constituents from Trans dermal patches of *M. charantia* (2cm<sup>2</sup>; 10 mg/patch) was found to be satisfactory. The Transdermal route exhibited negligible skin irritation and in vivo results revealed that the patches successfully decrease the blood glucose level and have been found to be effective for diabetes through modern pharmaceutical formulation techniques.

### 7. Micro pellets

Micro pellets is an agglomeration process that converts fine powder or granules of bulk drugs and excipients into small, free flowing semi spherical units. Pellets being multi particulate. systems are wildly used due to the technical as well as therapeutic advantages over single unit dosage form. Such as Inoherbs micropellets contain active herbal compound (Phytogranules). The extract of *Andrographis penniculata* was entrapped into micro pellets of calcium alginate. So formed pellets were evaluated for heaptoprotective activity in paracetamol induce hepatotoxicity in rat. The bitter alginate micro pellets loaded with alcoholic extract of A





*penniculata* were successfully inhibit the paracetamol induce hepatotoxicity by decreasing ASL, ALT, and liver weight.

### 8. Nano particle

In this system mean particle size of medicine is small up to 100nm. Due to reduction in size it gives increase compound solubility, reduce medicinal dosage and improve the absorption rate of herbal drug. Such as nanonized curcuminoides. Zedory turmeric oil, a traditional Chinese medication was loaded with nano structured lipid carriers after doing several *in vitro* drug test it indicate that prepared nanoparticle enhance the drug release rate which shows promising IV dosage form of water insoluble oily drug. These nano carriers have been made up of safe synthetic biodegradable polymer material. In this formulation both lipophilic and hydrophilic drugs can be loaded. fucose-chitosan/ heparin nanoparticle encapsulated berberine was prepared and delivery efficiency was monitored by confocal laser scanning microscopy. Analysis of stimulated gastrointestinal medium indicated that the propose drug carrier effectively controls the release of berberine, which interacts specially at the site of *H. pylori* infection, and significantly increases berberine's suppressive effect on *H. pylori* growth. In an *in-vivo* study, the berberine-loaded fucose-conjugated nanoparticles exhibited an *H. pylori* clearance effect and effectively reduce gastric inflammation in an *H. pylori* infected animal study.

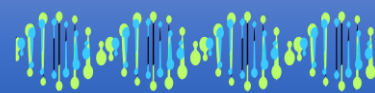
### 9. Polymeric Micelle formulation

These are formed from amphiphilic blocks have been successfully used for delivery of drug that lack of water solubility. the characteristic feature of micelles such as particle size, shape, drug loading, cellular internalization, stability and release kinetics of drug can be improved by altering the physicochemical properties of the constituents block copolymers and method of preparation. Thermo sensitive co-polymeric micelle synthesized by radical copolymerization and extract of *Nigella sativa* is entrapped in this polymeric system to evaluate its antibacterial activity. *Nigella sativa* loaded polymeric micelle found more effective than other form. The thermo sensitive polymeric system would more effectively release the drug into body when infectious status are functional.

Plants have been the basis of many traditional medicinal systems for thousands of years and continue to provide mankind with new remedies for each and every disease. Use of plants as a source of medicine has been inherited and regarded as an important component of the health care system in agricultural like India. Local plants are equipotent to medicinal plants and useful in the management of various diseases comprising microbial infections and immunosystem related disorders. *Polyalthia longifolia* (PL) is one of the most important indigenous medicinal plants in Indian medicinal literature which is found throughout Malaysia and widely used in traditional medicine as febrifuge and tonic. Almost all parts of this plant are used in Indian traditional system for the treatment of various ailments. PL leaves have been used in pyrexia as well as menorrhagia. *Bennicasa hispida* commonly known as Ash gourd belongs to Cucurbitaceae family, which is a single species of tender annual vine, believed to have originated in Java. It is valued for its medicinal properties and widely studied by Ayurvedic practitioners. It has special potency as nervine tonic. It alleviates nausea (*Vatta*) and acidity (*pitta dosha*). The properties of fruit changes according to stage of ripening. It is interesting to note that the tender fruits alleviates acidity, medium ripened fruit alleviates cough, where as fully







ripened fruit alleviates all of them. BH fruit juice is used in syrup and anti-anxiety tablets with combination of drugs. *Tabernaemontana alternifolia* is used as antihemetic for many years to treat tape worms in children with milk or curd as well as pain relievers.

The selected local plants namely *Polyalthia longifolia*, *Tabernaemontana alternifolia*, *Benincasa hispida* are widely known due to its uniqueness to exert ethnopharmacological activities comprising analgesic, anti-oxidant, anti-inflammatory, antibacterial which have well cited by the researchers in the studies .

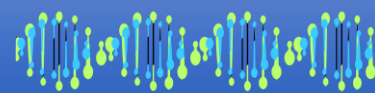
Herbal drugs constitute a major part of therapeutics in all the traditional systems of medicines like ayurveda, siddha, unani. Plants have been the basis of many traditional medicinal systems for thousands of years and continue to provide mankind with new remedies for each and every disease. Use of plants as a source of medicine has been inherited and regarded as an important component of the health care system in agricultural country like India. Most practitioners formulate and dispense their own recipes, which necessitates proper documentation and with utmost attention to research oriented services.

Across the world, the use of herbal medicines is steadily growing to treat medical illnesses comprising of major and minor ailments. Augmented incidence of the adverse reactions of synthetic drugs in humans and economic burden of the modern system of medicine on government has paved the interest in development of traditional medicine from local plants. It is estimated that approximately one quarter of prescribed drugs contain plant part derived extracts or active ingredients obtained from whole plants. Below are few examples of a plant derived drugs such as atropine, artimesinin, colchicine, digoxin, ephedrine, morphine, physostigmine, pilocarpine, quinine, quinidine, reserpine, taxols, tubocurarine, vincristine and vinblastine which proved its potential in important pharmacological categories.

Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing; however in many cases immediate onset of action is required than conventional therapy. To overcome these drawbacks, immediate release pharmaceutical dosage form has emerged as alternative oral dosage forms. There are novel types of dosage forms that act very quickly after administration. The basic approach used in development tablets is the use of superdisintegrants like Cross linked carboxymethylcellulose (Croscarmellose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone), starch 1500 are provides instantaneous disintegration of tablet after administration.

The development of immediate release therapy also provides an opportunity for a line extension in the marketplace, a wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs can be considered candidates for this dosage form. The objective of present study was to make immediate release herbal tablets which would contain a plant material equivalent to that found in traditional dosage form that would meet conventional pharmaceutical standards. Tablets are chosen as dosage form because they are easy to handle patient compliance and show immediate action.





**PROCEDURE**

**Part A: Collection, authentication and extraction**

Fresh leaves of *Polyalthia longifolia*, *Tabernaemontana alternifolia* and *Benincasa hispida* fruit peels were collected from Mumbai local market in month of April-May and shade-dried. The leaves were authenticated by Agarkhar Research Institute, Pune. A voucher specimen was deposited in the Botany department of Allahabad University, Allahabad. Further, they were subjected to extraction procedure as follows: Methanol was used as solvent for the extraction of *Polyalthia longifolia* and *Tabernaemontana alternifolia*. Fresh leaves were air-dried. The leaves of the plants were grounded into powder passed through sieve no. 40 to obtain fine powder.

The powder was soaked in methanol for 24 h with simultaneously shaking on orbital shaker at 50 rpm. Further they were filtered through Whatman filter paper no.1, the collected filtrate was evaporated to dryness using rotary evaporator at 40° C to obtain an alcoholic extract stored in amber colored air tight bottle in refrigerator until further use. Petroleum ether was used as primary solvent for the extraction of *Benincasa hispida*. The peels of the fruits were removed and air dried. The extraction was carried out at 40-60° C till the solution became colourless. Then it is filtered through Whatman filter paper no.1 and further macerated with ethanol for 8 days, the extracted material obtained was evaporated to dryness an alcoholic extract stored in amber colored air tight bottle in refrigerator until further use.

**Part B: Formulation development of Herbal tablets**

Herbal tablets were prepared separately by wet granulation using different proportions of various excipients and denoted as TA 1-TA2, PL1-PL2 and BH1-BH2. The procedure is described as below:

- **Sieving:** All excipients used were passed through 60# sieve along with lubricant and glidant.
- **Mixing :** The steps are described as follows:
  1. All the weighed excipients were taken in the mortar pestle, weighed amount of extract is added as depicted in Table no.1, the mixture was triturated till you get fine freely flowing powder form.
  2. PVP in IPA was added to get dough, passed through sieve mesh no. 8# and after drying finally through sieve mesh no. 20 #.
  3. Magnesium stearate was added and allowed to lubricate for 10 mins, followed by determination of micrometric properties for all the formulation are checked and compressed.
  4. % of disintegrants used and MCC was changed in the developed herbal formulation.
    - All three plants extracts of PL, TA and BH were subjected to the uniformity of the procedure described above.

The composition of the developed herbal tablets is described as,

**Table 1: Composition for *Tabermontana alternifolia* (TA) tablet**

Ingredient In (mg/tablet)	TA1	TA2
Plant extract TA	100	100
Lactose	104	-
MCC	-	154





Starch	30	30
Starch	1500	–
PVP in IPA	q.s	q.s
Magnesium stearate	3	3
Total	300	300

**Table 2: Composition of *Polyalthia longifolia* (PL) tablet**

Ingredient in (mg/tablet)	PL1	PL2
Plant extract PL	100	100
Lactose	92	116
MCC	60	60
Starch	15	-
Cp	-	6
Starch	1500	-
PVP in IPA	q.s	q.s
Magnesium stearate	3	3
Total	300	300

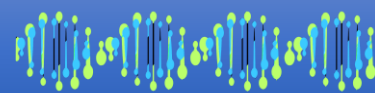
**Table 3: Composition of *Benincasa hispida* (BH) tablet**

Ingredient In (mg/tablet)	BH1	BH2
Plant extract BH	100	100
Lactose	92	116
MCC	60	60
Starch	15	-
Cp	-	6
Starch	1500	-
PVP in IPA	q.s	q.s
Magnesium stearate	3	3
Total	300	300

## CONCLUSION

There is great potential lied in development of novel drug delivery system for herbal formulation as it is safe, effective, convenient and economically affordable drug delivery. it can lead to overcome the problem associated with herbal formulation. results in enhance its efficiency and make is more bio available by increase its solubility, controlled release and target oriented Thus, the formulation developed from *Benincasa hispida*, *Polyalthia longifolia* and *Tabermontana alternifolia* had reasonable stability.





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## REVIEW ON INTRODUCTION OF PHARMACOVIGILANCE

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### ABSTRACT

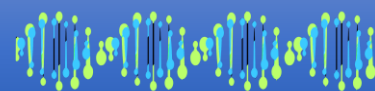
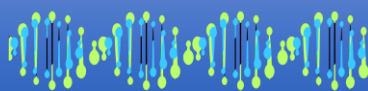
Pharmacovigilance outlined by the globe Health Organization (WHO) because the science and series of activities about the detection, evaluation, understanding rejection of Adverse impact or Associate in Nursing different drug connected problem' and a clinical test could be a analysis study in human volunteers to answer specific health queries. fastidiously conducted clinical trials square measure quickest and safest thanks to realize treatment that employment in individuals and thanks to improve health. play a crucial role in guaranteeing that patient be provide safe drug. The Pharmacovigilance have be recognize to play a crucial role in rational use of drug by providing data concerning the adverse impact possess by drug normally population. The information of drug Adverse Drug Reaction (ADRs) are often increased by numerous suggests that such information studies, intensive observation, spontaneous reportage and different new method at dictatorial and scientific level square measure being developed with the intention of step-up Pharmacovigilance. as a result of assessment strategies are not entirely void of individual judgements, interater reliableness are often low. In conclusions there's still no methodology universally accepted for casualty assessment of ADRs.

### INTRODUCTION

According to the world Health Organization, "Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effect or any other possible drug-related drawback, particular, long term and short term adverse effects of medicines". The history routes of the word "Pharmacovigilance" are: Pharmakon(Greek word of 'drug') and vigilare(Latin word for 'to keep watch').

Pharmacovigilance is not new to Asian nation and has infect been going on from 1983. when Asian nation decided to join the uppsala centre for adverse event monitoring. Spontaneous reporting of adverse drug reaction and adverse events is an important tool for gathering the safety data for early detection. it is widely accepted that a drug has to go through various phases of trial to establish its safety and efficacy before it is marketed commercially. However, the clinical trials offer various limitations, like; strict criteria of inclusion and exclusion make it to be used in a very selective group of patients; special population groups like kids, pregnant lady, and maturity population are not studied during the trials; and other factor causing drug reactions such as genetic factors, environmental factors, and drug-drug interactions may not have been studied during the clinical trials. These adverse drug reaction (ADRs) not only increase the suffering of patients but also increase morbidity and mortality in conjunction with a financial burden on society. the overall incidence of ADRs in hospitalized patients is estimated to be 6.7% (0.1-0.85%) . data indicates that in patients World Health Organization experience ADRs





death rates area unit 19.18% higher and the length of hospital stay is 8.25% higher. Total medical costs for patients with ADRs area unit increased by average of 19.86%.

**METHOD OF CAUSALITY ASSESSMENT**

Many researchers developed numerous ways of relation assessment of ADRs by mistreatment totally different criteria like written record relationship between the administration of the drug and also the incidence of the ADR, screening for non drug connected causes, confirmation of the reaction by in vivo or vitro tests, and former data on similar events attributed to the suspect drug or to its therapeutic category, etc. to outline ADRs in several categories. however as a result of there aren't any outlined diagnostic criteria or classes, inter-rater and intra-rater variability may be large. Currently, there's no universally accepted ways of accessing relation of ADRs. we tend to describe here 3 broad classes of varied ways of relation assessment: professional judgement/global contemplation, algorithms, and probabilistic ways (Bayesian approaches).

**HISTORY OF PHARMACOVIGILANCE IN ASIAN NATION**

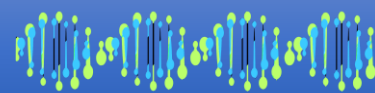
Pharmacovigilance in Asian nation started from 1986. a proper Adverse Drug Reaction (ADR) watching system was initiated with twelve regional centers, every covering a population of fifty million.

However, no noteworthy growth was created. later in 1997, Bharat joined the globe Health Organization (WHO) and Adverse Drug Reaction (ADR) scrutinized program primarily based at urban center, Kingdom of Sweden however got fail.

Hence when 2005 UN agency supported and World Bank fundd National Pharmacovigilance Programme (NPPV) of Bharat was created operational.2,10,11,12.

Year	Developments
1747	Very first known clinical trials by James Lind, proving the usefulness of lemon juice in preventing scurvy.
1937	Death of more than 100 children due to toxicity of sulfanilamide.
1950	Apalstic anemia reported due to chloramphenicol toxicity.
1961	Worldwide tragedy due to thalidomide toxicity
1963	16th World Health congregation recognize significant to rapid action on Adverse Drug Reactions (ADRs).
1968	WHO research project for international drug monitoring on pilot scale.
1996	Global standards level clinical trials initiated in India.
1997	India attached with WHO Adverse Drug Reaction Monitoring Program.
1998	Initiation of pharmacovigilance in India.





2002	67th National Pharmacovigilance Center established in India.
2004-05	India launched National Pharmacovigilance Program.
2005	Accomplishment of structured clinical trials in India.
2009-10	Pharmacovigilance Program (PvPI) started.

**Table 1:** The sequential pharmacovigilance developments with special reference to India<sup>1,13,14</sup>.

### AIM OF PHARMACOVIGILANCE

Improvement of patient care and safety in respect to use of medicines with medical and paramedical interventions remains to be a crucial parameter. The main objectives of pharmacovigilance involve exhibiting the effectuality of medicine by observation their adverse impact profile for several years from the research lab to the pharmacy; trailing any forceful impact of drug rising public health and safety respect to the utilization of medicines; encouraging the safe, rational and efficient use of drugs; promoting understanding, educations and clinical coaching in Pharmacovigilance; and effective communications to the generic public.

### METHODS UTILIZED IN PHARMACOVIGILANCE

The activities undertaken in the name of Pharmacovigilance can be roughly divided into three groups: regulatory, industry, and academia. Regulatory pharmacovigilance is driven by the aim to provide drugs with a positive benefit- harm profile to the public. Some of the problems related to regulatory post-marketing surveillance will be discussed in this context, followed by a description of the methods used to detect new ADRs and a discussion of the pros and cons of each method.

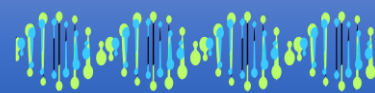
1. Dangaumou’s French method.
2. Kramer et al. method.
3. Naranjo et al. methodology (Naranjo scale).
4. Balanced assessment method.
5. Ciba-Geigy method.
6. Loupi et al. method.
7. Roussel Uclaf casualty assessment method.
8. Australian method.

### ADVERSE DRUG REACTION (ADRs)

An adverse drug (ADRs) is outline as AN fortuitous and harmful to a health product that causes at the doses sometimes or tested for the diagnosing, hindrance or treatment of a malady or the alteration of AN organic fuction;. Though , it's tough to acknowledge the actuating agent connected with the adverse drug reaction (ADRs) encountered contain quite ingredients.







The magnitude of risk must be thought-about together with magnitude of expected medical specialty advantages decide whether or to use a specific drug in an exceedingly given patient. Adverse drug (ADRs) are classified in to ways; thirty.

1. foreseeable (Type-A) Reaction
2. Unpredictable (Type-B) Reaction

**1.PREDICTABLE(TYPE-A) REACTION**

These square measure supported pharmacologic properties of the medicine like increased however quantitatively response to the drug that embody aspect effects, cyanogenic effects and consequences of drug withdrawal.

**2.UNPREDICTABLE(TYPE-B) REACTION**

These square measure supported peculiarities of patient and not on drug’s acknowledged actions; embody allergic reaction and specialty. they’re less common, usually non-dose connected, typically a lot of serious and need withdrawal of drug. an inventory of some suspected and acknowledged medicine related to adverse effect.

<b>Drug</b>	<b>Adverse Drug Reactions (ADRs)</b>
Thalidomide	Phocomelia, Multiple defects
Methotrexate	Multiple defects, Foetal death
Androgen	Virilization, limb, esophageal, cardiac defects
Progestins	Virilization of female foetus
Stilboestrol	Vaginal carcinoma in teenage female offspring
Tetracyclines	Discolored or deformed teeth, retarded bone growth
Warfarin	nose, eye and hand defects, growth retardation
Phenytoin	Various malformations
Lithium	Foetal goiter, cardiac and other abnormalities
Aspirin/ Indomethacin	Premature closure of ductus arteriosus

**Table 2:** Known drugs adverse effects.



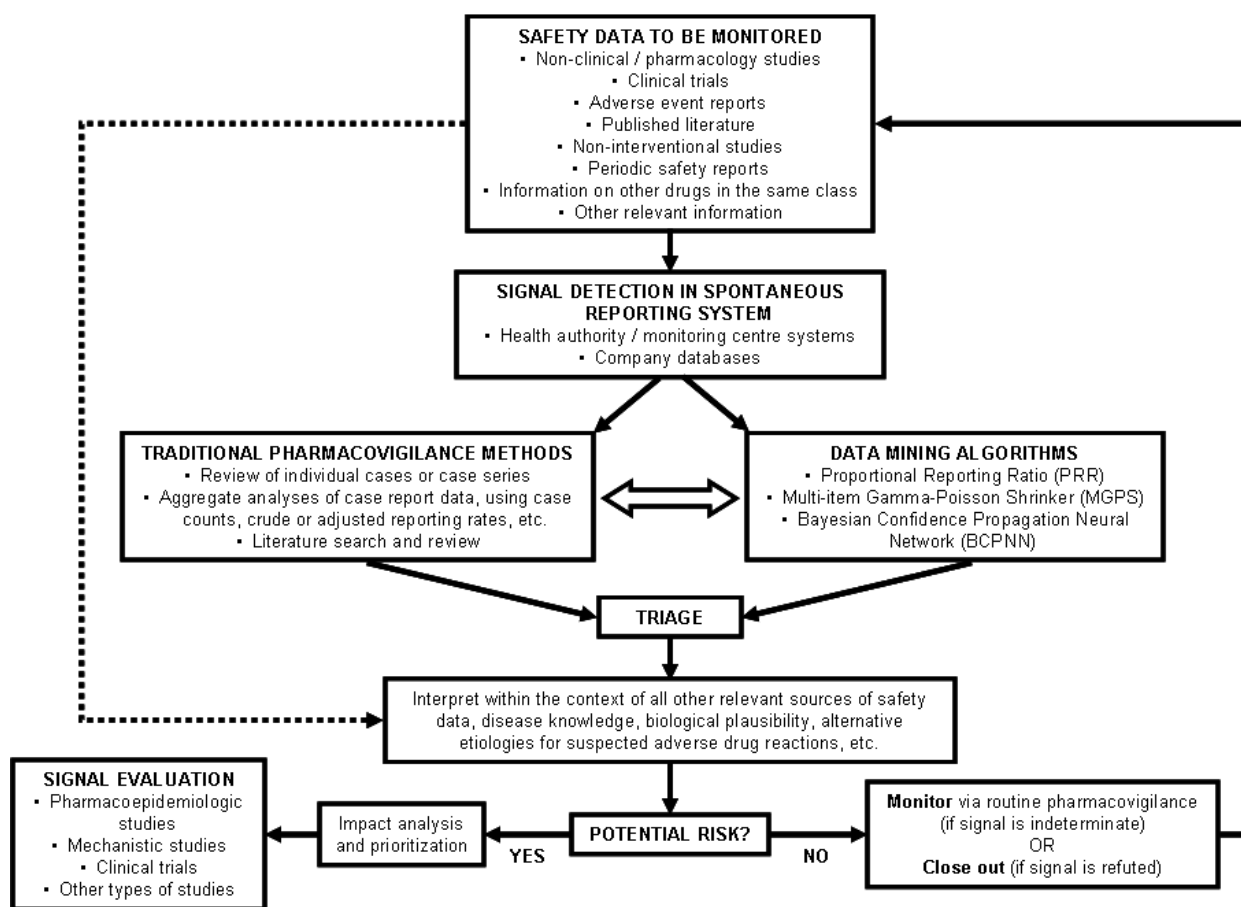
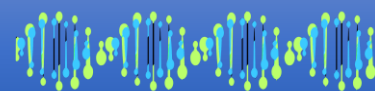
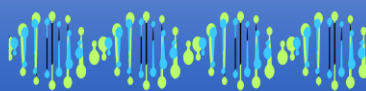
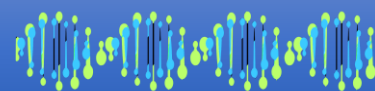
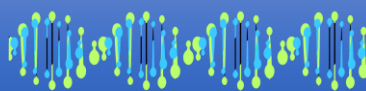


Figure 1. Signal detection and evaluation steps (reproduced with permission from the Report of CIOMS Working Group VIII © CIOMS)

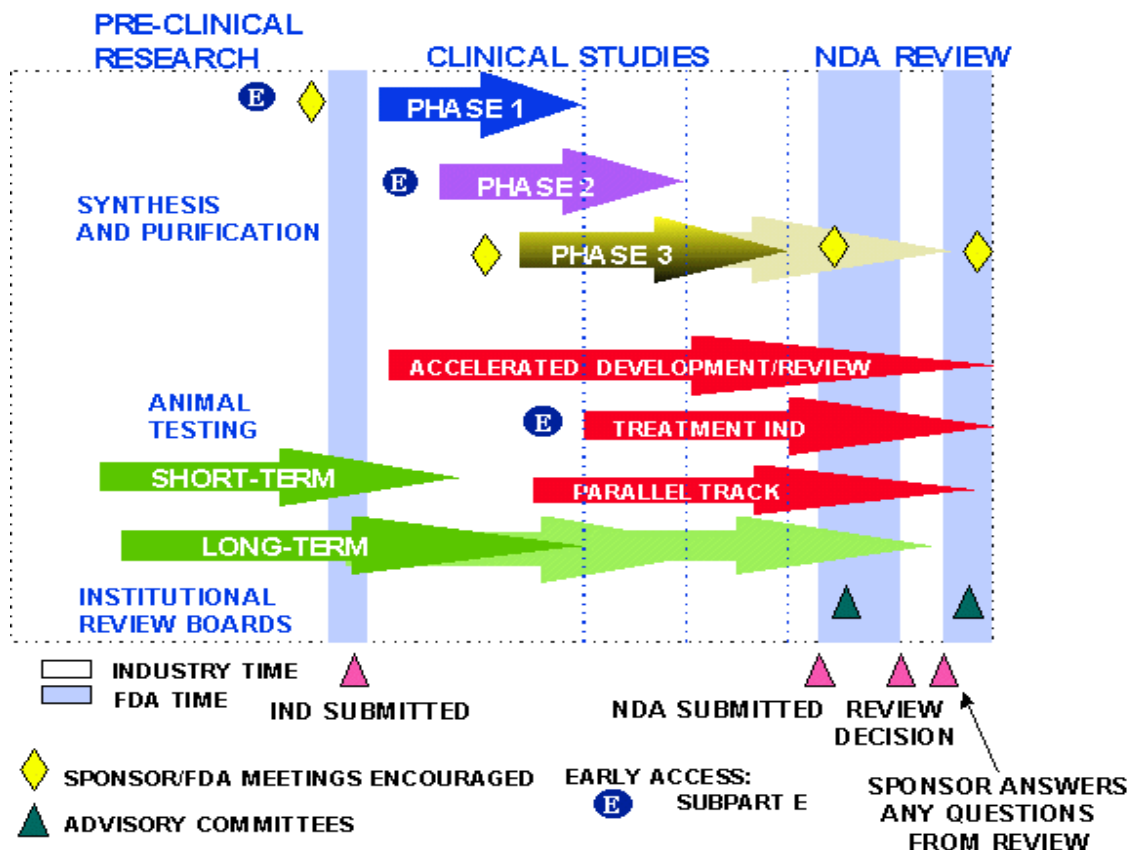
## CLINICAL TRIAL

A clinical trial could be a analysis study that tests a replacement medical treatment or a replacement manner of mistreatment Associate in Nursing existing treatment to ascertain if it'll be higher thanks to stop and screen for diagnose or treat disease. wide selection of dose of the study drug is given to Associate in Nursingimals subjects or to an in-vitro substrate so as to get preliminary effectuality, toxicity and pharmacokinetic information.





## PHASE OF CLINICAL TRIAL



Before pharmaceutical firms begin clinical test on a drug they conduct in depth pre-clinical studies.

### PRE-CLINICAL STUDIES

Pre-clinical studies involve in vitro ( i.e. tube or laboratory) studies and trial or animal population. Wide travel dose of the study in drug area unit given so as to get preliminary effectualness, toxicity and pharmacokinetic data and to help pharmaceutical firms decide whether or not it's worthy to travel ahead with more testing.

### PHASE 0

Phase zero may be a recent designation for exploratory , first-in-human trial conducted in accordance with U.S. food a drug administration (FDA) 2006 steerage on exploratory . Distinctive options of part zero trials embrace the administration of single sub-therapeutics doses of the study drug to alittle range of subjects (10-15) to collect preliminary information on the agent’s pharmacological medicine (how to body processes the drug) and pharmacodynamics(how the drug add the body).





## PHASE-I

Phase I path area unit 1st stage of testing in human subject. ordinarily alittle (20-80) cluster of healthy volunteers are going to be elite. This part includes trails designed to assess the security (Pharmacovigilances) tolerability, pharmacological medicine and pharmacodynamics of a drug.

There area unit totally different styles of clinical trial trials.

1. **SAD:-** Single Ascending Dose studies area unit those within which tiny cluster of subjects area unit given one dose of the drug whereas they're ascertained and tested for a amount of your time.
2. **MAD:-** Multiple Ascending Dose studies area unit conducted to raised perceive the pharmacological medicine of multiple dose of drug.

## PHASE- II

Once the initial safety of the study drug has been confirmed in clinical trial trials, clinical trial trials area unit performed on giant cluster (20-300) and area unit designed to assess however well the drug work in addition on continue clinical trial safety assessment in a very larger cluster of volunteers and patients. clinical trial studies area unit generally divided into clinical trial A and clinical trial B. clinical trial A is specifically style to access dosing necessities ( what proportion drug ought to be given), wherever as clinical trial B is specifically designed to check effectualness ( however well the drug work the prescribed dose (s)). Some trials mix clinical trial and clinical trial, and take a look at each effectualness and toxicity.

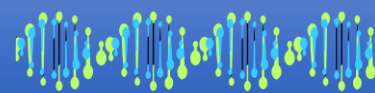
## PHASE-III

Phase III studies irregular controlled multi-center trials on giant patients cluster (300-3,000 or additional relying upon the disease/ medical condition studied) and area unit geared toward being the definitive assessment of however effective the drug is compared with current 'gold standard' treatment.

## PHASE-IV

Phase IV trial is additionally called Post promoting police work Trial. phase IV trials involves the security police work (Pharmacovigilance) and current technical support of a drug once it receive permission to sold . the security police work is intended to observe any rare or semipermanent adverse result over a far larger patient population and longer period than was potential throughout the harmful result discovered by phase IV trials might end in a drug being not sold , or restricted to bound uses. Recent example involves Baycol ( branch names Bycol and lipobay) trogelitazone (Rezulin and Vioxx (vioxx)).






Phase	Group
0	10-15
1	22-80
1A	Single Ascending Dose (SAD).
1B	Multiple Ascending Dose (MAD)
2	20-300
3	300-3000
4	Post Marketing Surveillance Trial.

**Table 3:** Phases of Clinical Trial

**CONCLUSION**

In conclusion there is still no method universally accepted for causality assessment of ADRs. Pharmacovigilance study of the science and series of activities relating to the detection, evaluation, understanding and avoidance of Adverse Effect or any other drug related problem. The knowledge of drugs Adverse Drug Reaction (ADRs) can be augmented by various mean such database studies, intensive monitoring, spontaneous reporting.

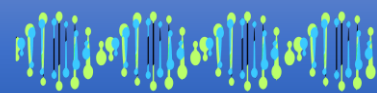
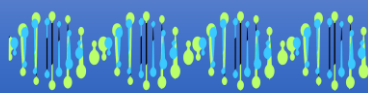
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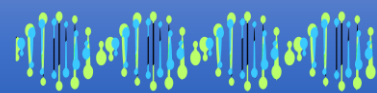
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## THERAPEUTIC POTENTIAL OF VITAMIN C IN DIABESITY AND ITS CO-MORBIDITIES

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### Abstract

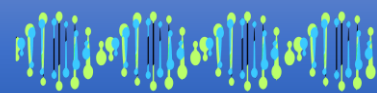
Vitamin C is a vital nutrient involved in many biological and biochemical processes as an antioxidant. As oxidative damage is implicated in the development of various diseases, vitamin C could have a preventive or even therapeutic effect. Vitamin C is the major water-soluble antioxidant and acts as first defense against free radicals in whole blood and plasma. Nowadays diabetes and obesity are emerging as a serious threat to human all over the world, it has been found that oxidative stress is involved in the pathogenesis of diabetes, obesity and their comorbidities. In diabetes due to hyperglycemia there is increased production of reacting oxygen species and reduction in antioxidant defenses which results in oxidative stress. Similarly in obesity due to excessive body fat accumulation there is production of reacting oxygen species which leads to oxidative stress. Therefore, antioxidant-based treatments with vitamin C could be considered as interesting approaches to possibly counteract diabetes, obesity fat accumulation and their complications. It has been suggested that this vitamin may inhibit the formation of reacting oxygen species or scavenge free radicals, it also increase the antioxidants defense enzyme capabilities and inhibit protein glycation (which occurs due to hyperglycemic condition), it also reduces the fat accumulation by modulating adipocyte lipolysis. There are many reports on effects of vitamin C in the management of diabetes and its comorbidities.

### Introduction

Diabetes is a group of chronic metabolic conditions, which are characterized by eminent blood glucose levels resulting from the inability of the body to produce insulin or resistance to insulin action or both. In the absence of effective insulin, hyperglycemia prevails which can lead to long term and short term complications of diabetes mellitus. (Abdel-Wahab et al., 2002). Type 1 diabetes occurs due to immense autoimmune damage of pancreatic beta cells which leads to a condition of complete insulin deficiency. Type 2 diabetes is marked by numerous metabolic defects, among which  $\beta$  cell secretory dysfunction and peripheral insulin resistance are considered as an emblem of the disease in human. Type 2 diabetes occurs due to defects in both insulin and secretion, which is now increasing at a very fast rate throughout the world, its intensity of occurrence can be figure out by the International Diabetes Federation (IDF). 2006 report stating that around 246 Million people worldwide are suffering from this disease and the prevalence is expected to cross the figure of 380 million within 20 years. Diabetes can affect many different organ systems in our body and also can lead to chronic complications, these complications may be micro vascular like nervous system damage, renal system damage, and





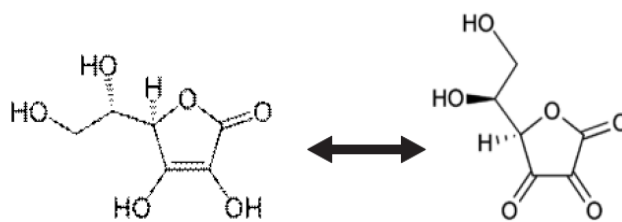
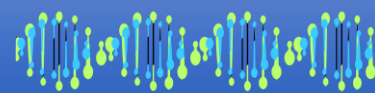


eye damage, or macro vascular like cardiovascular disease, stroke and peripheral vascular disease. The effects of diabetes on the central nervous system (CNS) result in cognitive dysfunction and cerebrovascular disease (Evans, 2003). Like diabetes, obesity has emerged a worldwide epidemic which is characterized by excess adipose tissue and that leads to several chronic diseases and early mortality. The adverse health consequences related to obesity include cardiovascular disease, stroke, type 2 diabetes mellitus, hypertension, dyslipidemia, cancers of the breast, endometrium, prostate, and colon, gallbladder disease, osteoarthritis, respiratory problems, including asthma and sleep apnea (Haslam et al., 2005). This epidemic has received both national and international attention because of obesity's detrimental impact on health, the enormous economic burden it imposes, and its increasing prevalence. Obesity is a global problem, affecting an estimated 300 million people worldwide. Approximately 325,000 deaths in the United States each year among nonsmokers are attributable to obesity (American Diabetes Association., 2006). Increased levels of indicators of oxidative stress in diabetic individuals suffering from complications suggest that enhanced production of free radicals and oxidative stress is the central event to the development of diabetic complications. Therefore, it seems reasonable that antioxidants like vitamin C can play an important role in the improvement of diabetes. In a similar way vitamin C has been demonstrated in the treatment of obesity by inhibiting lipolysis, thus decreasing fatty acid efflux to the system and by Modulating the lipid accumulation of adipocytes, either by direct effect on the differentiation machinery or by modulation locomotive behavior. Vitamin C is one of the important water-soluble vitamins. Vitamin C is widely distributed in fresh fruits and vegetables. Many health benefits have been attributed to vitamin C such as antioxidant, anti-atherogenic, anti-carcinogenic, immunomodulator and prevents cold (Arumugam et al., 2011). This article reviews the effects of vitamin C on treatment of diabetes and obesity associated metabolic disorders. This review well indicates that oxidative stress is involved in the pathogenesis of diabetes and its complications. Use of ascorbic acid reduces oxidative stress and alleviates obesity and diabetic complications, also will be pointed out here.

### **Chemistry of ascorbic acid**

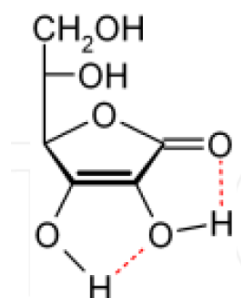
The trivial name of Vitamin C is L-ascorbic acid ( $C_6H_8O_6$ ) and its chemical name is 2-oxo-L-threo-hexono-1,4-lactone-2,3-enediol. Ascorbic acid is the enolic form of one  $\alpha$ -ketolactone. Ascorbic acid solution is easily oxidized to the diketo form known as dehydroascorbic acid, which can easily be converted into oxalic acid, diketogulonic acid or threonic acid.





**Figure 1.** Structure of Ascorbic acid and dehydroascorbic acid

L-ascorbic and dehydroascorbic acid are the major nutritional forms of vitamin C (Moser et al., 1990). Ascorbyl palmitate is used in commercial antioxidant preparations. All commercial forms of ascorbic acid except ascorbyl palmitate are soluble in water. In foods, pH effects the stability of ascorbic acid. It shows maximal stability between pH 4 and 6 (Moser et al., 1990). Structural elements that contribute to chemical behavior of Ascorbic acid are: The structure of the lactones and two enolic hydroxyl groups and a primary and secondary alcohol group. Ene diol structure prompts their antioxidant properties, as enediols can be oxidized easily to diketones. Ascorbic acid forms two bonds intermolecular hydrogen bonds (shown in red in the figure) that contribute significantly to the stability and antioxidant property.

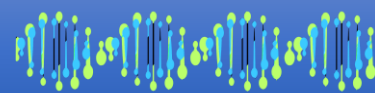


**Figure 2.** Hydrogen bond formed by ascorbic acid.

### Absorption

Ascorbic acid is absorbed in the body by active transport and simple diffusion. Sodium-dependent active transport: sodium-ascorbate co-transporters (SVCTs) and glucose transporters (GLUTs), are the two transporters required for absorption. SVCT1 and SVCT2 import the reduced form of ascorbate across plasma membrane (Rumsey et al., 1997). GLUT1 and GLUT3 are the two glucose transporters, and transfer only the dehydroascorbic acid form of vitamin C. Ascorbic acid present in diets is freely available and easily absorbed by active transport in the intestine. Ascorbic acid absorbed almost completely in the distal small intestine (Sauberlich, 1985). About 80-90% of it will be absorbed when the consumption is up to 100 mg/day, however at higher levels of consumption i.e 500 mg/day the efficiency of absorption of ascorbic acid quickly drops.



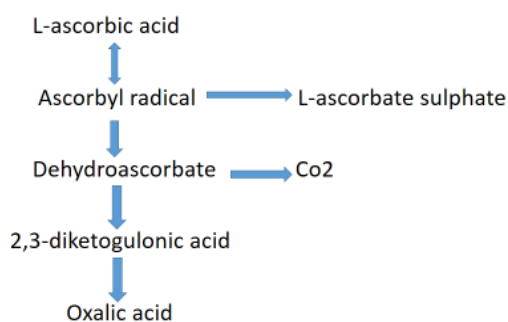


### Distribution

Being water soluble compound ascorbic acid is easily absorbed but it is not stored in the body. . The average adult has a body pool of 1.2-2.0 g of ascorbic acid that may be maintained with 75 mg/d of ascorbic acid. About 140 mg/d of ascorbic acid will saturate the total body pool of vitamin C (Sauberlich, 1985). Ascorbic acid is distributed throughout the water-soluble compartments. Adrenal cortex, leukocytes, platelets, and pituitary gland contain high concentrations of ascorbic acid. Although the body's maximal store of vitamin C is largely determined by the renal threshold for blood, yet there are many tissues that maintain vitamin C concentrations far higher than in blood. Biological tissues that accumulate over 100 times the level of vitamin C in blood plasma are the adrenal glands, pituitary, thymus, corpus luteum, and retina (Hediger., 2002). Those with 10 to 50 times the concentration of vitamin C present in blood plasma include the brain, spleen, lung, testicle, lymph nodes, liver, thyroid, small intestinal mucosa, leukocytes, pancreas, kidney, and salivary glands.

### Metabolism

The major metabolites of ascorbic acid in human are dehydroascorbic acid, 2,3-diketogulonic acid and oxalic acid (Fig 2). Ascorbic acid is metabolized in the liver, and to some extent in the kidney, it involves a series of reactions. The principal pathway of ascorbic acid metabolism involves the loss of two electrons (Tolbert et al., 1975). The intermediate free radical reversibly forms dehydroascorbic acid, which leads to the irreversible formation of the physiologically inactive 2,3-diketogulonic acid (Packer et al., 1997). Diketogulonic acid may be either cleaved to oxalic acid and threonic acid, or decarboxylated to carbon dioxide, xylose, and xylulose, leading finally to xylonic acid and lyxonic acid (Arrigoni et al., 2002). All of these metabolites and ascorbic acid itself are excreted in the urine (Villacorta et al., 2007).

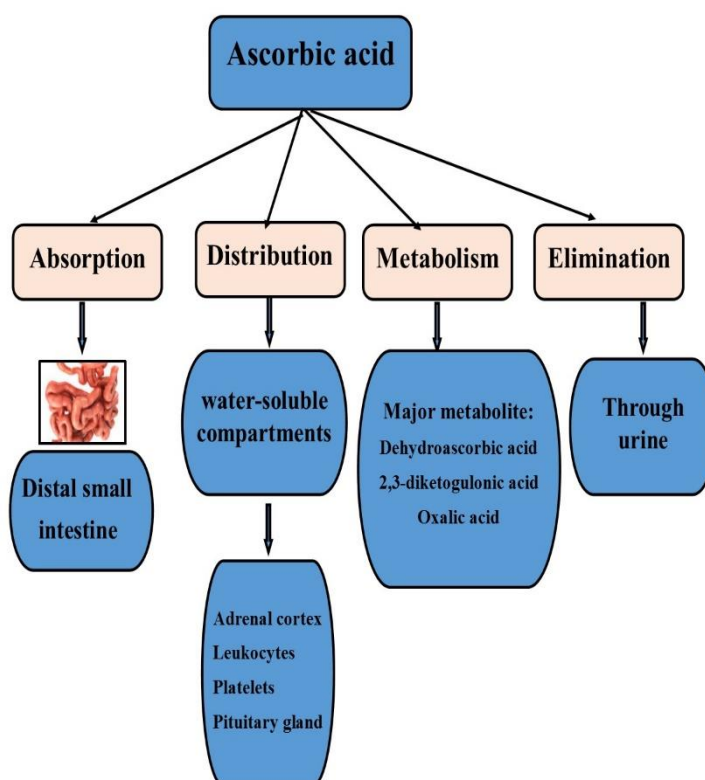


**Figure 3:** Catabolism of ascorbic acid



### Elimination

The main route of elimination of ascorbic acid and its metabolites is through urine. It is excreted unchanged when high doses of ascorbic acid are consumed. Ascorbic acid is generally non-toxic but at high doses (2-6 g/day) it can cause gastrointestinal disturbances or diarrhea (Barnes et al., 1975).



**Figure 4:** ADME of Ascorbic acid

### Role of vitamin C for the treatment of diabetes and its co-morbidities

For diabetes, the importance of vitamin C has been validated in both humans and animals. A study on diabetic rats found that vitamin C supplementation leads to defense against oxidative processes. In another study, it was found that vitamin C supplementation decreases insulin resistance and recovers glucose regulation in diabetic mice (Abdel-Wahab, 2002). Diabetic blood sugar curves were also seen in humans with vitamin C deficiency but these values resumed to normal after supplementation with vitamin C. Vitamin C plays a crucial role in the treatment of diabetes and its related complications as vitamin C functions as an antioxidant, and also this vitamin inhibits the intracellular accumulation of sorbitol, hence vitamin C



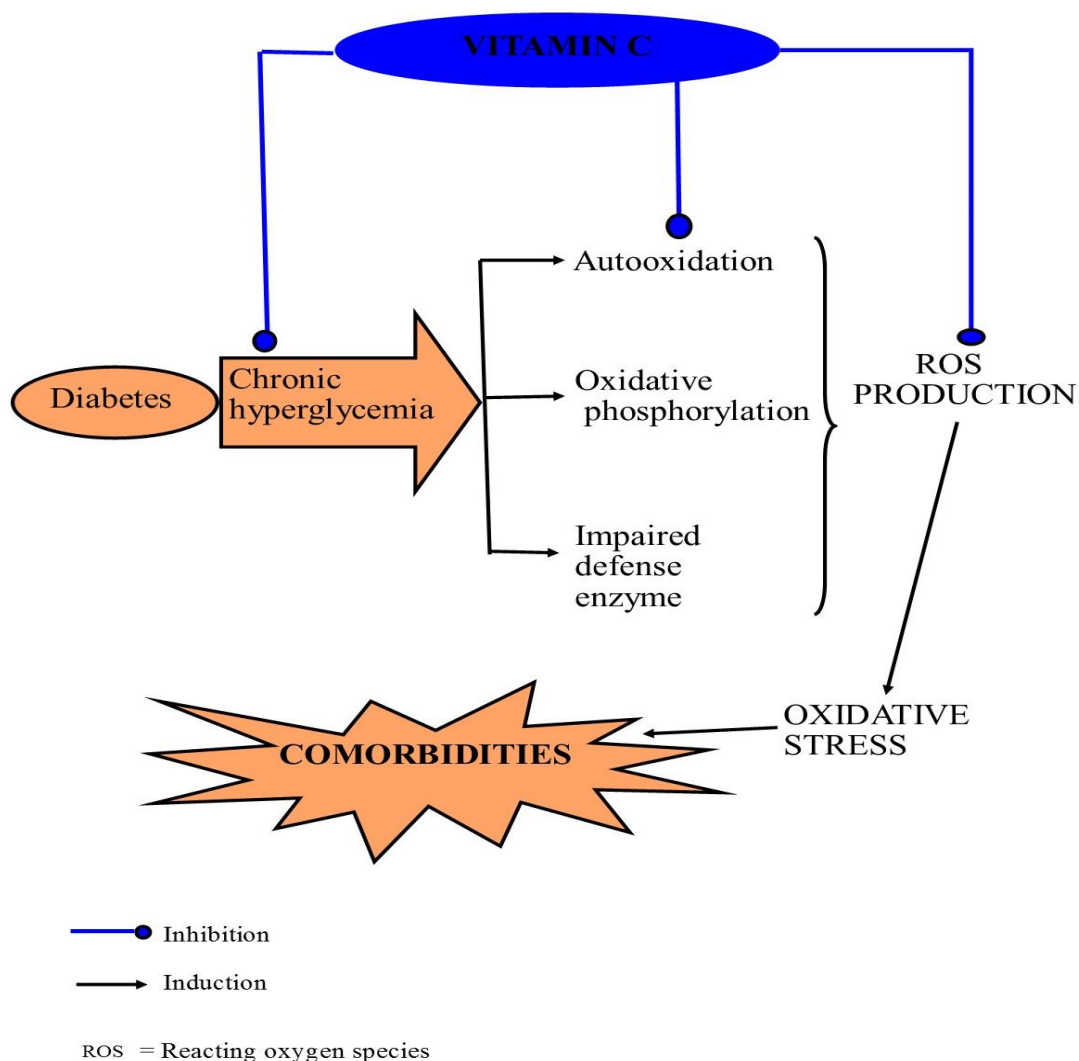
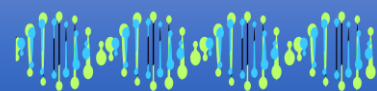
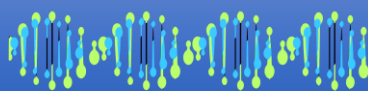


decreases oxidative stress and improves blood vessel function and other complications in diabetic patients.

### **Mechanism involved in the treatment of diabetes and its co-morbidities**

The antioxidant property of vitamin C play a crucial role in the treatment of diabetes and its related complications. In diabetes chronic hyperglycemia occurs. High blood glucose levels results in the production of reacting oxygen species (ROS) by various processes like auto-oxidation of glucose, shifts in redox balances, oxidative phosphorylation, decreased tissue concentrations of low molecular weight antioxidants, such as reduced glutathione (GSH) and vitamin E, and impaired activities of antioxidant defense enzymes such as superoxide dismutase (SOD) and catalase (CAT) (Haskins et al., 2003). Levels of ROS are under tight control by the protective actions of antioxidant enzymes and nonenzymatic antioxidants in normal and healthy cells. However, in diabetes, excessive cellular levels of ROS induced by hyperglycemia causes oxidative stress. ROS include free radicals such as superoxide ( $\bullet\text{O}^{2-}$ ), hydroxyl ( $\bullet\text{OH}$ ), peroxy ( $\bullet\text{RO}_2$ ), hydroperoxyl ( $\bullet\text{HRO}^{2-}$ ) as well as nonradical species such as hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) and hydrochlorous acid (HOCl) (Turko et al., 2001). These oxygen free radicals are mediator of diabetes-associated complications. Current studies have specified that a hyperglycemia-induced overproduction of superoxide appears to be the major event in the development of complications of diabetes. Superoxide overproduction is associated with increased generation of nitric oxide and, as a result, formation of the strong oxidant peroxynitrite and by poly (adenosine diphosphate-ribose) polymerase activation, which in turn further initiates the pathways implicated in the development of diabetes-related complications. This procedure consequence in severe endothelial dysfunction and initiation of inflammation in blood vessels of individuals with diabetes, and these aspects contribute to the development of complications of diabetes. Vitamin C has been proved to inhibit all this processes by acting as an antioxidant hence inhibiting the formation of ROS or scavenge free radicals, it also increase the antioxidants defense enzyme capabilities and inhibit protein glycation (which occurs due to hyperglycemic condition), as a result there is decrease in the formation of advanced glycation end product (AGEs) and hence it protects from diabetic complications like peripheral vascular disease, nervous system damage, renal system damage, and eye damage, cardiovascular disease and stroke. Vitamin C inhibits the action of interferon alpha, a substance that inhibits the release of insulin and hence prevents hyperglycemic condition (Hamilton et al., 2007).



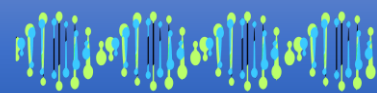
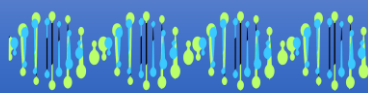


**Figure 5:** Mechanism of action of vitamin C in diabetes.

### CNS regulation in diabetes

Diabetes is characterized by hyperglycemia and is associated with long-term vascular complications such as retinopathy, nephropathy, cardiopathy, and neuropathy. Diabetes causes ischemic damages in various brain regions because of increased oxidative stress caused by hyperglycemia (Dalal et al., 2002). Increased reactive oxygen species can amend neuronal function because of neuronal death through protein oxidation, elevated nonenzymatic glycosylation, DNA damage, peroxidation of membrane lipids (Ozkan et al., 2005). It has been found that treatment with vitamin C prevent neuronal cell damage caused by diabetes-induced oxidative stress by reducing the concentration of free radicals (Hawkins et al., 2001). Many studies have shown that the CNS can indirectly or directly control the three main regulators of glucose homeostasis: the liver, pancreas, and skeletal muscles Subsequent denervation studies





suggested a role for the CNS in other important aspects of glucose regulation, including hepatic glucose production and skeletal muscle glucose uptake. CNS controls key aspects of peripheral glucose homeostasis by monitoring various peripheral signals that are recognized by neural and endocrine mechanisms. These signals are integrated and processed by a sensor in the CNS, which corrects hepatic glucose production, pancreatic hormonal secretion and glucose uptake to maintain stable glucose levels in response to rapidly changing conditions (Wallis et al., 1999).

### **Role of vitamin C in treatment of obesity and its co-morbidities**

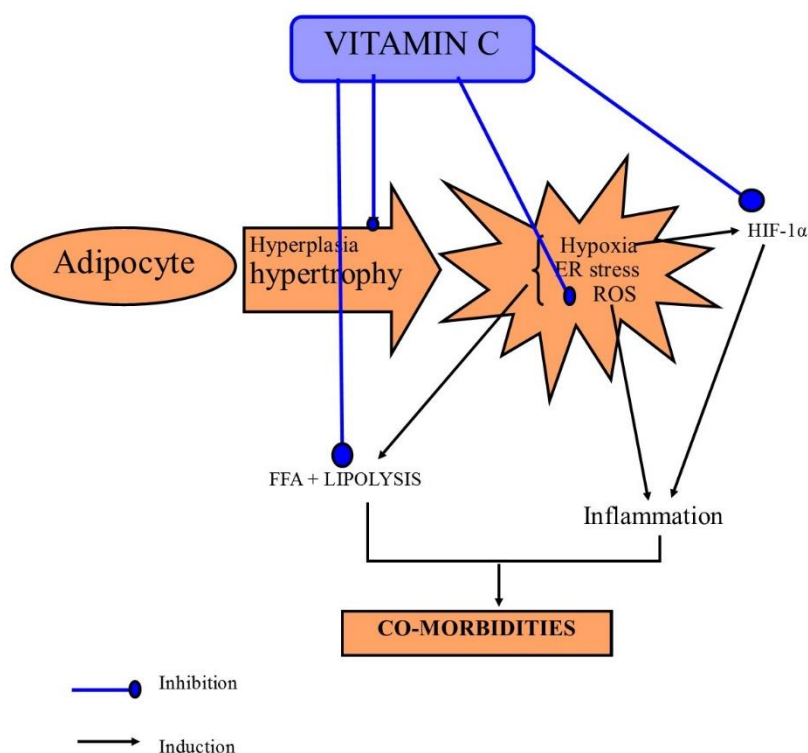
Indeed obesity has emerged as one of the serious health problem worldwide. As we know in obesity there is a sharp increase in the fuel reservoir in the organism in respect of fat content, accompanied by larger total body weight due to imbalance between energy intake and energy expenditure (Martinez, 2000). All these mass increment has been related with the increase of white adipose tissue deposits. This hypertrophy leads to oxidative stress which lead to several associated clinical manifestation such as cardiovascular disease, type 2 diabetes, inflammation, and some type of cancer also. Since these co-morbidities has been related to an unbalanced oxidative stress, therefore antioxidant-based treatment could be considered as to counteract obesity fat accumulation complications. In this context, it has been observed that vitamin C intake play a crucial role in the treatment of obesity and its co-morbidities. It has been found that this vitamin 1.regulate the glucocorticoid release from adrenal glands, 2.modulate adipocyte lipolysis, 3.inhibit glucose metabolism and leptin secretion on isolated adipocytes, 4.decreases oxidative stress. So it is clear that vitamin C intake can prevent obesity and its related complications.

### **Mechanism involved in the treatment of obesity and its co-morbidities**

The antioxidant property of vitamin C play a crucial role in the treatment of obesity .As in obesity there is severe increase in the white adipose tissue i.e hypertrophy. White adipose tissue, in addition to storage of energy, is an endocrine organ which secretes a large number of molecules which are involved in a variety of physiopathological processes. White adipose tissue overgrowth results in the dysregulated production of many endogenous products which have pro-inflammatory activity and may also modulate mitochondrial status, and also many inflammatory products derived from this tissue, such as tumor necrosis factor-alpha (TNF-a), interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), and inducible nitric oxide synthase (iNOS), are correlated with amplified body adiposity (Haslam et al., 2005). It has been found that in obesity, inflammatory-related pathways are also activated. Besides the production of pro inflammatory cytokines, adipose tissue also produces some substances like leptin and adiponectin which has important local and systemic effect. Thus induced monocyte migration to the adipose tissue and high secretion levels of several white adipose tissue adipokines are main reason for ROS production which leads to obesity-associated oxidative stress, hypoxia and endoplasmic reticulum stress (Kurl et al., 2002).



This pathological condition causes inflammatory state in the tissue, by prompting the migration of pro-inflammatory macrophages from bone marrow and the interaction between occupant adipocytes and macrophages. This interaction results to a deregulated cytokine and adipokyne secretion. Hypoxia-inducible factor alpha (HIF-1a) activation by hypoxia, and glucocorticoids contribute to this phenomenon. Ultimately, prolongation of this chronic state will leads to comorbidities like cardiovascular disease, stroke, hypertension, dyslipidemia, endometrium, prostate, and colon, gallbladder disease, osteoarthritis, respiratory problems, including asthma and sleep apnea insulin-resistance at the local and at the systemic level. Vitamin C has been proved to inhibit all this processes by reducing the lipid accumulation of adipocytes, either by direct effect over the differentiation machinery or by modulation locomotive behavior, inhibiting lipolysis, thus decreasing fatty acid efflux to the system, inhibiting glucocorticoid production, directly interfering with the adipocyte-macrophage interaction inhibiting the HIF-1a pathway, and the most important scavenging reactive oxygen species and thus reducing oxidative stress and inhibiting other comorbidities (Sturm, 2007).



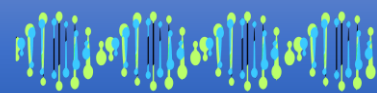
**Figure 6:** Mechanism of action of vitamin C in obesity.

### CNS regulation in obesity

Obesity is characterized by alteration in the energy balance and increased body weight. CNS play a crucial role in the regulation of energy balance. The central nervous system (CNS) influences body weight and energy stability through three mechanisms: (1) effects on behavior,







including feeding and physical activity; (2) effects on autonomic nervous system activity, which regulates energy expenditure and other aspects of metabolism; and (3) effects on the neuroendocrine system, including secretion of hormones such as growth hormone, thyroid, cortisol, insulin, and sex steroids (Schwartz et al., 2000). Mechanical, endocrine, neural, and metabolic signals from the periphery provide information to the CNS regarding the intake and utilization of nutrients (Haslam et al., 2005). The CNS then integrate this information and direct changes in energy intake and expenditure to maintain energy balance. The CNS responds to signals from stored fuel (adipose tissue), such as changes in the levels of leptin and free fatty acids (FFAs); to changes in the levels of circulating hormones, such as insulin; and to the nutrients released during a meal, such as glucose, to regulate hepatic glucose production and storage, pancreatic insulin secretion and skeletal muscle glucose uptake. Vitamin C inhibit leptin secretion on isolated adipocytes and hence maintain energy stability. It has been found that treatment with vitamin C prevent neuronal cell damage caused by obesity-induced oxidative stress by reducing the concentration of free radicals (Hawkins et al., 2001).

### **Gut mediated signal inducing satiety in obesity**

The GI tract is the largest endocrine organ in the body and is thought to have an important appetite-regulating role as a source of various regulatory peptide hormones (Chaudhri et al., 2008). Post-prandial satiety is thought to be regulated by a sensory system that connects between the gut and appetite-regulating centers in the brain, with the hypothalamus being responsible for nutrient and energy sensing and corresponding adjustments in food intake. In the gut, there exists a group of endocrine cells, which synthesize and release various hormones in response to nutrient and energy intake, Gut hormones which are responsible for maintaining energy balance are mainly cholecystokinin (CCK), oxyntomodulin (OXM), pancreatic polypeptide (PP), Ghrelin, glucagon-like peptide-1 (GLP-1) (Murphy et al., 2004). It has been found that these hormones influence appetite in humans and rodents when administered at physiological levels. Peptide hormones produced in the gastrointestinal tract and adipose tissue modify appetite in both animal and human. Peptides released, in response to food intake, from multiple locations in the gut (including the stomach, proximal/distal small intestine, pancreas and colon), activate vagal afferent nerves that innervate brain regions which involved in the immediate need for food intake. Peripheral signals from adipose tissue and the gut are integrated in the hypothalamus to effect short-term food intake and long-term energy balance; centrally released hormones and neurotransmitters also participate in appetite regulation. Cross-talk between peripheral satiety signals and hypothalamic and brainstem centres represents an integrative regulatory system for feeding, energy balance and body composition (Konturek et al., 2004).

### **Discussion**

Vitamin C, is widely regarded as an essential antioxidant in the human body and also regarded as “the most important antioxidant in human plasma”. Apart from its antioxidant properties, vitamin C has other important functions, such as the enzymatic function (proline, lysine, and





dopamine  $\beta$ -hydroxylase are examples), hydroxylation of amino acids, and nonenzymatic functions such as increasing gastric iron absorption. As an antioxidant, vitamin C has mainly two primary actions: First, vitamin C reacts with and inactivates free radicals in the water-soluble compartments of the body, areas such as the cytosol, plasma, and extracellular fluid. Second, vitamin C regenerates oxidized vitamin E (Sturm, 2007). It is well documented that there is an increased production of damaging free radicals in diabetes and obesity. Glucose autooxidation, protein glycosylation, formation of advanced glycation end products, and polyol pathway are involved in generation of oxidative stress. The protection against such damage can be offered by free radical-scavenging antioxidants (vitamin C). . It has been suggested that vitamin C may inhibit the formation of reacting oxygen species or scavenge free radicals, it also increase the antioxidants defense enzyme capabilities and inhibit protein glycation (which occurs due to hyperglycemic condition) (Haslam et al., 2005).

### Conclusion

Vitamin C shows positive effects on numerous metabolic disorders acting primarily as an antioxidant. On the basis of current evidence, it is justified to promote diets rich in vitamin C for the prevention of diabetes and obesity. Vitamin C supplements are beneficial in wound healing, reducing the incidence of common cold primarily in heavily physically stressed persons. It is also effective in preventing plasma lipid peroxidation, and decreasing serum fibrinogen and cholesterol values as risk factors for obesity. However, some positive effects could be achieved only by intra-arterial or intravenous administration of vitamin C, such as in patients with diabetes mellitus and some types of obesity. Despite contradictory reports, the consensus from extensive literature is that adverse health effects are not induced in healthy persons by ingesting high doses of vitamin C. However, there should be a caution in persons with some specific metabolic disorders. As an antibacterial effects of vitamin C, it promotes to increase concentration of some beneficial gut microbiota. And healthy gut microbiota directly or indirectly associated with gut-brain axis, which is responsible for healthy routine life. On the basis of above literature search, we may concluded that vitamin C could be useful for the treatment of diabetes and obesity and its associated disorders.

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## NOVEL ROUTES OF INSULIN FOR DIABETES TREATMENT

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### Abstract

Diabetes is a chronic disease characterized by inadequate insulin secretion with resulting hyperglycemia. Diabetes complication include both microvascular and macrovascular disease, both of which are affected by optimal diabetes control. Many individuals with diabetes rely on subcutaneous insulin administration by injection or continuous infusion to control glucose levels. Novel routes of insulin administration are an area of interest in the diabetes field, given that insulin injection therapy is burdensome for many patients. This review will discuss pulmonary delivery of insulin via inhalation. The safety of inhaled insulin as well as the efficacy in comparison to subcutaneous insulin in the various populations with diabetes is covered. In addition, the experience and pitfalls that face the development and marketing of inhaled insulin are discussed.

### Introduction

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels.

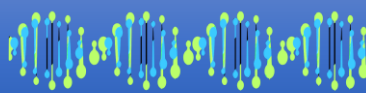
In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2015, diabetes was the direct cause of 1.6 million deaths and in 2012 high blood glucose was the cause of another 2.2 million deaths .

Two major types of diabetes mellitus are:

**Type I** Insulin-dependent diabetes mellitus (IDDM)/juvenile onset diabetes mellitus: There is  $\beta$  cell destruction in pancreatic islets; majority of cases are autoimmune (type 1A) antibodies that destroy  $\beta$  cells are detectable in blood, but some are idiopathic (type 1B)—no  $\beta$  cell antibody is found. In all type 1 cases circulating insulin levels are low or very low, and patients are more prone to ketosis. This type is less common and has a low degree of genetic predisposition.

**Type II** Noninsulin-dependent diabetes mellitus (NIDDM)/maturity onset diabetes mellitus: There is no loss or moderate reduction in  $\beta$  cell mass; insulin in circulation is low, normal or even high, no anti- $\beta$ -cell antibody is demonstrable; has a high degree of genetic predisposition; generally has a late onset (past middle age). Over 90% cases of diabetes are type 2 DM. Causes may be:





- Abnormality in gluco-receptor of  $\beta$  cells so that they respond at higher glucose concentration or relative  $\beta$  cell deficiency. In either way, insulin secretion is impaired; may progress to  $\beta$  cell failure.
- Reduced sensitivity of peripheral tissues to insulin: reduction in number of insulin receptors, ‘down regulation’ of insulin receptors. Many hypertensives are Hyperinsulinaemia, but normoglycaemic; and have associated dyslipidaemia, hyperuricaemia, abdominal obesity (metabolic syndrome). Thus, there is relative insulin resistance, particularly at the level of liver, muscle and fat. Hyperinsulinaemia per se has been implicated in causing angiopathy.
- Excess of hyperglycemic hormones (glucagon, etc.)/obesity: cause relative insulin deficiency—the  $\beta$  cells lag behind.

**Preparation of insulin**

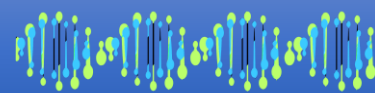
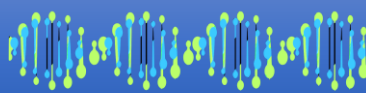
Insulin is used to control the level of blood glucose in patients with DM. It is an essential therapy for patients suffering from T1DM, and T2DM (especially in late-stage disease). Insulin was discovered in 1921 by Frederick Banting and Charles Best, went through its first clinical use in 1922 and helped revolutionize the treatment of T1DM which was fatal at that time. Initially, insulin was isolated from bovine and porcine pancreata, until the 1980s. Later on, recombinant DNA techniques allowed the manufacture of human insulin. Modifications of the amino acid sequence of the insulin molecule by rDNA and protein engineering methods have recently allowed the production of monomeric insulin analogues (e.g. lispro, aspart) which have a more rapid absorption profile. Since DM results in a defect in insulin function, the ideal treatment is to allow diabetics to regain normal insulin function. However, current research and technology has not been able to achieve this. The current insulin treatment involves exogenous administration, with the aim of achieving effective glycaemic control (i.e. prevention of hyper- and hypoglycemia) and avoidance of the complications of DM. Current modes of delivering insulin include intravenous (IV) infusion and subcutaneous (SC) injections. SC insulin preparations, which are more commonly used, include rapid-, intermediate- and long-acting insulin, which are used in different combinations (1 to 4 times or more daily). Table 1 lists the different insulin preparations together with their durations of action.

These are classified into rapid-, short-, intermediate- and long-acting insulin.

**Table 1: Durations of action of different insulin preparations.**

Insulin preparation		Onset (h)	Peak (h)	Duration (h)
Rapid acting	lispro, aspart, glulisine	< 0.5	0.5 – 2.5	3 – 4.5
Short acting	soluble insulin	0.5 – 1	1 – 4	4 – 8
Intermediate acting	Isophane (NPH), lente	1 – 3	3 – 8	7 – 14
Long acting	Bovine ultralente	2 – 4	6 – 12	12 – 30
	Glargine, detemir	1 – 2	None	18 – 24





**Table 2: Novel routes of insulin formulations and details of their respective experimental results**

	<b>Insulin formulation</b>	<b>Experimental model</b>	<b>Results</b>
<b>Pulmonary (inhaled)</b>	Afrezza®	Clinical trials (market available)	Acceptable HbA1C reduction in T1DM when used pre-meals with another basal insulin, but less HbA1C reduction [vs. insulin aspart]. Greater HbA1C reduction in T2DM when used with other OHA [vs. placebo]. May cause bronchospasm in asthma & COPD.
	Insulin microcrystal	In vivo (STZ-induced diabetic rats)	Prolonged hypoglycemic effects over 7h. Addition of zinc increases hypoglycemic effect [17% minimum reductions in blood glucose].
	Insulin + HA dry powder + (Zn <sup>2+</sup> or HPC)	In vivo (beagle dogs)	Addition of Zn <sup>2+</sup> & HPC improved mean residence time by >9-fold & >7-fold, respectively [vs. spray dried pure insulin].
	Insulin + DPPC	In vivo (rats)	Greater hypoglycemic effect [vs. insulin + liposome].
	Insulin + (bacitracin, Span 85, or citric acid)	In vivo (rats)	Bacitracin & Span 85 improved insulin solution bioavailability to ~100% [not effective in dry powder forms]. Citric acid increased the hypoglycemic effect, with bioavailability of 42-53% for dry powders. No acute toxicity to lung cells by citric acid.





	Insulin + (TDM or DM $\beta$ CD)	In vivo (rats)	Relative bioavailability: [TDM] 0.34-0.84% [DM $\beta$ CD] 0.19- 0.48%. Both have reversible effects on respiratory epithelium [normalises 120min post-exposure]
	Insulin + H-MAP	In vivo (rats)	Dose-dependent effect [maximum at 16mg/kg H-MAP & 1.3 U/kg insulin]. At maximum doses: relative bioavailability increased by >2.5-fold, maximum insulin concentration by 2-fold, blood glucose reduction by 2-fold [vs. same dose of insulin alone].
	Insulin/liposome	In vivo (alloxan-induced diabetic rats)	Homogeneously distributed throughout lung. Increased drug retention times. Hypoglycaemic effect
	Insulin-CAP-PEG particle suspensions	In vivo (rats)	Increased half-life & residence times [vs. insulin solution. Spray instillation was more efficient than intratracheal instillation.
	Insulin/PLGA nanospheres	In vivo (guinea pigs)	Substantial prolonged hypoglycemic response over 48h [3.9 IU/kg insulin] [vs. 6h by aqueous insulin]
	Insulin/PBCA NP	In vivo (healthy rats)	Improved bioavailability. Significant hypoglycemic responses. Minimum blood glucose concentrations of 46.9/30.4/13.6% of initial







			levels for 5/10/20 IU/kg insulin in PBCA NP.
Nasal	Insulin + 0.5% sucrose cocoate	In vivo (rats)	Improved insulin absorption, with resulting hypoglycemic effects.
	Insulin + carbopol-based gel	In vivo (rabbits)	Significant hypoglycemic effect. Relative bioavailability of 20.6% [vs. IV insulin]
	Insulin + 2% CS gel + EDTA	In vivo (diabetic rabbits)	Improved insulin absorption. Hypoglycaemic effect up to 46% of that caused by IV insulin
	Insulin + AGMS	In vivo (rats)	Insulin released slower from AGMS [cumulative release of 18.4% within 30min, 56.9% within 8h], compared to GMS [cumulative release of 32.4% within 30min, 75.1% within 8h]. AGMS increased nasal insulin absorption significantly when given in dry powder form.
	Insulin/PEGylated TMC NC	In vivo (rats)	Reduced blood glucose levels by 34-47%. Less toxic on nasal epithelium [vs. non-PEGylated].
	Insulin/CS-TBA microparticles + reduced glutathione (permeation mediator)	In vivo (rats)	Controlled-release of insulin over 6h. Absolute bioavailability of 7.24% [higher than using unmodified CS].
	Insulin + alkylglycosides dodecylmaltoside, tridecylmaltoside, tetradecylmaltoside, ordodecylsucros	In vivo (hyperglycemic rats)	Improved insulin absorption. Rapid hypoglycemic effects, maximum between 60-120min post-administration.





			Tetradecylmaltoside increases insulin absorption even when administered 15min before insulin.
	Insulin/p(LAMA-r-AAPBA) NP	In vitro & in vivo (diabetic rats)	Modification of glycopolymers affects insulin release. Good cytocompatibility. NP internalization via clathrin- & lipid raft/caveolae-mediated endocytosis. Significant hypoglycemic effect.

**Abbreviations:** T2DM: Type 2 Diabetes Mellitus, T1DM: Type 1 Diabetes Mellitus; HbA1C: glycated haemoglobin; OHA: Oral Hypoglycemic Agents; COPD: Chronic Obstructive Pulmonary Disease; STZ: Streptozotocin; HA: Hyaluronic Acid; HPC: Hydroxypropyl Cellulose; Zn<sup>2+</sup>: Zinc Ions; DPPC: 1,2-Dipalmitoyl Phosphatidylcholine; TDM: Tetradecyl-β-maltoside; H-MAP: Hydroxy-Methyl-Amino-Propionic Acid; CAP: Calcium Phosphate; PEG: Polyethylene Glycol; PLGA: Poly(lactide-co-glycolide); PBCA: Polybutylcyanoacrylate; NP: Nanoparticles; EDTA: Ethylenediaminetetraacetic Acid; AGMS: Aminated Gelatin Microspheres; GMS: Gelatin Microspheres; PEG: PolyethyleneGlycol; TMC: Trimethyl Chitosan; NC: Nanocomplexes; CS-TBA: Chitosan-4-Thiobutylamidine; p(LAMA-r-AAPBA): Poly(2-lactobionamidoethylmethacry-late-random-3 acrylamidophenylboronic acid).

**Pulmonary (inhaled) insulin**

Inhaled drugs are absorbed into the alveolar-capillary network, which has the advantage of having a large surface area (~140m<sup>2</sup>), thin diffusion barrier (~0.1-0.5mm), as well as being non-invasive. Drugs can be aerosolized and delivered with a median aerodynamic diameter smaller than 5µm, effectively targeting the alveoli as sites for absorption. Pulmonary delivery bypasses digestive enzymes and first-pass metabolism associated with oral delivery. Although enzymes are present in the lungs, they are involved in different metabolic pathways than those in the GIT.

Insulin microcrystal with a mean diameter of 3µm were prepared and administered to STZ-induced diabetic rats by using a sieve-type ultrasonic nebulizer. Prolonged hypoglycemic effects were observed over 7 hours. This may be explained by a sustained-release profile of insulin from the microcrystal that was deposited throughout the lungs. Further studies on insulin microcrystal found that the addition of zinc caused an enhancement of the hypoglycemic effect in rats (17% minimum reductions in blood glucose).

Hyaluronic acid (HA) exhibits valuable properties to aid in pulmonary insulin delivery, including its mucoadhesivity, which prolongs contact of the drug delivery system with absorption sites in the lungs, improving insulin absorption. In vivo studies on beagle dogs suggested that the addition of zinc ions (Zn<sup>2+</sup>) or hydroxypropyl cellulose (HPC) to insulin/HA





dry powder system improved the mean residence time of the preparation by >9 times and >7 times, respectively, as compared to spray dried pure insulin.

A number of absorption enhancers have been experimented upon, to improve insulin delivery via the pulmonary route. In vitro and in vivo studies suggested that phospholipids enhance pulmonary absorption of insulin. When 1,2-dipalmitoyl phosphatidylcholine (DPPC) was physically mixed with insulin and administered to anaesthetized rats, greater hypoglycemic effects were seen compared to insulin and liposome mixture [8,12]. Another study investigated the effect of additives to insulin absorption. A dry powder form of insulin was found to have a higher bioavailability than a pH 7.4 insulin solution. Bacitracin (1.4mg/dose) and Span 85 (1mg/dose) improved insulin (solution form) bioavailability to almost 100%, but are not effective in dry powder forms. However, citric acid added to insulin dry powder increased the hypoglycemic effect, with bioavailability of 42% and 53% for dry powders containing 0.025 and 0.036mg/dose citric acid, respectively. Moreover, citric acid was not found to cause acute toxicity to lung cell. Another group of absorption enhancers belong to the family of cyclodextrin (CD) derivatives, namely tetradecyl- $\beta$ -maltoside (TDM) and dimethyl- $\beta$ -cyclodextrin (DM $\beta$ CD), which have been tested on anaesthetized rats. The relative bioavailability of insulin preparations with TDM was higher (0.34-0.84%) than those containing DM $\beta$ CD (0.19-0.48%), indicating that TDM is a more effective absorption enhancer. It was also found that both agents have reversible effects on the respiratory epithelium, which was restored 120 minutes post-expos. Hydroxy-methyl-amino-propionic acid (H-MAP) was investigated as a potential pulmonary absorption enhancer in fasted anaesthetized rats. It was discovered that co-administration of H-MAP with insulin affects pharmacokinetics and pharmacodynamics in a dose-related manner, with maximum effects at 16mg/kg H-MAP and 1.3U/kg insulin. At these doses, there was a >2.5- fold increase in relative insulin bioavailability, achieving twice the maximum insulin concentration, with twice the reduction of blood glucose, compared to the same dose of insulin alone.

Nanoparticulate delivery systems have helped improve pulmonary insulin delivery as well. One such formulation involves insulin-loaded poly (lactide-co-glycolide) (PLGA) nanospheres with a mean diameter of 400nm, prepared by modified emulsion solvent diffusion method in water. These NP were prepared as aqueous dispersions (6mg/ml), nebulised by a sieve type ultrasonic nebulizer, and administered to fasted guinea pigs through a spacer by using a constant volume respirator for 20 minutes. Administration of 3.9IU/kg insulin caused substantial prolonged hypoglycemic responses over 48 hours, in contrast to 6 hours by nebulised aqueous insulin solution. This suggested that insulin was released in a sustained manner from PLGA nanospheres that were distributed throughout the lung . Insulin loaded in polybutylcyanoacrylate NP prepared by emulsion polymerization also improved bioavailability in studies on normal rats. Intratracheal administration caused significant hypoglycemic responses, with minimum blood glucose concentrations of 46.9%, 30.4% and 13.6% of initial levels after administration of 5, 10 and 20 IU/kg insulin (in polybutylcyanoacrylate NP), respectively.

A recently FDA-approved product called Afrezza® has been developed by Mankind Corp. This rapid-acting insulin is delivered as an inhalational powder before meals. Studies to assess its safety and effectiveness were carried out in 3017 participants (1026 with T1DM, 1991 with





T2DM). When Afrezza® was used as part of the basal-bolus regimen with basal insulin in T1DM patients, HbA1C reduction in 24 weeks was acceptable but not as much as that achieved by insulin as part. When used in combination with oral hypoglycemic drugs in T2DM patients, Afrezza® achieved a greater reduction in HbA1C after 24 weeks (compared to placebo).

The ideal pulmonary delivery system would have good insulin-loading efficiency, avoidance of insulin break down, predictable and reproducible release profile, as well as minimal side effects. These are the challenges faced by researchers searching for an inhaled form of insulin therapy. It is important to consider the adverse effects of inhaled insulin including the greater risk of hypoglycemia, greater weight gain, and mild to moderate cough in 25% of patients. Insulin doses are also dependent on patient co-morbidities, as smokers and asthmatics require lower and higher doses, respectively. Furthermore, to achieve a comparable glycaemic response, inhaled insulin needs to be given at much higher doses compared to SC administration. There is also the issue of insulin-directed antibodies. Nevertheless, inhaled insulin appears to be a reasonable alternative to short-acting insulin injections in diabetic patients.

### **Nasal insulin:**

The nasal cavity is lined by an epithelial layer that has a large surface area due to the existence of microvilli on the epithelial cells. Together with the high total blood flow and porous endothelial membrane, this facilitates absorption of molecules into the sub epithelial capillary beds, directly into the general circulation. This route also bypasses the liver and avoids first-pass metabolism. All together, these can allow fast absorption (comparable to intramuscular or even IV injections) and onset at lower doses, and fewer side effects. Nasal administration is also convenient and less invasive, which can lead to better patient compliance. Administering intranasal insulin post-meals result in pulsatile increases in blood insulin levels, mimicking normal physiological secretion. Considering all these advantages, intranasal insulin has great potential to be used in the treatment of patients with T1DM and T2DM.

Difficulties faced by nasal drug delivery include mucociliary clearance, enzymatic activity, as well as the epithelial lining itself that prevents passage of peptide molecules with high molecular weights and hydrophilic natures. Nasal bioavailability can be increased by use of absorption enhancers, proteolytic enzyme inhibitors, mucoadhesive formulations, as well as dry powder systems to deliver insulin via the nasal route.

One study investigated the potential use of alkylglycosides as absorption enhancers for the nasal absorption of insulin, as in vivo studies in rats made hyperglycemic by xylazine/ketamine anesthesia. When drops containing 2U insulin and 0.03-0.5% alkylglycosides were instilled, rapid hypoglycemic effects were observed, together with increased levels of immune reactive insulin in the blood, with maximal hypoglycemia between 60-120min post-administration.

Dodecylmaltoside, tridecylmaltoside, tetradecylmaltoside and dodecylsucrose (a compound that differs from dodecylmaltoside by only one carbohydrate residue) effectively enhanced insulin absorption. However, nonylglucoside needed higher concentrations of 0.25-0.5% to behave as an effective absorption enhancer. Further experiments on glycosides, made up to maltose or sucrose linked to longer alkyl side-chains (C<sub>13-16</sub>), were tested on anaesthetised rats, and their efficacy as absorption enhancers were compared with previously tested





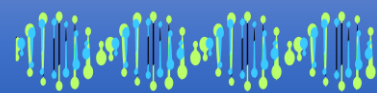
alkylglycosides with shorter alkyl side-chains ( $C_{8-12}$ ). Results indicate that for alkylmaltoside derivatives, tetradecylmaltoside ( $C_{14}$ ) caused maximal enhancement in insulin absorption. Longer-chained pentadecylmaltoside ( $C_{15}$ ) and hexadecylmaltoside ( $C_{16}$ ) were less potent and required higher concentrations for maximal effect. On the other hand, for alkanoylsucrose derivatives, tridecanoylsucrose ( $C_{13}$ ) and tetradecanoyl sucrose ( $C_{14}$ ) were most potent. In addition, tetradecyl maltoside increased insulin absorption even when administered 15 minutes before insulin. It was determined that the potency of the enhancers depended more on the alkyl side-chain length rather than the glycoside moiety.

Emollients such as sucrose cocoate (SL-40), which is a mixture of sucrose esters of coconut fatty acids in aqueous ethanol solution, has also been tested as a absorption enhancer for nasal insulin administration in vivo on anaesthetized Sprague-Dawley rats. A 0.5% sucrose cocoate formulation increased nasal insulin absorption, with resulting hypoglycemic effects. Mass spectrometry identified sucrose monododecanoate as the most common ester in the sucrose cocoate mixture.

Mucoadhesive delivery systems can aid in improving bioavailability by countering the nasal mucociliary clearance mechanism. These systems prolong drug residence times at absorption sites and protect the drug molecules from enzymatic degradation. These include gels, liposomes and microspheres, which absorb water from the mucus layer lining the nasal cavity and forming a gel-like layer over the nasal mucosa. In addition, the absorption of water causes the nasal epithelial cells to be dehydrated, resulting in the separation of tight junctions between cells, increasing their permeability to drugs via paracellular absorption. An example of a gel preparation is a carbopol-based nasal gel spray, containing insulin, which caused a significant drop in blood glucose levels in rabbits. The bioavailability of insulin administered in the nasal gel preparation was 20.6% compared to IV insulin. Another insulin gel formulation uses bioadhesive chitosan (CS) gel containing 4000 IU/dl insulin, administered to diabetic rabbits. Results show that gels made up of 2% medium molecular weight CS with ethylenediaminetetraacetic acid (EDTA) enhanced insulin absorption and caused a drop in glucose levels by up to 46% of that caused by IV insulin.

Microsphere preparations for nasal insulin include insulin/CS microspheres made by emulsification-cross linking process. In vivo studies on diabetic rats found that microspheres with 400mg CS and 70mg ascorbylpalmitate (used as a cross-linker) resulted in an absolute bioavailability of 44%, with a corresponding 67% decrease in blood glucose compared to IV insulin. A separate study tested aminated gelatin microspheres (AGMS) to deliver intranasal insulin to rats. Fluorescein isothiocyanate (FITC)-labelled insulin was used in this study, which was released slower from AGMS (cumulative release of 18.4% within 30min, 56.9% within 8h), compared to native gelatin microspheres (GMS) (cumulative release of 32.4% within 30min, 75.1% within 8h). Additionally, AGMS increased nasal insulin absorption significantly when given in dry powder form. It was suggested that AGMS works by absorbing water from the nasal mucosa, temporarily dehydrating the epithelium, hence, opening tight junctions. The cationic nature and mucoadhesivity of AGMS also contributes to its absorption enhancing effects. A separate microparticle-based delivery system using a thiolated chitosan conjugate, known as chitosan-4-thiobutylamidine (CS-TBA) was tested to deliver insulin nasally in rats. The nasal preparation consisted of FITC-labelled insulin, CS-TBA and reduced glutathione (as





a permeation mediator). The insulin showed a controlled-release profile over 6 hours, with an absolute bioavailability of 7.24%, which is higher compared to using unmodified CS.

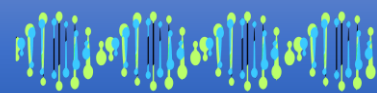
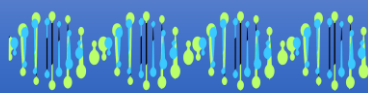
Nanotechnology has opened up new pathways in researching novel nasal insulin delivery systems. One formulation tested insulin/CS NP prepared by ionotropic gelation of CS glutamate and tripolyphosphate pentasodium, and by simple complexation of insulin and CS, but found that the enhancing effect was not as great as CS in powder form. Another formulation involves a CS derivative: PEGylated trimethyl CS (TMC) Nanocomplexes (NC). These insulin/PEGylated TMC NC managed to reduce blood glucose levels by 34- 47% in anaesthetized rats, and were found to have less toxic effects on nasal epithelium compared to the non-PEGylated counterparts, suggesting its suitability to be used as a nasal insulin delivery system. Another set of NC tested for this same purpose were made from amine-modified poly (vinyl alcohol)-graft-poly(L-lactide), and prepared by spontaneous self-assembly of insulin and the water-soluble amphiphilic polymer. In vivo studies on fasted healthy rats, found that the NC decreased blood glucose levels by 50% (from basal levels), 50 to 80 minutes post-administration, and studies on STZ- induced diabetic rats observed a 30% decrease in blood glucose within 75-95 minutes. There was no evidence of nasal mucosal damage 4 hours post-administration, as confirmed by histological examination. An amphiphilic glycopolymer poly (2-lactobionamidoethyl methacrylate-random-3-acrylamidophenylboronic acid) (p (LAMA- r-AAPBA)) was used in the manufacture of NP to deliver insulin intranasally. It was demonstrated that modification of the glycopolymers affects insulin release in vitro. Further tests show good cytocompatibility, with NP internalization into Calu-3 cells via clathrin-mediated and lipid raft/caveolae-mediated endocytosis. In vivo studies on diabetic rats show significant hypoglycemic effect after nasal administration.

Nasally delivered insulin seems to be a possible non-invasive method of administering insulin. However, there are certain problems that need to be addressed. There are large amounts of intra- and inter- individual variability in bioavailability, as well as limitations to the amount of insulin that can be administered for each nasal instillation. More importantly, the preparation must be safe to be used in the long run, as insulin is used in long-term diabetic management. Nasal irritation and possible damage to the nasal mucosa and ciliary function are concerning drawbacks. Absorption enhancers are useful to increase nasal insulin bioavailability, but are also associated with adverse effects, especially at effective concentrations and/ or prolonged use. Surfactants and bile salts, popular absorption enhancers, can cause irreversible nasal mucosa damage. Another potent enhancer is dimethyl- $\beta$ -cyclodextrin (DM $\beta$ CD), a cyclodextrin derivative, which was shown to increase insulin absorption via the nasal route in rats at a concentration of 5% (w/v), with a bioavailability of almost 100%. However, in vitro studies show that DM $\beta$ CD affects ciliary movement. Hence, further studies are needed before nasal insulin delivery systems are ready for clinical use.

## Conclusion

These novel routes of insulin therapy provide opportunities to overcome the disadvantages of current insulin regimens. Ultra-long acting insulin (e.g. degludec) may lead to a convenient reduction in dose frequency, whereas ultra-short acting forms (e.g. Linjeta™) can avoid hypoglycaemic effects after meals. Artificial pancreas systems resemble physiological insulin,



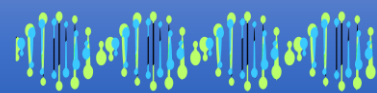


and with improved algorithms, have come ever closer to achieving physiological insulin levels and response to meals, especially when used in combination with new ultra-short acting insulin formulations. Other routes such as Transmucosal route have shown promising results and may soon allow non-invasive insulin delivery for all diabetic patients. Finally, oral insulin seems to be the ideal formulation, which is being extensively researched by numerous companies and institutions worldwide. Nanotechnology has aided substantially in the improvement of insulin delivery as well.

However, it is wise to be cautious with exploring alternative and novel routes for insulin delivery, as insulin may produce unwanted local effects. It is well known that subcutaneous injections of insulin cause local lipodystrophy, damaging subcutaneous fat tissue and causing a degree of disfigurement. Since insulin is a growth factor, it has the tendency to be mutagenic, which is a concern, as insulin therapy is usually life-long. Such prolonged exposure to a potentially mutagenic drug may adversely affect local tissues. In addition to adverse effects inherent to insulin, the use of absorption enhancers may present their own problems. The barriers to absorption of drug molecules function to prevent penetration of toxins and pathogenic microorganisms. Disrupting such barriers may not only facilitate insulin absorption, but also transport of unwanted molecules and organisms. In addition to that, hepatic first-pass metabolism may reduce bioavailability of insulin, but this process takes place in normal individuals to reduce hepatic glucose production as well as prevent peripheral hyperinsulinaemic effects. Bypassing the liver to increase insulin bioavailability might cause adverse effects in the long run.

In conclusion, much work needs to be done to achieve a safe, non- invasive, convenient insulin formulation. With the release of Oral- lyn™ and Afrezza®, and preliminary research in countless non-invasive insulin delivery systems, much progress has been made towards achieving this goal. Aided by the advancements in nanomedicine, the vision of an ideal insulin tablet may soon be realized, thus, making insulin injections a thing of the past.



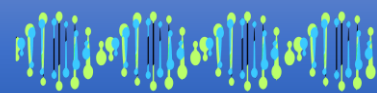


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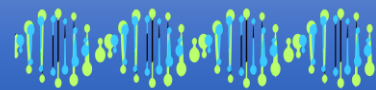
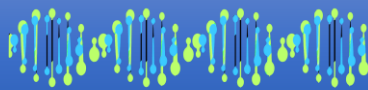
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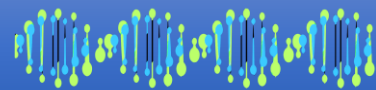
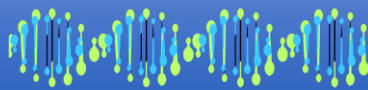
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# SELECTED ORAL PRESENTATION





## LIQUID CRYSTALLINE DRUG DELIVERY SYSTEM FOR POORLY SOLUBLE DRUGS

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Poorly soluble drug molecules often have low bioavailability issues and absorption problems in the clinical setting. As the number of poorly soluble drugs increases from discovery, developing technologies to enhance their solubility, while also controlling their release is one of the many challenges facing the pharmaceutical industry today. Liquid crystalline systems, nanoparticles or macro-matrix, self-assemble in the presence of an aqueous environment and can provide a solubility enhancement, while also controlling the drug release rate. Liquid crystals are thermodynamically stable and possess long shelf life. It show bio adhesive properties and sustained release effects. The focus is on the potential of utilizing liquid crystalline systems for poorly soluble drugs followed by water soluble molecules.

### KEYWORDS:

Drug delivery; Liquid crystal; Poorly soluble drug; cubic crystal hexagonal crystal





## SYNTHESIS AND EVALUATION OF ANTICONVULSANT ACTIVITY OF SOME IMIDAZOLE CONTAINING COMPOUNDS.

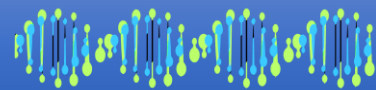
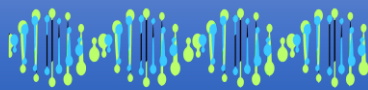
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Dr. KNMIPER, Modi Nagar, Ghaziabad*

### ABSTRACT

Epilepsy is one of the most common disorders of the brain, affecting about 50 million individuals worldwide. Although 70-80% of all epileptics are adequately treated by current available drugs, seizure protection is often accompanied by numerous side effects including drowsiness, ataxia, gastrointestinal disturbances, gingival hyperplasia, hirsutism and megaloblastic anaemia<sup>2</sup>. Thus search of new epileptic drugs is very essential. Epilepsy is a chronic disorder that causes unprovoked, recurrent seizures. A seizure is a sudden rush of electrical activity in the brain. Imidazole (1,3-diazacyclopenta-2,4-diene) is an organic compound with the formula  $C_3H_4N_2$ . This aromatic heterocyclic is classified as an alkaloid. This ring system is present in important biological building blocks such as histidine, and the related hormone histamine.. Imidazole is also one of the most versatile nuclei in medicinal chemistry with a wide range of biological properties including antimicrobial, antitumor, Analgesic, anti-inflammatory, antidepressant and anticonvulsant activities. On the basis of these observations we have synthesized some derivatives of Nafimidone [1-(2-naphthyl)-2-(imidazole-1-yl) ethanone] which is a potential anticonvulsant compound containing imidazole and studied their anticonvulsant and antimicrobial properties. The synthesized compounds were characterized by elemental analysis, IR, NMR and MASS-spectroscopy. Three of the five synthesized compounds showed anticonvulsant activity when screened against MES taking Phenytoin and carbamazepine as the standard drugs.

**KEYWORDS:** Imidazole, anticonvulsant activity, nafimidone, spectral analysis





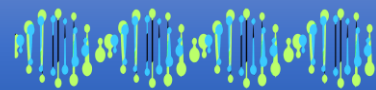
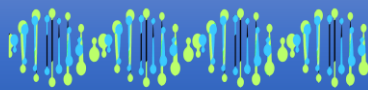
## X RAY IMAGING AS AN AID IN DIAGNOSIS AND TREATMENT OF OSTEOPOROSIS

*Sudhanshu Gupta\*, Prakash Mishra, Adarsh kesarwani,  
Arvind Kumar Srivastava  
United institute of Pharmacy Naini Allahabad*

Bone Mineral Density of the spine and hip which have an important role in estimation of individual patients of osteoporosis (it is a common age related disorder proved clinically by Skeletal fractures, especially fractures of the vertebrae, hip, and forearm) and in helping of patients about the appropriate use of anti-fracture treatment. Actual diagnosis of osteoporosis, estimation of fracture risk and monitoring of patients can be performed by Dual energy X-Ray Absorptiometry (DXA). Hip and Spine examinations by this technique provides number of advantage over other techniques. T-score definition of osteoporosis, given by World Health Organisation justified ability to predict fracture risk, proven effectiveness for targeting anti-fracture therapies, and the ability to monitor response in treatment. The WHO has established Dual energy X-Ray Absorptiometry the Best Densitometric Technique for examining Bone Mineral Density in Post-menopausal women and based the definitions of osteopenia and osteoporosis of its result. This review discusses the evidence for these and the other clinical aspects of Dual energy X-Ray Absorptiometry for scanning, including its role in the new WHO principle for treating patients on the basis of their individual fracture risk. DXA is presently acknowledged as the leading Bone Densitometric Technique because it has the efficiency to measure axial and appendicular sites with superior monitoring capabilities and more sophisticated reference databases and in quality control procedures.

**Key Words:** Dual energy X-Ray Absorptiometry, Osteoporosis, bone mineral density.





## IMMUNOSUPPRESSIVE DRUGS AFTER SOLID ORGAN TRANSPLANTATION

*Kishan Singh, Manoj Kumar Mishra, Anil Kumar Patel*

*Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

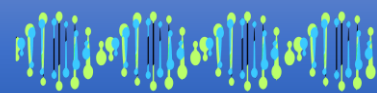
### ABSTRACT:

In recent years solid organ transplantation has been rapidly developed as a therapeutic intervention that is life-saving and greatly contributes to a better quality of life in organ recipients. The rapid development has been made possible because of a drastic expansion in the immunosuppressive repertoire. Unfortunately, the side effects of these drugs can be severe, which is one of the reasons that life expectancy of transplant patients still significantly falls short of that of the general population. In this review manuscript we will discuss current and future immunosuppressive strategies that are employed in solid organ transplantation. Expanding our understanding of the human immune system will hopefully provide us with newer, smarter drugs that promote immune-tolerance without the side effects observed today.

**KEYWORDS:** Solid organ transplantation, renal transplantation, immunosuppressive drugs







## PHARMACOGNOSTICAL AND PHYTOCHEMICAL STANDARDIZATION OF *POTENTILLA FULGENS* WALL EX. HOOK

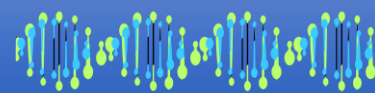
Harinath Dwivedi<sup>1</sup>, AKS Rawat<sup>2</sup>, Anupam<sup>\*1</sup>,  
Babu Banarasi Das University, Faizabad Road, Lucknow<sup>1</sup>,  
Pharmacognosy & Ethnopharmacology Division, CSIR-National Botanical  
Research Institute, Lucknow<sup>2</sup>

### Abstract

*Potentilla fulgens* belongs to the rosaceae family. It is an erect perennial herb, grows in Jammu and Kashmir, Himachal Pradesh, Uttarakhand, West Bengal, Sikkim, Assam and Meghalaya. Whole herb is used for gum and tooth ailments, cough, cold, diarrhoea, stomach problems, diabetes and cancer. Roots are used in wounds and anthelmintic. Root contain novel bioflavonoid potifulgene, epicatechin. Aerial parts yielded triterpenes, potentene A and potentene B along with afzelchin -4  $\alpha$  - 8'' catechin, epiafelchin and rutin. Identification of the drug is desired for obtaining its maximum therapeutic effects. The aim of the present study was to scientifically establish a standard monograph on the basis of pharmacognostical and phytochemical aspects. The present study comprises macroscopical, microscopical characters, physico-chemical parameters, florescence analysis and HPTLC finger printing of the roots of *Potentilla fulgens*. The diagnostic characters of root showed the presence of cork cells, cortex region, secondary phloem, lignified xylem, elongated medullary rays, starch grains, calcium oxalate crystals. HPTLC fingerprinting detected the presence of  $\beta$ -sitosterol, a biomarker compound in ethanolic extract of root. Phytochemically the plant was found to contain flavonoids, saponin, phenolics and tannins. The present study will provide referential information for correct identification and standardization of this medicinal plant.

Key Words: *Potentilla fulgens*, Pharmacognosy, HPTLC,  $\beta$ -sitosterol





## THE MARKETING CHANNELS OF PHARMA CIRCUMFERENCE

*Nitin Kumar Pandey*

*Shambhunath Institute of Pharmacy, Allahabad*

### **Abstract:**

The observation, learning & expansion of marketing channels is the requisite for not only economical growth of pharmaceutical companies but also for health and social enrichment of our country especially regarding people of under poverty line & middle class. We have to explore or improve the things such as distribution network and net promoter score so that we can reach to all the diversities of people. Either it is product life cycle management, marketing research, R & D sector or sales & promotion we need an influential team possessing all courage along with continuous motivation to deliver their best. This all needs sharp & deep ethnographic, demographic studies, relationship focus so that our pharma companies of India can gain/retain the topmost positions of the world. The utmost important thing that must revolve in the mind of every youth is that right and firm motivation to deal with all obstructions upcoming to pave the way for growth of pharma organizations & their country preserving the pride and welfare.

**Keywords:** Ethnographic effect, Customer profile, Demographical analysis, Net promoter score (NPS)





## NANOROBOTICS

*Rahul Ashok Tiwari, Raj Keshwar Prasad  
Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

### Abstract

Nanorobotics is the study of robotics at the nanometer scale, and includes robots that are nanoscale in size and large robots capable of manipulating objects that have dimensions in the nanoscale range with nanometer resolution. With the ability to position and orient nanometer-scale objects, nanorobotic manipulation is a promising way to enable the assembly of nanosystems including nanorobots.

This generally focuses on nanorobotic manipulation systems and their application in nanoassembly, biotechnology and the construction and characterization of Nano-Electro Mechanical Systems (NEMS) through a hybrid approach. Because of their exceptional properties and unique structures, carbon nanotubes (CNTs) and SiGe/Si nanocoils are used to show basic processes of nanorobotic manipulation, structuring and assembly, and for the fabrication of NEMS including nano tools, sensors and actuators. Nanorobotics provides novel techniques for exploring the biodomain by manipulation and characterization of nanoscale objects such as cellular membranes, DNA and other biomolecules. Nano tools, sensors and actuators can provide measurements and/or movements that are calculated in nanometers, gigahertz, piconewtons, femtograms, etc., and are promising for molecular machines and bio- and nanorobotics applications. Efforts are focused on developing enabling technologies for nanotubes and other nanomaterials and structures for NEMS and nanorobotics.

**Keywords:** NEMS, CNTs, Sensors, Actuators





## DEFENSIVE EFFECT OF NF-KAPPA B INHIBITOR (NDDCT) IN NEURODEGENERATION INDUCED BY LEAD

*Sudhir Kumar<sup>\*</sup>, Harikesh Maurya<sup>#</sup>*

*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow*

### ABSTRACT

Globally the economic burden for brain (neuro-disorders) disorders continuously is increasing due to unavailability of proper medicine without influencing complication and management guideline, hence the quest for a new medicine that can reserve neuronal activity and protect the further neuron damages. The study was designed to evaluate pharmacological potential of NDDCT (Natrium Diethyl Dithio Carbamate Trihydrate) in Lead induced neurotoxicity rat model. The neurotoxicity induced with lead 1mg/Kg b.w. mixed with dist. water for 35 days, significantly increased the level of serum nitrite and lead concentration in blood and in brain homogenate, the antioxidant activity like superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) were observed; the thiobarbituric acid reactive substances (TBARSs), total (brain) protein, acetyl-cholinesterase (AChE) activity were decreased with lead treatment. Histopathological changes including neurons degradation, neuronal necrosis, clumps formation of protein on neurons, were observed after lead administration. Result shows that, the treatment with NDDCT (50mg/kg b.w./day for 35 days) significantly attenuated all the elevated biochemical and histopathological parameters induced by lead. Finally it was concluded that NDDCT-50mg protected lead-induced neurotoxicity through enhancement of brain antioxidant system and confirms by histopathological investigation.

**Keywords:** NDDCT, Lead, Neurotoxicity





## SCOPE OF PHARMACOVIGILANCE AND ITS FUTURE TRAINED IN INDIA

*Akanksh Sharma, Harikesh Maurya\**

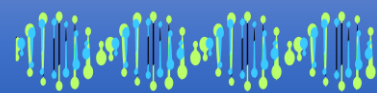
*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow*

### **Abstract**

The word pharmacovigilance defined as the science and activities related to the detection, assessment, understanding, prevention of adverse effects or any other drugs related problems. It is design to create ADR database for human population, insufficient evidence of safety from clinical trials and insure optimum safety of drug products in Indian market. The global pharmacovigilance market is expected to reach USD 10.27 billion by 2025, and grown at 14.20% (CAGR) between 2014 and 2020. In India about 179 ADR monitoring centers which are highly involving to development phase IV rules with 60% market share and expected to maintain dominance in future, phase III expected to grow in coming years because rising need to conduct risk assessment studies. Few top Indian firms involved in providing improved pharmacovigilance frameworks with the help of national coordination centre, which taking measures to enhance patient safety including monitoring, surveillance, and collaboration with national health programs. At present, India is fourth largest producer of pharmaceuticals in world and includes drug brands more than 6,000 licensed drug manufacturers and over 60,000 branded formulations, which provide great career option for life science and Pharmacy graduates in sectors-pharmaceutical companies, biotech companies, clinical research organizations etc.

**Keywords:** Pharmacovigilance, compound annual growth rate (CAGR), of national coordination centre, national health programs.





## SIGNIFICANCE OF STEM CELL IN ADVANCE HEALTH CARE SYSTEM

*Anjali Gupta, Arvind Kumar, Harikesh Maurya\**

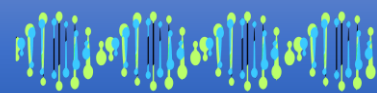
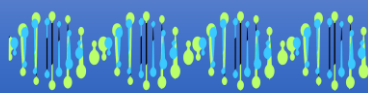
*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow*

### **Abstract**

Stem Cells are the preliminary cells to develop into mature cells which specialized in definite functions. The main characteristic of stem cell is the ability to undergo division to develop additional stem cells. Throughout human lives rely on stem cell to replace injured tissue and cells that are lost every day such as skin, hair, blood and lining of gut. Stem cells have two important properties; (a) The ability to self renew dividing in a way that make copy of themselves, (b) The ability to differentiate giving rise to the mature types of cells that build up organs and tissues. There are two major types of stem cells i.e. tissue specific stem cell and embryonic stem cell. The reason behind more valuable of embryonic stem cells are that, they derived from a variety of species and described as “Pluripotent” i.e. cells derived from any of three germ layer (ectoderm, mesoderm and endoderm). Embryonic stem cells can be obtained from the blastocyst a very early stage of development that consist of mostly hollow ball of approximately 1.5 lac cells and is barely visible to the naked eye. Thus stem cell technology is rapidly developing fields that combine the effort of cell biologist, genetics, clinical and offers hope of malignant and non-malignant diseases.

**Keywords:** Stem cell, Embryonic, Pluripotent, Malignant.





## THE CURRENT SCENARIO OF CLINICAL TRIAL IN INDIA

*Pragya Shukla, Arvind Kumar, HarikeshMaurya\**

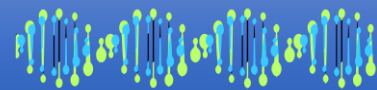
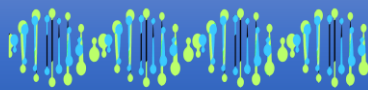
*Hygia institute of Pharmaceutical Education & Research, Ghaila road, Lucknow*

### **Abstract**

The clinical research industries are being in the state of dilemma with changing regulatory scenario in India. It started with an increase of projects between 2005 & 2010 and then got steady decline in the last five years. The government has reacted to the underlying assumptions by instituting new set of regulations with more strict measures to check compliance and conduct of the clinical research activities. The major focus has been increases in the field of regulatory vigilance over investigator, sponsors, ethics committee & institutions, thus ensuring protection of the subject right, safety and wellbeing. The main aim must be to cover aware of their rights and responsibilities. Our endeavour is to cover the current healthcare, clinical research status and the regulatory reforms in India and also propose the ways to achieve this goal with spreading education and public awareness regarding clinical research. The major growing healthcare needs the changing trends of the disease burden and the great potential of the nation for supporting clinical research activities. It is essential to map to enable the general population to contribute to the scientific developments and healthcare advancements without affecting their rights and safety. The new regulations would then act as an agonist to aid in making India a nation that delivers fair, scientific and good quality research.

**Keywords:** Clinical research in India, healthcare status, public awareness, regulatory reforms, research scenario.





## LIPOSOME-BASED DRUG DELIVERY IN BREAST CANCER TREATMENT

*Shailendra Tiwari, Harikesh Maurya, Santosh Kumar\**

*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow*

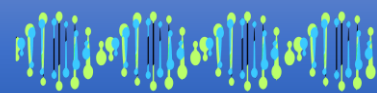
### Abstract

Drug delivery system is one of the principles to provide enhanced efficacy and/or reduced toxicity for anticancer agents. Long circulating macromolecular carriers such as liposomes can exploit the 'enhanced permeability and retention' effect for preferential extravasations from tumor vessels. Liposomal anthracyclines have already achieved highly efficient drug encapsulation, resulting in significant and improved anticancer activity with reduced cardiotoxicity, which include versions with greatly prolonged circulation such as liposomal daunorubicin and pegylated liposomal doxorubicin. The Pegylated liposomal doxorubicin has shown substantial efficacy in treatment and/or management of breast cancer as in both monotherapy and combination therapy with other chemotherapeutic agents. Additional liposome constructs or formulations are being developed for the delivery of other drugs at targeted points. The next generation of drug delivery systems will include true molecular targeting; immunoliposomes and other ligand-directed constructs represent an integration of biological components capable of tumor recognition with new drug delivery technologies.

**Keywords:** Drug delivery, immuno-liposomes, liposomesm onoclonal, antibody, polymers







## PHARMACOLOGICAL POTENTIAL OF BCCTFV-25 IN CCL<sub>4</sub> INDUCED NEPHROTOXIC RAT

*Sunil Kumar, Harikesh Maurya\**

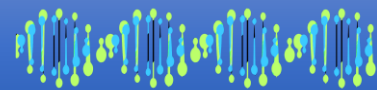
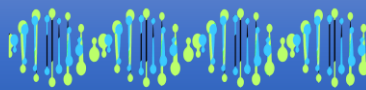
*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj, Lucknow*

### ABSTRACT

In India the economic burden for kidney disease continuously increasing due to unavailability of proper medication guideline and treatments, hence the quest for herbal medicine formulation that can reverse and protect the kidneys damages. The present study was designed to evaluate pharmacological potential of BCCTFV-25 in CCL<sub>4</sub> induced nephrotoxicity in Wistar rats to validate its folklore use in kidney diseases. The nephrotoxicity induced with 5ml CCl<sub>4</sub>/Kg b.w. mixed with olive oil in ratio of 1:9 each week for six weeks, significantly increased the level of serum creatinine, urea and reduced the level of uric acid. In kidney homogenate, the activity of superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) were decreased while thiobarbituricacid reactive substances (TBARSs) were increased with CCl<sub>4</sub> treatment. Histopathological changes including glomerular atrophy, tubular necrosis, necrosis of epithelium, interstitial edema and congestion in capillary loops was observed after CCl<sub>4</sub> administration. Result shows that, the treatment with BCCTFV-25 (25mg/kg b.w./day for six weeks) significantly attenuated all the elevated biochemical and histopathological parameters induced by CCl<sub>4</sub>. Finally it was concluded that BCCTFV-25 protected CCl<sub>4</sub>-induced nephrotoxicity through enhancement of renal antioxidant system and confirms by histopathological investigation.

**Keywords:** BCCTFV-25, CCL<sub>4</sub>, Nephrotoxicity, creatinine, thiobarbituricacid





## ROLE OF PHARMACIST IN MEDICATION SAFETY

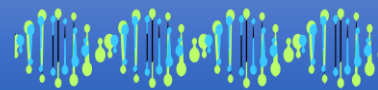
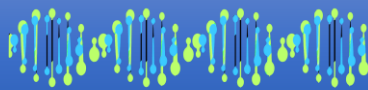
*Shivam pandey , Rishabh keshari*

### **Abstract :**

Pharmacists have great role to prevent these impacts and ensure the patient safety. Pharmacist: A professional who prepare and dispense drug and medicines. Medication Errors are unintended mistakes in the prescribing, dispensing and administration of a medicine that could cause harm to a patient. Each of these nodes of the medication system, with its many components, is prone to failure, resulting in harm to patients. The pharmacist is uniquely trained to be able to impact medication safety at the individual patient level through medication management skills that are part of the clinical pharmacist's role, but also to analyze the performance of medication processes and to lead redesign efforts to mitigate drug-related outcomes that may cause harm.

**Keywords :** Pharmacist, Medication error, Patient safety, Drug .





# SELECTED POSTER PRESENTATION





## ADVANTAGES OF INSULIN DRUG DELIVERY: A NOVEL PROSPECT

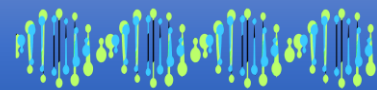
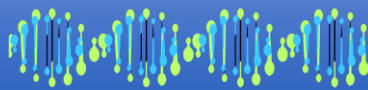
*Prabhat Kumar Tiwari\*, Arpit Maurya, Aman Kumar, Shobhit prakash Srivastava*

*Dr M.C.Saxena College of Pharmacy*

### **Abstract:**

Diabetes mellitus (DM) ,commonly referred to as diabetes is a group of metabolic disorder in which there are high blood sugar level overall prolonged period. Acute complication can include diabetic ketoacidosis, hyperosmolar hyperglycemic state or death. Type 1 diabetic mellitus (T1DM) is also on increase like type 2 diabetic, even through not in the same proportion, but still with a trend of 3-5% increase/year. Insulin therapy via subcutaneous or other parenteral route in diabetic patient is preferred but on continuous administration there may be chance of peripheral hyperinsulinemia, formation of thrombus, inflammation & irritation at the site. Also patient suffering from needle phobia hesitate to take it. But the new therapy of the transdermal patches developed now. A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. Often, this promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of medication delivery such as oral, topical, intravenous, intramuscular, etc. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive.





## Formulation and Evaluation of Topical Herbal Gel Containing *Nardostachys jatamansi* Rhizome Extract for Antimicrobial Activity.

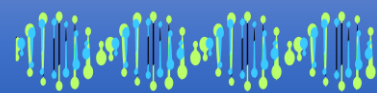
Nargis Ara\*, Neelam Datt, Shailendra K. Saraf.

Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology.

**Abstract:** The plant *N. jatamansi* is a critically endangered rhizome bearing medicinal property. It has been traditionally used in the treatment of many disorders like sun burns, wound healing and skin problems. In the current study, a herbal topical gel containing ethanolic extract of *Nardostachys jatamansi* rhizomes was developed by incorporating the ethanolic extract in a gel base. Four batches were prepared using Carbopol 940, Carbopol 934 and Sodium carboxymethyl cellulose as polymers and evaluated on various parameters like pH, spreadability, extrudability, drug content, *in-vitro* release and antimicrobial activity. Among all the batches, F3 showed good physical appearance, homogeneity and spreadability. Drug content and *in-vitro* drug release for F3 was found to be higher in comparison to the other batches, as 0.206 mg/g and 72.7% respectively. Antimicrobial study was done by cup-plate method using different microbial strains and among all F3 showed significant growth inhibition zone against *E. coli* and *S. aureus*. Thus from the study it was concluded that *N. jatamansi* can be used as an alternative for the treatment of topical problems.

Keywords: *Nardostachys jatamansi*, Herbal formulation, Gel, Antimicrobial.





## TO REDISCOVER STEM CELLS: AS FUTURE OF MEDICAL SCIENCE

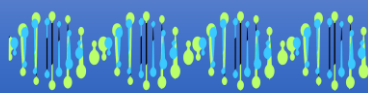
*Ekta Singh Chauhan\*, Mayank Kulshreshtha  
School of Pharmacy, BBD University, Lucknow (U.P.), India.*

### Abstract

Most of the cells of our body are unable to replicate but stem cells are specialized cells having a capacity to reproduce itself as well as other specialized cells of the body. The clonogenic and self-renewing property of stem cells differentiate it from the other cells because of this unique property it has gained attention of various scientists related to medical science to use it as “SEED”. This seed is used to regenerate tissues whenever any organ is damaged. The applications of stem cells is not only limited to tissue regeneration but also used to treat various abnormal condition of the body. The most popular stem cell therapy is Bone marrow transplantation. Recently stem cells are used in the treatment of many life threatening diseases and disorders such as dysfunction, AIDS etc. Therapies involving stem cells has opened a new path for the treatment of spinal cord (disease and injuries). Scientists of medical science uses stem cells in the screening of new drug entities. They have also developed models regarding normal growth as well as risk factors which causes birth defects. Stem cells play a vital role in regenerative treatment , drug discovery, biomedical research, neurodegeneration treatment, brain and spinal cord injuries, muscle regeneration, blood cell formation , Regrowing of teeth, Wound healing and Infertility lead to stem cells to serve as a powerful candidate to start a new clinical trials and can be future prospective of Modern Medical Science.

**Keywords:** Tissue regeneration, spinal cord injuries, clonogenic.





## AN OVERVIEW ON ANTIDIABETIC NATURAL PRODUCTS

Pragati Mishra and Parmesh K. Dwivedi

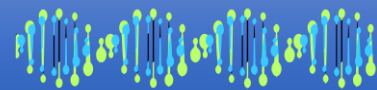
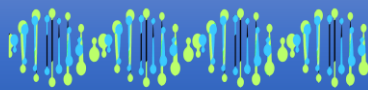
Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow campus

### Abstract

To serve as “lead” molecules for the synthesis of bioactive compounds or to be used as drug, Phytochemicals from the natural sources have a great importance. Today in the search for new therapeutic agents, bioactives plants, animals and microflora continues to play an important role. Diabetes mellitus is a group of etiologically and clinically heterogeneous disorders which results in metabolic defects and serious pathological consequences and is generally characterized by persistent hyperglycemia. With thousands of plant species, we are blessed with many natural products used as medicinal remedies in modern therapeutics. The herbaceous plant, *Galega officinalis* has been used since thousands of years ago for relieving the symptoms of diabetes mellitus. The effective use of acarbose, an alpha-glucosidase inhibitor is well documented in the large number of patient with type-2 diabetes. In this context, various terpenoids isolated from plant *Fagara tessmannii*, *Luculia pinceana*, *Gypsophila oldhamiana*, *Glinus oppositifolius* exhibited good  $\alpha$ -glucosidase inhibitory activity. The alkaloids isolated from *Adhatoda vasica*, *Lobelia sessilifolia*, *Commelina communis*, *Hyacinthus orientalis* are also found to be strong inhibitors of  $\alpha$ -glucosidase. Researches on various plants like *Capparis spinosa*, *Cinnamomum cassia*, *M. charantia*, *Aloe barbadensis*, *Theobroma cacao*, *T. foenum-graecum* have also been carried out to investigate their antidiabetic potential.

**Key words:** Diabetes, natural product, bioactive, alpha-glucosidase





## RECENT DEVELOPMENTS ON ANTIHYPERTENSIVE AGENTS

*Shivam Yadav, Parth Rastogi, Shreya Verma, Abhishek Kumar Nayak and Parmesh K. Dwivedi*

*Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow campus*

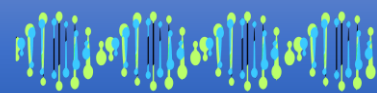
### Abstract

Because of growing rate of obesity and diabetes, a large number of population have been suffering from hypertension which is the most common cardiovascular disease and also a major cause of death worldwide. Despite the large number of antihypertensive drugs available, demand for new antihypertensive compounds is increasing day by day. The hypertension is treated with various established drugs belonging to the class of diuretics, calcium channel blockers, ACE inhibitors, angiotensin II antagonist, adrenergic receptor antagonist, vasodilators, aldosterone receptor antagonist etc. In the search of an alternate option, vaccinations are being trialed with some successful studies. In the search of new therapeutic targets, advancements in the signalling pathways that modulate vascular smooth muscle cell contraction has also provided valuable insight. Molecule MC-1 which is a metabolite of vitamin B<sub>6</sub>, is less toxic and reduces the heart damage. This in combination with lisinopril have been trialed for the treatment of hypertension with co-existing type 2 diabetes. Recently, some angiotensin II receptor antagonist such as azilsartan has also been investigated for the treatment of hypertension.

**Key words:** Hypertension, advancement, drugs







## **APTAMERS: PROSPECTIVE AS FUTURE PHARMACEUTICAL DOSAGE FORM**

Syed Abul Kalam<sup>1\*</sup>, Pranati Srivastava<sup>1</sup>, Manish Yadav<sup>1</sup>, Ved Prakash<sup>1</sup>, Ekta Singh Chauhan<sup>2</sup>

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2. School of Pharmacy, BBD University, Lucknow,

### **Abstract**

Aptamers are short stretches of Ribonucleic acid or Deoxyribonucleic acid having a specific 3D shape which form complexes with the target site with high affinity. Systemic Evolution of Ligands by Exponential Enrichment (SELEX) is responsible for the high affinity and specificity of aptamers to bind the target molecules. Due to some unique features of Aptamers, it attracts the attention of many scientists to use them as a tool in the treatment & diagnosis of various diseases and syndromes.

The results obtained from the various clinical data shows that Aptamers can be used in the treatment and diagnosis of various diseases including cancer and syndromes like AIDS, severe acute respiratory syndrome etc. Many viral infections like human immunodeficiency virus, hepatitis B virus and ebola virus are now treated or diagnosed with the help of aptamers. Along with viral infections, aptamers are also promising Chemical antibodies in the treatment of various kinds of cancer like breast cancer, lung cancer, colorectal cancer, etc. Aptamers have several advantages over conventional antibodies in context to its size, thermal stability, immunogenicity, ease of modification, etc. Aptamers are smaller than conventional antibodies, this property allows aptamers to access in tissue and cell. Aptamers are synthetic agents and we scale up its production as per requirement and it eliminate the various regulatory requirements associated with bio-production.

The various roles of aptamers in the treatment and diagnosis of many life threatening diseases, syndromes and viral infections like cancer, AIDS, ebola virus lead aptamers to serve as Future Pharmaceutical dosage form or prospective Future of Modern Medical Science.

**Keywords:** SELEX, Chemical antibody, Chronic diseases, Bio-production, Targetting.





## COMBINED ANTICOAGULANT EFFICACY OF *OCIMUM SANCTUM* AND *ZINGIBER OFFICINALE* AQUEOUS EXTRACTS

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Pharmacy College, Azamgarh, Itaura Chandeshwar 276001, U.P.

### ABSTRACT

Conventional anticoagulant therapy is the mainstay of medical treatment for deep vein thrombosis disorders. However, there are many complications found with conventional medicines specially bleeding. Hence, the search for newer novel anticoagulant derived from natural substances specifically plants origin is in high demand now-a-days. *Ocimum sanctum* (Tulsi) from Lamiaceae family and *Zingiber officinale* (Ginger) from Zingiberaceae has been extensively used in Ayurveda and Unani systems for thousands of years to cure or prevent a number of illnesses. The objective of our work is to investigate the combined effect of *O. sanctum* and *Z. officinale* (ginger) aqueous extract on clotting time in human blood. The plasma was tested against different ratio of aqueous extract of *O. sanctum* and *Z. officinale* as follows: 0:0, 0:1, 1:0, 1:1, 1:2, 2:1. Result showed promising activities for aqueous extract of *O. sanctum* and *Z. officinale* on clotting time.

### Keywords

*Ocimum sanctum*, *Zingiber officinale*, anticoagulation





## NOVEL ROUTES OF INSULIN FOR DIABETES TREATMENT

*Adarsh Mishra, Astha, Saurav Ghoshal*

*Shambhunath Institute of Pharmacy, Jhalwa Allahabad*

Subcutaneous insulin has been used to treat diabetes since the 1920s; however, despite a number of different formulations, intensive insulin therapy with multiple daily injections has not gained widespread clinical acceptance. Attempts to find effective, well-tolerated, nonenteral routes for delivering insulin began in the 1920s, and, over the years, have included ocular, buccal, rectal, vaginal, oral, nasal and uterine delivery systems. Until recently, many researchers believed that insulin delivered noninvasively was associated with too low a bioavailability to offer a realistic clinical approach. However, a growing body of evidence suggests that inhaled insulin is an effective, well-tolerated, noninvasive alternative to subcutaneous regular insulin. Critically, inhaled insulin shows a more physiological insulin profile than that seen with conventional insulin. Further studies are needed to confirm long-term efficacy and pulmonary safety, to compare the different approaches, and to characterize better their relative places in practice. As a result of the recognition of the importance of tighter control of glycaemia and the growing number of patients with type 2 diabetes who receive insulin, inhaled insulin could become an increasingly integral part of managing diabetes.

**Keywords:** Diabetes, Insulin





## POLYHERBAL FORMULATION OF PUSHKAR MOOL USED IN ASTHAMA

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*Shambhunath Institute of Pharmacy Jhalwa, Allahabad*

### **Abstract:**

Formulations containing two or more than two herbs are called polyherbal formulation. Drug formulation in Ayurveda is based on two principles: Use as a single drug and use of more than one drug. The latter is known as polyherbal formulation. Popularity of polyherbal formulation is due to their high effectiveness in a vast number of diseases. It is obtained from the root of the plant *Inula racemosa* belonging to family Asteraceae. Pushkarmool is an Ayurvedic herb which offers path breaking results in chest pain, cough and respiratory discomfort. It is a useful herb that is used for treating bronchitis and heart diseases. The botanical name of this herb is *Inula racemosa* and it is probably one of the powerful herbs. It is basically an Asian plant belonging to the daisy family. The roots of this plant are used in the form of indigenous medicine and even as an expectorant. It is widely used in various health problems like asthma, chronic cough, sinusitis, cold, emphysema, lung collapse and COPD. It is probably one of the most versatile herbs that can be used for its multiple medicinal benefits. Inulin, alantolactone, isoalantolactone. Pregnant/Lactating women, children or any with Known pre-existing condition should take under the advice of health care provider.

**Keywords:** Polyherbal formulation, COPD, sinusitis.





## **AUTOMATED DRUG DELIVERY SYSTEM**

*Shambhunath Institute of Pharmacy, Jhalwa Allahabad*

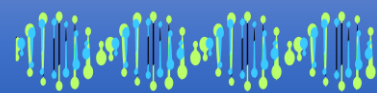
*\*Ambalika Yadav and Ajay Oraon*

### **Abstract**

Now a days usually the drug delivery during the surgeries is done manually by giving injection to the patient. During this drug delivery process some can commit minute mistakes in the quantity of drug release which leads to critical condition and can influence the health of the patient, so to decide and delivery the quantity of drug, it requires significant effort from the clinical stand point not guaranteeing an optimal performance. The proposed system involves automated drug delivery to the patient based on some health parameters, such as fever, sugar, etc.

**Keywords:** Drug delivery system





## STEM CELLS AS VEHICLES AND TARGETS OF NANOPARTICLES

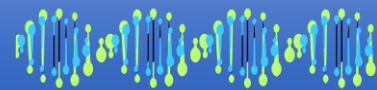
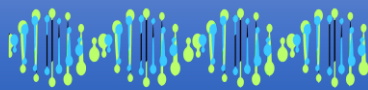
*\*Shivangi Singh, Anjali Dubey, Saurabh Ghoshal*

*Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

Modulation of endogenous adult stem cell niches represents a promising strategy for regeneration of tissues and to correct cell abnormalities, including cancer. Recent advances show the possibility to target endogenous stem cells or their progenies by using nanoparticles conjugated with specific biomolecules. In addition, the targeting of the stem cell niche can be accomplished by using stem cells loaded with nanoparticles. This review examines principles for the targeting of endogenous stem cells as well as factors for the modulation of stem cells. Nanoparticles such as manganese, polystyrene, silica, titanium oxide, gold, silver, carbon, quantum dots, and iron oxide have received enormous attention in the creation of new types of analytical tools for biotechnology and life sciences. Labeling of stem cells with nanoparticles overcame the problems in homing and fixing stem cells to their desired site and guiding extension of stem cells to specific directions. Although the biologic effects of some nanoparticles have already been assessed, information on toxicity and possible mechanisms of various particle types remains inadequate. The aim of this review is to give an overview of the mechanisms of internalization and distribution of nanoparticles inside stem cells, as well as the influence of different types of nanoparticles on stem cell viability, proliferation, differentiation, and cytotoxicity, and to assess the role of nanoparticles in tracking the fate of stem cells used in tissue regeneration.

**Keywords:** Nanoparticles, Stem Cells, Cytotoxicity, Tracking





## SYNTHESIS, CHARACTERISATION AND BIOLOGICAL EVALUATION OF PYRAZOLE DERIVATIVES AS ANTI-INFLAMMATORY AGENTS

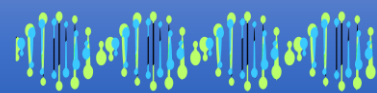
*Anjali Singh\*, Princee Kesarwani, Poonam Kumari, Bhumika Yogi, Sujeet Kumar Gupta  
Department of Pharmaceutical Chemistr Hygia Instiute of Pharmaceutical Education and  
Research, Lucknow*

### ABSTRACT

In the present study we have made an attempt to synthesize novel pyrazole derivatives (**2a-i**) and evaluate them for anti-inflammatory activity using carrageenan induced rat paw edema model. In the first step, 2-acetylnaphthalene (**1**) was allowed to react with substituted benzaldehyde (**2**) in equimolar amount with sodium hydroxide to form various substituted chalcone derivatives (**1a-i**). Further pyrazole derivatives on treatment with thiosemicarbazide in the presence of ethanol corresponding pyrazole derivatives (**2a-i**). The structure of the final analogues has been confirmed on the basis of elemental analysis, FTIR, <sup>1</sup>H NMR. All the values of elemental analysis, FTIR, <sup>1</sup>H NMR were found to be prominent. Among all synthesized compounds, compounds **2d** and **2h** were found to be most potent in comparison with standard diclofenac.

**Keywords:** Pyrazole, Anti-inflammatory, chalcone, carrageenan induced rat paw edema model.





## SYNTHESIS OF NEW POLYMERS LIKE PGA, CAPROLACTON AND PENTADECALACTONE AND THEIR USE IN NANOPARTICLES OF ANTI-CANCER DRUG

*Anoop Tiwari\*, Ravindra Yadav, Pragya Dubey  
Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

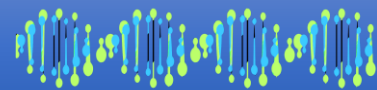
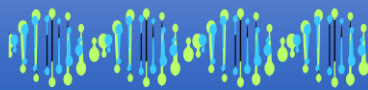
### **Abstract:**

The majority of anticancer drugs have poor aqueous solubility, produce adverse effects in healthy tissue, and thus impose major limitations on both clinical efficacy and therapeutic safety of cancer chemotherapy. To help circumvent problems associated with solubility, most cancer drugs are now formulated with co-solubilizers. However, these agents often also introduce severe side effects, thereby restricting effective treatment and patient quality of life. A promising approach to addressing problems in anticancer drug solubility and selectivity is their conjugation with polymeric carriers to form polymer-based prodrugs. These polymer-based prodrugs are macromolecular carriers, designed to increase the aqueous solubility of antitumor drugs, can enhance bioavailability. Additionally, polymer-based prodrugs approach exploits unique features of tumor physiology to passively facilitate intratumoral accumulation, and so improve chemodrug pharmacokinetics and pharmacological properties. This review introduces basic concepts of polymer-based prodrugs, provides an overview of currently emerging synthetic, natural, and genetically engineered polymers that now deliver anticancer drugs in preclinical or clinical trials, and highlights their major anticipated applications in anticancer therapies.

**Keywords:** prodrugs; macromolecules; drug delivery; cancer therapy; genetically engineered biopolymers







## REVIEW ON THE PHARMACOLOGICAL PROPERTIES OF THE PLANT *ZINGIBER OFFICINALE*

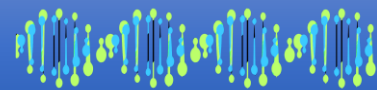
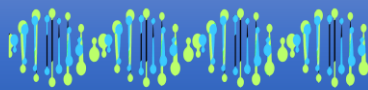
Arpita Yadav\*, Avadh Biharee, Anoop Tiwari, Parjanya Kumar Shukla.  
Department of pharmacognosy Krishnarjit Institute of Pharmacy, Allahabad U.P. India

### Abstract

Ginger is a flowering plant whose rhizomes, ginger root or simply ginger, is widely used as a spice or a folk medicine. The English origin of the word, "ginger", is from the mid 14 century, from old *English gingifer*, from medieval *latin gingiber*, from *greek zingiberis* from prakrit. Ginger likely originated as ground flora of tropical lowland forests in region from the Indian sub continental to southern Asia. It produces clusture of white and pink flower buds that bloom into yellow flowers. The fragrant perisperm of the zingiberaceae is used as sweetmeats by Bantu and also condiment and sialogouge. In ginger the whole B complex vitamins C, E, various minerals and other phytochemicals are found which shows their relative activity. It has a sialogouge action, stimulating the production of saliva, which makes swallowing easier. Zingerone is produced from gingerols during drying, having lower pungency and spicy-sweet aroma. Studies have found no clear evidence of harm from taking ginger during pregnancy, though its safety has not been established and it is a suspected risk for mutagenicity.

**Key words:** *zingiber officinale*, fragrant, sialogouge, minerals, phytochemicals, mutagenicity.





## RECENT UPDATES ON EPILEPSY AND ITS TREATMENT

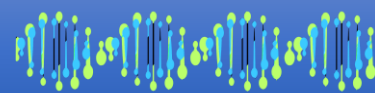
*Chandrashekhar Prajapati\* , Karuna S Shukla  
School of Pharmacy, BBD University, Lucknow (U.P.), India.*

### ABSTRACT

An epileptic seizure is an transient paroxysm of uncontrolled discharges of neurons causing an event which is discernible by the person experiencing the seizure and/ or an observer. Seizure is para-oximal abnormal discharge at high frequency from an aggregate of neurons at cerebral cortex. The incidence of epileptic seizure is around 50 cases per 100,000 of the population and about 70-80% of all those who develop epilepsy will become seizure free on treatment and about 50% will eventually withdraw their medication successfully. Seizure occurs when there is an imbalance or deficient in (a) sodium or calcium ion conductance of the neuronal membrane, (b) deficit in GABA transmission, (c) excitatory mechanism involving NMDA receptor channel to produce depolarization,(d)other functions related to pre and post post synaptic activity. Epilepsy is treated by anti-epileptic drugs such as (i) Phenyton, carbamezipine, valvproate-they blocks sodium channel that remain open due to repetitive neuronal firing,(ii) phenobarbitol, vigabatrin, tigabine, ganoxdone -they enhance the GABA ergic action,(iii) felbmate- it blocks the NMDA receptor,(iv) Ethosuximide-they inhibit T-type calcium channel. Treatment of epilepsy usually for at least 3 years and, depending on circumstances, sometimes for life. Treatment aims to control seizure using one drug without causing side effects and minimizing the use of polypharmacy. Oral absorption of these drugs is slow but complete. It is not given by Intramuscular (IM) or Intraveinuous (IV) route except for fos-phenytoin.IM injection causes pain and IV injection can cause thromboavitis and hypertension.

**Key words:** Epilepsy, seizures, phenynton, carbamezipine.





## HERBAL FORMULATIONS: NOVEL DRUG DEVELOPMENT AND DESIGN

*Suraj Kumar Prajapati, Gopal Dubey, Manoj Kumar Mishra  
Shambhunath Institute of Pharmacy Jhalwa, Allahabad*

### Abstract

Herbal drug is growing fast but somewhere due to its unconventional drug dosage it's not widely used by people. The drug of herbal origin can be utilize in better advanced formed with enhance efficacy by incorporating in modern dosage form. With the use of these advance techniques it gives us protection from toxicity, enhancement in stability improved bioavailability of herbal formulations. Protection from physical and chemical degradation can be achieved. Prove beneficial to combat with life threatening disease more rapidly. The importance of these herbal development industries has immensely gained momentum due to the underlying side effects associated with allopathic medicines ranging from minor problems such as ulcerations to major life threatening problems such as growth retardation. In the present research studies the aim was to develop oral herbal tablets from *Polyalthia longifolia* (PL), *Tabernaemontana alternifolia* (TA), *Benincasa hispida* (BH) plant extracts and perform its evaluation as per ICH guidelines. Thus, article discusses and encompasses the readers vision that in future local plants developed formulations could be probable prove to be equipotent with medicinal plants formulations useful for various therapeutic purposes.

**Keywords:** *Ethanosomes, Polyalthia longifolia, Tabernaemontana alternifolia, Benincasa hispida.*





## NEWER APPROACHES TOWARDS FIGHT AGAINST ANTIBIOTIC RESISTANCE

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*School of Pharmacy, BBD University, Lucknow*

### ABSTRACT

Antibiotic resistance has been called one of the world's most pressing public health problem present in every country. Antibiotic have been considered one of the wonder discoveries of 20<sup>th</sup> century. This is true, but the real wonder is the rise of antibiotic resistance in hospitals, communities and the environment concomitant with their use. WHO classified antimicrobial resistance as a serious threat and no longer a prediction for future. Antibiotic resistance is now among every part of the world and its affecting everyone irrespective to the age. The US CENTERS FOR DISEASES CONTROL AND PREVENTION (CDC) said today that antibiotic resistant pathogen sicken 2 million American a year and listed the three most urgent threat as *Clostridium difficile*, carbapenam-resistant enterobactericeae (CRE) and *Neisseria gonorrhoeae*, *S. aureus*, *Mycobacterium* species. In 2009, the ECDC and the European medicine agency (EMA) estimated that the overall cost for the EU in term of extra health care cost and productivity losses totaled at least EUR 1.5 billion each year. The global systemic antibiotic market was valued at 39.6 billion dollar in 2013 and is expected to reach 41.2 billion dollars by 2018.

**Key words:** Antibiotic, WHO, global systemic.





## TELEMEDICINES IN HEALTH SECTOR

*Karan Jaiswal, Juhi Singh, Saurav Ghoshal  
Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

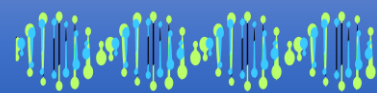
### **Abstract:**

Pharmacists play a vital role in the health care system through the medicine and information they provide. Pharmacist responsibilities include a range of care for patients, from dispensing medications to monitoring patient health and progress to optimize their response to medication therapies. Many patients with diseases difficult to diagnose and treat come to hospitals for medical help, and the cost of traveling and accommodation is high for them, especially for those from the poor or remote border areas.

As networks become more advanced and increase in speed, various energetic activities have begun to emerge. New networks will cause a major revolution in society, and one area, which is expected to be an effective application of new networks, is telemedicine. In general, Telemedicine can be defined as the delivery of health care and sharing of medical knowledge over a distance using telecommunication means. Telemedicine provides medical information exchange at a distance, to support medical procedure, with the ultimate goal for improving community health care. In these experiments, integrated functions such as the transmission of medical images, collaboration and video conferencing, and provided superb human interfaces for telemedicine. As high-speed broadband networks spread, telemedicine support functions and areas where telemedicine services are available will increase. In the medical field, the emergence of a new format for medicine is expected, to include an equalization of opportunities to receive advanced medical treatment, and providing exacting medical care by linking hospitals and clinics.

Keywords: Pharmacists, Telemedicine, Diagnose





## PRODRUG CONCEPT AND THEIR CLINICAL APPLICATIONS

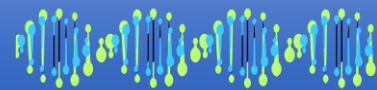
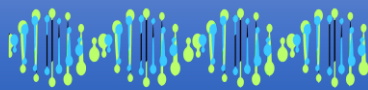
*Kashish Kapoor, Sristi Raj, Pravin Kumar Singh and Parmesh K. Dwivedi  
Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow campus*

### Abstract

A pharmacological inactive derivative of a drug molecule that after administration, converted into a pharmacologically active drug due to enzymatic or spontaneous reaction in the body is known as prodrug. On the basis of conversion, there are two major types of prodrugs. Anti-viral nucleoside analogs and statins comes under Type-I prodrugs as they are bioactivated intracellularly while the antibody, gene or virus-directed enzyme prodrugs used in chemotherapy or immunotherapy are bioactivated extracellularly and also known as Type-II prodrugs. A prodrug strategy can be used to increase the permeability of a drug, to improve bioavailability when a drug itself is poorly absorbed from the g.i.t. The prodrug strategy has been employed for the delivery of biologics to the CNS, to solve the formulation problems, to improve the skin permeation of drug, local delivery of drugs etc. In addition to this the prodrugs have their wide applications in improving patient acceptability, stability and membrane transport.

**Key words:** Prodrug, bioavailability, chemotherapy





## ROLE OF NATURAL PRODUCTS IN THE HEPATIC DISEASES AND PROTECTIVE ACTION

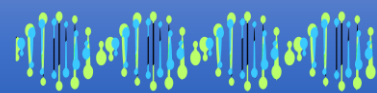
*\*Keerti Mishra, Alina Beg, Manoj Kumar Mishra  
Shambhunath Institute of Pharmacy, Jhalwa, Allahabad, U.P. India*

### **Abstract**

In the human body the liver is one of the most important organs in the body. It performs a very important role in the regulation of various processes, they are metabolism, secretion, storage and detoxification of endogenous and exogenous substances are major. Due to the all work liver can be infected by any type of disorders, and till now a day various types of medicine not treating properly. Liver have the self healing ability to one third part of itself. Liver is a very major organ of body due to the improper work of it, can cause severe types of some other disease. Hepatic cells can be regenerate if the liver is affected half of their part. But in severe hepatic conditions Allopathic medicines not treating properly and in place of these drugs natural agents gives a very good response with their low toxicity and very reduced adverse effect. In all the hepatoprotective natural products the phytochemicals are present which shows their action against the disease and by nature they are very less toxic. Some natural products which improves the functioning and regulation of liver (grapefruit, cranberries, and grapes) and plants cactus pear (nopal) and cactus pear fruit, chamomile, silymarin and spirulina.

**Key words:** Hepatoprotective, detoxification, phytochemical, hepatic cells





## TARGETED DRUG DELIVERY SYSTEM

*\*Neha Mishra, Varsha Verma, Manoj Kumar Mishra  
Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

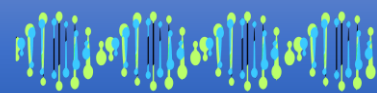
### ABSTRACT

Targeted drug delivery, also known as smart drug delivery, is a method of treatment that involves the increase in medicament in one or few body parts in comparison to others. Two strategies are widely used for drug targeting to the desired organ/tissue: passive targeting and active targeting. Drug delivery vehicles transport the drug either within or in the vicinity of target. An ideal drug delivery vehicle is supposed to cross even stubborn sites such as a blood brain barrier. Recently, nano medicine has emerged as the medical application of nanotechnology. Since nanoparticles are very small in size, nano drug delivery can allow for the delivery of drugs with poor solubility in water and also aid in avoiding the first pass metabolism of liver. Nanotechnology derived drug delivery can cause the drug to remain in blood circulation for a long time, thereby leading to lesser fluctuations in plasma levels and therefore, minimal side effects. These include polymer- drug conjugates and nano particulate systems such as liposomes, quantum dots, dendrimers, etc. There are several other approaches as well. These also include the strategies wherein the therapeutic agents are coupled with “targeting ligands” that possess the ability to recognize antigens associated with tumors.

**Keywords:** Targeted drug delivery, Nanoparticles, Therapeutic, Conjugates, Cancer







## **pH RESPONSIVE ANTI-HIV NANOPARTICLES**

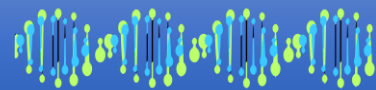
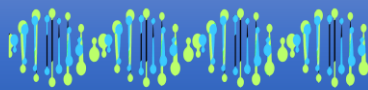
*\*Nikita Gupta, Roshni Bhatt, Manoj Kumar Mishra, Saurav Ghoshal*

*Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

A pH responsive novel nano-lipid complex delivery system targeted to lymphoid tissues and HIV host cells will greatly improve cell and tissue selectivity, and thus overcome drug insufficiency of anti-HIV drugs in lymphoid tissues, leading to maximum viral suppression. We will test this hypothesis with a well-established HIV-infected primate model to determine the effects of this novel drug delivery strategy targeted to lymphoid tissue and cells on disease progression. To do so, we will design pH-responsive lipid-nanoparticles composed of anti-HIV drug combination for enhanced activity in virus host cells.

The second aim is designed to compare the most potent anti-HIV nanoparticles containing inhibitors of HIV protease and reverse transcriptase with respect to target tissue and cell selectivity and resident time. The data collected from time-course and dose-dependent pharmacokinetic and tissue localization studies will be used to define a safe and effective dosing schedule for the proof-of-principle study in HIV-infected primates. Finally, we will evaluate the impact of the optimized, pH-responsive anti-HIV nanoparticles on HIV infection and disease progression. The proposed targeted novel drug delivery strategy will accelerate clearance of residual virus in lymphoid tissues and cells, which received limited exposure to orally administered drugs. A primate model is used to probe questions that could not be addressed in humans. The results obtained from these studies hold promise for making a profound advance in anti-HIV drug therapy and providing a proof-of-principle for first-in-human clinical testing. Successful completion of this study will have significant impact on treatment paradigms and outcome of HIV infections. With an established investigative team, we could proceed with first-in-human studies when a positive outcome is achieved. While combination antiviral drug therapies have extended the life of individuals infected with HIV, the residual virus in tissues and virus reactivation leads to disease progression. The proposed novel strategies are designed to address this unmet medical need and may eventually lead to a cure for HIV/AIDS.





## NEW DRUG TREATMENT OF MALARIA TREATMENT

*Shambhunath Institute of Pharmacy*  
*Prateek Mishra, Vishal Patel, Manoj Kumar Mishra*

### **Abstract:**

Malaria is a major public health problem in India, accounting for sizeable morbidity, mortality and economic loss. From preventive measures, early diagnosis and complete treatment are the important modalities that have been adopted to contain the disease. In view of widespread chloroquine resistance in *Plasmodium falciparum* infection, and other recent developments, the national policy has been revised to meet these challenges.

**Keywords:** *Plasmodium falciparum*, chloroquine





## LIGAND BASED PHARMACOPHORE MODELING AND VIRTUAL SCREENING OF SOME NOVEL ANTIMALARIAL AGENTS

Rachna Bishl<sup>\*</sup>, Jyotsna Vishwakarma, Avinash C. Tripathi, Savita Upadhyay, Shailendra K. Saraf

Division of Pharmaceutical Chemistry, Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, Lucknow-226028, U.P., India

Rapid increase of resistance to the available antimalarial drugs has led to the re-emergence of malaria in many parts of the world; this creates an urgent need to identify new anti-malarial drug targets for both, prophylaxis and chemotherapy. Currently, virtual screening methods have emerged as valuable tools in discovering novel compounds. Naturally occurring sesquiterpene lactone (SLT) class of compounds were found to be very effective against *Plasmodium falciparum* in the recent past. Considering this, a series of twenty eight SLTs with a wide range of antimalarial activity was selected to generate a pharmacophore model (using PHASE module of Schrodinger Software Package). Best model was selected on the basis of survival score, difference between survival and inactive score and the predicted pIC<sub>50</sub> values. The potential hits were retrieved from ASINEX database compound library using pharmacophore based virtual screening protocol. Validation of the virtual screening protocol and robustness of the hypothesis was carried out with the help of different parameters (such as; average rank of actives; EF; ROC; BEDROC; AUAC; and RIE), demonstrating excellent metrics. The obtained hits were subjected to docking studies against various antimalarial targets such as, Falcipain (FP), Plasmepsin (PL), Dihydroorotate Dehydrogenase (DHODH), Dihydrofolate Reductase (DHFR), Enoyl Acyl Carrier Protein Reductase (ACP) and Lactate Dehydrogenase (LDH) to predict their probable mechanism of action. Thereafter, the ADMET and Lipinski's rule filters were applied and filtered hits were ranked on the basis of fitness score (> 1.5), Glide score and conserved interactions. Finally, *in-silico* toxicities of some top ranked candidates were predicted using OSIRIS and LAZAR programs. The compound, ASINEX ID: 335646, having fitness score of 2.03 and a Glide score of -8.427 was selected as the best among all with probable *pf*DHODH inhibition activity. The outcomes of the *in-silico* studies are being verified in the wet lab using various *in-vitro* and *in-vivo* screening protocols for antimalarial activity.





**Key word:** *Plasmodium, virtual screening, pharmacophore model, sesquiterpene lactone.*

## NUTRITIONAL REQUIREMENTS FOR PEPTIC ULCER

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*School of Pharmacy, BBD University, Lucknow*

### ABSTRACT

Ulcer disease is a condition in which open sores develops in the lining of the gastrointestinal tract. They can occur in the upper portion of the small intestine (duodenal ulcer), stomach (gastric ulcer), and esophagus (esophageal ulcer). Contrary to long-standing common belief, stress does not cause ulcers. Instead, the leading cause of ulcer disease is a bacterium called *Helicobacter pylori* (*H. pylori*). These bacteria damage the protective mucosal barrier of certain areas within the gastrointestinal tract, making it easier for acidic digestive fluids to injure and inflame the gut's lining. Other causes include smoking and chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen; Patients suffering from peptic ulcers are undernourished and therefore, need an increased energy intake. In case of patients at bed rest, the energy needs for activity are not utilized and make up the extra needs. Research shows that a high fibre diet decreases the risk of developing ulcer disease. Although both insoluble and soluble fibres demonstrate this association, there is a stronger association between diets high in soluble fibre and a decreased risk for developing ulcers. Foods that are high in soluble fibre include oats, psyllium husk, legumes, flax seeds, barley, nuts, and certain vegetables and fruits, such as oranges, apples, and carrots. A high protein diet is advised as this promotes healing. Proteins also have a buffering action. Though milk protein has a good buffering action, the high calcium content of milk stimulates acid production. A high milk intake delays the healing of the ulcers and thus milk should be used in moderation. Eggs and other high protein foods can be included to meet the requirements.

Keywords; Ulcer, *Helicobacter pylori*, *nutritional requirements*.





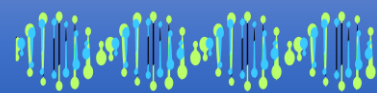
## DRUG METABOLISM IN THE BRAIN: BENEFITS AND RISKS

*\*Ratnakar Garg, Amit Singh, Raj keshwar Prasad, Manoj Kumar Mishra  
Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

The brain is protected against chemical assault by cerebral endothelial cell membrane systems, forming a blood–brain barrier (BBB) that prevents the influx of most polar molecules. However, some lipophilic potentially toxic drugs and environmental pollutants can reach the central nervous system (CNS). Therefore, other efficient mechanisms of protection are needed to protect the brain from chemical insult. It has been clearly established that xenobiotic metabolism is catalyzed by a series of enzymes located both in the brain parenchyma and at blood–brain interfaces. Moreover, efficient transport mechanisms resulting from multidrug resistance protein (MRP) and P-glycoprotein (Pgp) activities can export both xenobiotics and some of their polar metabolites from the brain to the blood of the cerebral circulation. Therefore, to protect the central nervous system from foreign molecules that might disturb its homeostasis or display some toxicity, three different components are required: (a) a *physical barrier*, preventing the entry of polar and high molecular weight molecules; (b) a *metabolic barrier*, resulting from the activity of oxidases, reductases, or conjugating enzyme systems; and (c) an *active, ATPdependent barrier*, due to the activity of multidrug resistance–related transport systems. Drug metabolism results both in inactivation of potentially toxic or pharmacologically active molecules.

**Keywords:** P-glycoprotein, *ATPdependent barrier*, blood brain barrier





## PRELIMINARY PHYTOPHARMACOGNOSTICAL EVALUATION OF LEAVES OF *THUJA ORIENTALIS*

Ruby Tripathi\*, Krishanu Samanta, Emdad Hossain

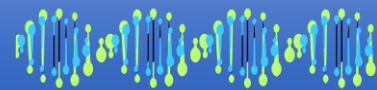
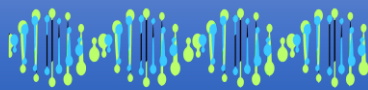
Pharmacy College, Itaura, Chandeshwar, Azamgarh 276128, Utter Pradesh, India

### ABSTRACT

Under the family- Cupressaceae, *Thuja orientalis* L., is very important plant for its traditional uses. It is commonly known as Morpankhi or Thuja. In Latin it is known as 'tree of life'. The leaves have been used traditionally as antibacterial, antitussive, antipyretic, astringent, emmenagogue, expectorant, emollient, febrifuge, haemostatic, stomachic, refrigerant, diuretic and also used in alopecia. The present study was to determine different pharmacognostical parameters along with preliminary phytochemical screening of petroleum ether, chloroform, ethanol and aqueous extracts of *Thuja orientalis*. The macroscopical and some microscopical characters of leaves were also studied. In the transverse section of leaves showed the arrangement of various cells in epidermis, hypodermis, palisade cells, spongy parenchyma and vascular bundles etc. Preliminary phytochemical screening of various extracts revealed the presence of different secondary metabolites. Loss on drying, extractive values, fluorescence analysis of extracts and powder treated with different chemical reagents were also studied under ordinary light, short and long ultraviolet light. The foaming and swelling index of leaves were also determined. These studies will be helpful in developing standards for quality, purity and sample identification of this plant.

**Keywords:** Cupressaceae, pharmacognostical, physico-chemical parameters, pharmacognostical, *Thuja orientalis*





## NOVEL ROUTES OF INSULIN FOR DIABETES TREATMENT

*Mohammad Salman, Mohan Yadav*  
*Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

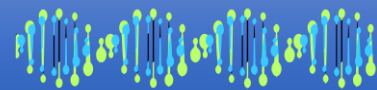
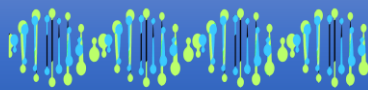
### **Abstract:**

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Diabetes is a chronic disease characterized by inadequate insulin secretion with resulting hyperglycemia. Diabetes complications include both microvascular and macrovascular disease, both of which are affected by optimal diabetes control. Many individuals with diabetes rely on subcutaneous insulin administration by injection or continuous infusion to control glucose levels. Novel routes of insulin administration are an area of interest in the diabetes field, given that insulin injection therapy is burdensome for many patients. This review will discuss pulmonary delivery of insulin via inhalation. The safety of inhaled insulin as well as the efficacy in comparison to subcutaneous insulin in the various populations with diabetes are covered. In addition, the experience and pitfalls that face the development and marketing of inhaled insulin are discussed.

**Keywords:** Glycemic control, insulin, diabetes





## AN UPDATE ON GREY BABY SYNDROME

*Sandeep Kumar Pandey\**, *Satendra Prabhakar*, *Rishabh Bajpai*, *Karuna S Shukla*

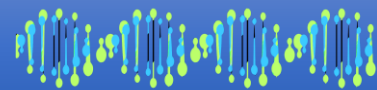
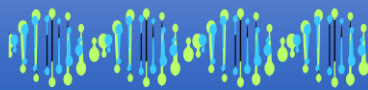
*School of Pharmacy, BBD University, Lucknow*

### ABSTRACT

The incidence of dose related chloramphenicol toxicity was determined in 64 neonates from 12 hospitals. Ten of the 64 exhibited symptoms attributed clinically to chloramphenicol toxicity. Nine received the dose prescribed and one an overdose. Symptoms of the grey baby syndrome were observed in five of the 10 babies; four babies suffered reversible haematological reactions; and one baby was described as very grey. Peak serum chloramphenicol concentrations in these 10 babies ranged from 28 to 180 mg/l and trough concentrations from 19 to 47 mg/l. Serum chloramphenicol concentrations above the therapeutic range (15-25 mg/l) were observed in a further 27 neonates (two had received a 10-fold overdose), none of whom showed signs of toxicity. Serious toxicity was associated with either prescription of dosages greater than that recommended or overdosage of chloramphenicol. High concentrations in young neonates may be avoided by prescribing and giving the recommended dose and then careful monitoring; concentrations should be maintained between 15 and 25 mg/l. No babies with concentrations within this range showed clinical signs of toxicity.







## SMART CONTACT LENS AND BLOOD GLUCOSE LEVEL; A CORRELATION

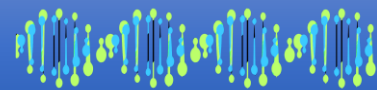
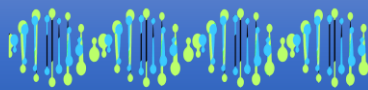
*ShivamVerma<sup>\*</sup>, Sushil Kumar Maurya, Karuna S Shukla  
Scool of Pharmacy, BBD University, Lucknow, U.P., India*

### ABSTRACT

A report published by WHO which states that 422 millions of people are affected by diabetes mellitus and in India 62 million people are affected from this disease and mostly it affect the age of 42. Every year 1 million of Indians die due to diabetes mellitus. The treatment for Diabetes mellitus is not developed till date but insulin injections are commercially available. This disease occurs due to insufficient secretion of insulin from  $\beta$  islets of pancreas. Insulin regulates the blood glucose level. Hyperglycaemia is a condition in which blood glucose level exceed from normal range while in hypoglycaemia the blood glucose level decreases. Insulin is the hormone which is secreted by pancreas and used in metabolism of glucose. A recent advancement in the diagnosis of blood glucose level the contact lens is designed which indicate the blood glucose level. The mechanism lies behind these lens is “wireless glucose sensors “which detect the glucose level of body. The lens consists of LED which remain flashing when blood glucose level in human body get increased above certain limit. This is a non-invasive method for determination of blood glucose level. The commercially available method for determination of blood glucose level is invasive type so the patient convenience in smart lens is very high.

**Key words;** Diabetes mellitus, Insulin, contact lens.





## ***MORINGA OLEIFERA*: HEALTH BENEFITS TARGETED TOWARD MANY SYSTEM**

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*Department of Pharmacognosy, Krishnarpit Institute of Pharmacy, Allahabad, U.P. India.*

*Moringa oleifera* is also known as drumstick tree. It's medicinal plant widely used in folkloric medicine of Africa and Asia for the treatment of various diseases such as inflammation, obesity, ulcer, anaemia, wound, liver problem etc. *Moringa oleifera* leaves, seeds, bark, roots, and flower are widely used in traditional medicine, and the leaves and immature seed pods are used as food products in human nutrition. It's rapidly growing number of studies have shown that extracts of *moringa oleifera* leaves possess a wide range of additional biological activities includes antioxidant, tissue protective, analgesic, antihypertensive, radioprotective and immunomodulatory actions. The phytochemical constituents includes phytol, oleic acid, ascorbic acid, methyl ester- hexadecanoic acid, heptacosane, pentacosane, flavonoids quercetin, essential oil, carbohydrates, protein, fibers, mineral and phenolic contents. *Moringa oleifera* has been clinically proven to increase the production of breast milk whether it is consumed before or after the birth of a baby. In more recent times, *Moringa oleifera* has gained notoriety as a very nutritious plant that can feed the needy and, in fact, save lives. *Moringa oleifera* leaves or leaf powder can be used successfully as a supplement. Traditional cultures in various parts of the world have long used *Moringa oleifera* in their herbal medicine repertoire for ailments ranging from gout to various inflammation and fevers.





## EXTRACTION, ISOLATION AND EVALUATION OF *ABELMOSHUS ESCULANTUS* L. (BHINIDI) MUCILAGE USED AS EXCIPIENT IN PREPARATION OF HERBAL DOSAGE FORM

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<sup>\*1</sup>Pharmacognosy & Ethnopharmacology Division, CSIR-NBRI, Lucknow.

<sup>2</sup>School of Pharmacy, BBD University, Lucknow.

### Abstract

The objective of the present work is to develop a novel polymer which is used for preparation of herbal and conventional dosage forms as well as novel drug delivery system for the targeting of particular body organ or disease. The polymer or mucilage was extracted, isolated from ripe seeds of *Abelmoshus esculantus* L. (Bhindi) and the total phenolic and flavonoid content was estimated. The extraction of mucilage from *Abelmoshus esculantus* L. was done by Acetone Precipitation method. Brown color, characteristic odour, tasteless, rough fracture and irregular texture of the mucilage was found after performing organoleptic properties. The percentage yield of mucilage was found 9.05% w/w. Physicochemical characterization of *Abelmoshus esculantus* L. (Bhindi) mucilage was swelling index  $14 \pm 0.2$ , in cold water the mucilage swelled to form a gel, soluble in hot water, insoluble in organic solvents. Total ash value was 7.52% and pH value was  $7.1 \pm 0.1$ . Chemical characterization of isolated mucilage was found to positive carbohydrates, polysaccharides and mucilage test. The present investigation showed *Abelmoshus esculantus* L. mucilage has high pharmaceutical significance in herbal dosage forms.

**Keywords:** *Abelmoshus esculantus* L., mucilage, novel polymer, targeted drug delivery system, herbal dosage forms, novel drug delivery system.





## SIRTUIN AS AN ANTI-AGEING AGENT

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*United Institute of Pharmacy, Naini, Allahabad*

### ABSTRACT

Sirtuins are ancient proteins widely distributed in all lifeforms of earth. These proteins are universally able to bind NAD(+), and activate it to effect ADP-ribosylation of cellular nucleophiles. The most commonly observed sirtuin reaction is the ADP-ribosylation of acetyllysine, which leads to NAD(+)-dependent deacetylation. Other types of ADP-ribosylation have also been observed, including protein ADP-ribosylation, NAD(+) solvolysis and ADP-ribosyltransfer to 5,6-dimethylbenzimidazole, a reaction involved in eubacterial cobalamin biosynthesis. This review broadly surveys the chemistries and chemical mechanisms of these enzymes.

The sirtuins are highly conserved NAD-dependent deacetylases that were shown to regulate lifespan in lower organisms and affect diseases of aging in mammals, such as diabetes, cancer, and inflammation. Here we discuss several diseases of aging for which SIRT1 has been recently shown to confer protection. Sir2 is an NAD-dependent deacetylase that connects metabolism with longevity in yeast, worms and flies. Mammals contain seven homologs of yeast Sir2, SIRT1–7. Here, we review recent findings demonstrating the role of these mammalian sirtuins as regulators of physiology, calorie restriction, and ageing.

**KEYWORDS:** Sirtuin, anti-ageing, deacetylation, NAD-dependent, metabolism, Sir2, SIRT1-7, calorie restriction and ageing.





## NANOROBOTICS IN DRUG DELIVERY SYSTEM FOR TREATMENT OF CANCER

*Som Shukla\*, Kuldeep Tiwari, Raj Keshwar Prasad*

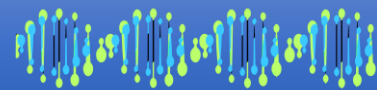
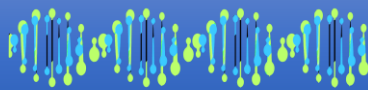
*Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

### **Abstract**

The poster gives an overview of the present status of nanorobotics in cancer therapy. With aid of biotechnology, molecular biology and molecular medicine can develop fully self-sufficient nanorobots. The nanorobotics considered, as a wonderful vision of medicine in the future are an advanced submicron device generally made of bio- nanocomponents. It has an eminence future in the drug delivery technology target in cancer. Nanorobots could carry and deliver large amounts of anti-cancer drug into cancerous cell without harming healthy cell, reducing the side effect related to current therapies like damage of conventional chemotherapy. This paper presents a study on different approaches employed toward cancer treatment using nanorobots.

**Key word-**Nanorobotics, Cancer therapy, Application of nanorobotics





## ORGAN TRANSPLANTATION TECHNIQUES

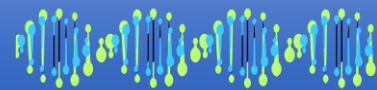
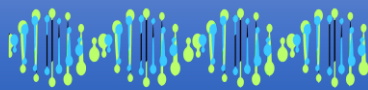
*\*Sumit Kumar Pandey, Saurabh Kesarwani  
Shambhunath Institute of Pharmacy, Jhalwa, Allahabad*

### **Abstract:**

Over the course of the last century, organ transplantation has overcome major technical limitations to become the success it is today. The breakthroughs include developing techniques for vascular anastomoses, managing the immune response (initially by avoiding it with the use of identical twins and subsequently controlling it with chemical immunosuppressants), and devising preservation solutions that enable prolonged periods of ex vivo storage while preserving function. One challenge that has remained from the outset is to overcome the shortage of suitable donor organs. The results of organ transplantation continue to improve, both as a consequence of the above innovations and the improvements in peri- and postoperative management. This review describes some of the achievements and challenges of organ transplantation.

Keywords: Organ transplantation, Immunosuppressants, ex vivo





## SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF ISOINDOLE DERIVATIVES

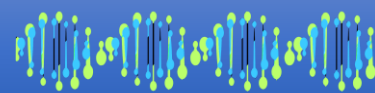
*Surendra Kumar Gautam\**, Mamta Agrahari, Utkarsh Chaturvedi, Nirankar Pandey,  
Bhumika Yogi, Sujeet Kumar Gupta  
Department of Pharmaceutical Chemistry Hygia Instiute of Pharmaceutical Education and  
Research, Lucknow

### **ABSTRACT**

In the present study we have made an attempt to synthesize Isoindole derivatives (Mannich base) (**4a-c**) and evaluate them for anti-convulsant activity using Maximal Electroshock Method (MES model). In the first step, Phthalic anhydride (**1**) was allowed to react with different amino acid (**2**) with glacial acetic acid form various substituted Isoindole derivatives (**3a-d**). Further isoindole derivatives on treatment with formaldehyde and different primary/secondary amine in the presence of methanol corresponding isoindole derivatives (**4a-c**). The structure of the final analogues has been confirmed on the basis of elemental analysis, FTIR, <sup>1</sup>H NMR. All the values of elemental analysis, FTIR, <sup>1</sup>H NMR were found to be prominent. Among all synthesized compounds, compounds **4b** were found to be most significant in comparison with standard Phenytoin.

**KEY WORDS:** Phenytoin, Anti-convulsants, Phthalic anhydride, Maximal electroshock method (MES model)





## ALZHEIMERS'S DISEASE AND ITS TREATMENT: CURRENT SCENARIO

*Suryansh Mishra\*, Ashutosh Kumar Mishra, Karuna S Shukla*

*School of Pharmacy, BBD University, Lucknow*

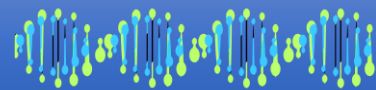
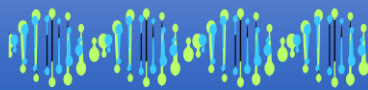
### ABSTRACT

Alzheimer's disease (AD) is a type of dementia that causes problems with memory, thinking and behavior. Majority of people with AD are 65 and older. In its early stage, memory loss is mild but with late stage AD individuals lose the ability to carry on a conversation and respond to their environment. AD is 6<sup>th</sup> leading cause of death in U.S. and those suffering from it live an average of 8 years. It has no current cure, but treatment for symptoms is available. Although current treatment can't stop disease from progressing they can temporarily slow the worsening of dementia symptoms. Two abnormal structures called plaques and tangles are prime suspects in damaging and killing neurons. Plaques are deposits of a protein fragment called beta-amyloid that builds up in the spaces between the neurons. Tangles are twisted fibers of another protein called tau that build up inside. USFDA has approved two types of medications- Cholinesterase inhibitors (ARICEPT, EXELON, RAZADYNE), Memantine (NAMENDA). All of the prescription medications currently approved to treat AD. Symptoms in early to moderate stages are from a class of drugs called cholinesterase inhibitors. These are prescribed to treat symptoms related to memory, thinking, language, judgment and other processes. Three cholinesterase inhibitors are commonly prescribed- Donepezil (Aricept) to treat all stages. Rivastigmine (Exelon) and Galantamine (Razadyne)- treat mild to moderate.

**Keywords;** Alzheimer's disease, plaques, Donepezil.







## **AUTOMATIC DRUG DELIVERY IN ANESTHESIA**

Swati Rai\*, Ajay Kushawaha, Sagar Bansal  
Shambhunath Institute of Pharmacy Jhalwa, Allahabad

### **Abstract:**

The main goals of general anesthesia are adequate hypnosis, analgesia and maintenance of vital functions. For some special kinds of operations neuromuscular block is essential. Furthermore the patient safety and cost reduction as a case of minimized drug consumption and shortened postoperative recovery phases are part of the main issues to motivate automation in anesthesia. Since the beginning of the eighties engineers and physician are working together in the field of the development of closed-loop systems for drug delivery. The work gives a short overview about the development of the automation in drug delivery systems over the last years without the claim of completeness and expressed the much more vision.

Keywords: Drug delivery systems, closed loop systems





## ZIKA VIRUS THROUGH AN EYE OF A PHARMACY STUDENT: A REVIEW

*Anil Verma\**, *Karuna S Shukla*

*School of Pharmacy, BBD University, Lucknow*

### ABSTRACT

Since the beginning of this century humanity has been facing a number of new emerging as well as life threatening diseases every year. Most of the population is being suffered by these deadly diseases like west nile, Influenza, avian flu, dengue, chikanguniya, SARS, MERS, Ebola and now Zika. Zika virus is a mosquito transmitted by *A. aegypti* and *A. albopictus* belongs to family Flaviviridae which became the focus of an ongoing pandemic and public health emergency all around the world. The same mosquito also transmits 3 other vector-borne diseases -- dengue, chikungunya and yellow fever – across tropical and subtropical regions around the world. Hence, it is often misdiagnosed with above diseases due to its similar manifestation. It was firstly reported in 1947 from zika forest of Africa while its first case on Human was reported in 1952 in Uganda and United republic of Tanzania. The epidemic history of zika virus began in 2007, with its emergence in Yap Island in the western Pacific, followed in 2013-14 by a larger epidemic in French Polynesia, south Pacific, where the first severe complications and non-vector borne transmission of the virus were reported. Zika virus emerged in Brazil in 2015 and was declared a national public health emergency after local researchers and physicians reported an increase in microcephaly cases. In 2016, WHO declared the recent cluster of microcephaly cases and other neurological disorders reported in Brazil a global public health emergency. Last year three cases of Zika virus was found in Ahemdabad city of Gujrat.

**Keywords;** Zika virus, Flavivirus, Mosquito borne virus, arbovirus, Microcephaly, Guillian's Barr's syndrome, replication of zika virus and pathogenesis





## RECENT AND ADVANCE TECHNOLOGIES USED IN PARKINSON'S DISEASE

*Anish Kumar, Neha Srivastava, Harikesh Maurya\**

*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow*

### ABSTRACT

Parkinson's disease is a slowly progressive neurologic disease of the nervous system marked by tremor, muscular rigidity, and slow imprecise movement and chiefly affecting middle-aged and elderly (60 year) people. Parkinsonism is a clinical syndrome comprising combinations of motor problems and degeneration of dopamine producing cells in the substantia-nigra leads to a decrease dopamine production, Levodopa induce motor complications, including motor fluctuations and dyskinesia. A pathologic hallmark is the presence of cytoplasmic eosinophilic inclusions in monoamine neurons, sometimes it is genetic, but most cases do not seem to run in families. Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease, and it affect over 1 percent of the population over age 55 year while no one currently knows what causes brain cells to the die due to parkinson's disease. According to US statistical project it shows the globally increases in the prevalence of Parkinson's disease in 2005 and 2030. It is estimated, that the number of Parkinson's disease patient will increase from 4.1 million in 2005 to 8.7 million in 2030. Approximately 60,000 American are diagnosed with Parkinson's disease each year. More than 10 million people worldwide are living with Parkinson's disease.

**Keywords:** Parkinson's disease, substantia-nigra, ganglia, Alzheimer's disease





## DEVELOPMENT OF NEW GRANULATION TECHNIQUE FOR TABLET

*Hiroshima, Arvind Kumar, Santosh Kumar\**

*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow*

### **Abstract**

The development of a strong, active granular sludge bed is necessary for optimal operation of up flow anaerobic sludge blanket reactors. The mechanical & microbial structures of the granules may have a strong influence on desirable properties such as growth rate, settling velocity and shear strength. Theories have been proposed for granule's microbial structure based on the relative kinetics of substrate degradation, but contradict some observations from both modeling and microscopic studies. The study designed to examine structures of four types of granules from full-scale UASB reactors, treating waste water from a cannery, a slaughter house, and two breweries. Microbial structure was determined using fluorescence in situ hybridization probing with 16S rRNA-directed oligonucleotide probes, superficial structure and microbial density (volume occupied by cells and microbial debris) assessed using scanning electron microscopy (SEM), and transmission electron microscopy (TEM). The granules were also modeled in distributed parameter of biofilm model. The results reflected the trophic structures indicating possibly determined by kinetics in particular interest from simulations of the protein grown granules, which were predicted to have slow growth rates, low microbial density, and no trophic layers, the last two of which were reflected by microscopic observations. The primary cause of this structure, as assessed by modeling, was the particulate nature of the waste water, and the slow rate of particulate hydrolysis, rather than the presence of proteins in the wastewater.

**Keywords:** Granular sludge, oligonucleotide, biofilm model, trophic structures





## AN UPDATES ON CHROZOPHORA TINCTORIA FOR ITS MEDICINAL VALUES

Pooja Mishra, Harikesh Maurya\*

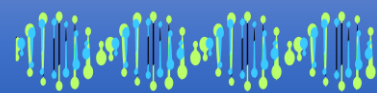
Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow

### ABSTRACT

*Chrozophora tinctoria* commonly known as dyer's croton, giradol, or turnsole belonging to the family Euphorbiaceae, the plant species is native to the Mediterranean, the Middle East, India, Pakistan and Central Asia. The plants generally grow on loam and clayey-loam, neutral to slightly alkaline soils with rich in calcium carbonate, slightly saline, moderately rich in organic matter, phosphorus and very high in potassium content. *Chrozophora tinctoria* produced the blue-purple colorant "turnsole" used as a food colorant. Twelve compounds were isolated from *Chrozophora tinctoria* (L.) Raf., Which are identified as kaempferol, kaempferol 3-*O*- $\beta$ -glucopyranoside, kaempferol 3-*O*-(6"- $\alpha$ -rhamnopyranosyl)- $\beta$ -glucopyranoside, quercetin, quercetin 3-*O*- $\beta$ -glucopyranoside, quercetin 3-*O*-(6"- $\alpha$ -rhamnopyranosyl)- $\beta$ -glucopyranoside, apigenin, apigenin 7-*O*- $\beta$ -glucopyranoside, acacetin, gallic acid, methyl gallate and  $\beta$ -sitosterol-3-*O*- $\beta$ -glucopyranoside. Pharmacologically it was reported as the plant possess wound healing, anti-inflammatory and antioxidants properties, while traditionally used as treatment of warts.

**Keywords:** *Chrozophora tinctoria*, turnsole, wound healing, acacetin, gallic acid





## INCREDIBLE HEALTH BENEFITS OF PAPAYA PLANT

*Vaibhav dwivedi, Sarika gupta, Shivram Krishna, Harikesh Maurya\**

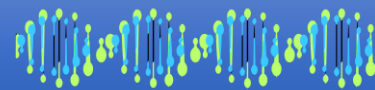
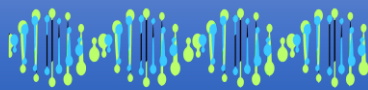
*Hygia Institute of Pharmaceutical Education & Research, Prabandh Nagar, Faizullah Gunj,  
Lucknow*

### ABSTRACT

*Carica papaya* is a popular and economically important fruiting tree of tropical and subtropical Asian countries belonging to the family Caricaceae. The ripe papaya fruit consumed in whole world as a source of nutrition, food, vegetable or processed products for medicines. Its flesh is sweet, juicy and similar in taste to other melon which is highly used as flavoring in candies, jellies and ice cream. *C. papaya* has a wide range of alleged medicinal properties including antiseptic, antiparasitic, anti inflammatory, antidiabetic, and contraceptive activity. *Carica papaya* contains many chemical constituents of papain, chymopapain, papayotin, malic acid, photokinase, calcium malate, sucrose, dextrose, levulose, pectin, malic acid, and citrate. *Carica papaya* also contains various phytoconstituents; alkaloids, glycosides (saponin, anthraquinone, cardiac, cyanogenetics, tannins & phenolic compounds), flavonoids, proteins, amino acids, sterols, triterpenoids, carbohydrates, fats & fixed oils. The medicinal properties of each part of papaya like fruit, latex, leaves, seed, stem, bark and root possess economic value, and grown on commercial scale. It can be chosen as a source of papain for the development of various pharmaceutical products for various diseases.

**Keywords:** *Carica Papaya*, Caricaceae, Papaya, cyanogenetics, anthraquinon





## AN EMERGENCE OF *SWIETENIA MACROPHYLLA* IN NATURAL WORLD

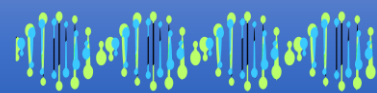
Salahuddin, Renu Gautam, Harikesh Maurya\*  
Hygia Institute of Pharmaceutical Education & Research

### ABSTRACT

*Swietenia macrophylla* is medicinally important plants belonging to the family *meliceae*, among two other species are also available in same family i.e. *Swietenia humilis*, *Swietenia mahagoni*. Geographically the plant is native to North America and grown in following countries i.e. Brezil, Maxico, Peru, Malaysia and located in tropical to subtropical regions mainly in open rain forest. Its fruits seem to point upwards to the sky so that it is basically known as sky fruit. In Ayurvedic medication system the different parts such as fruits, leaves, barks, seeds are highly used to treat the human ailments because its contains alkaloids, flavonoids, tannins, terpenoids, phenol, steroids, saponins, carbohydrate amino, acids and proteins, oil. The phyto-constituent of plant extracts like limonoids (swietenolide), swietenine, augustineolide, andirobin, proceranolide, himachalene have been accounted for antidiabetic, antimicrobial, anti-inflammatory, antifungal, antiulcer, antimalarial, antidiarrhoeal, antioxidants, antitumour, antimutagenic and Anti-Nociceptive activities. The researchers have been reported several health benefits like healthy heart, controlling blood sugar, insect deterrent, overcoming constipation, reduce alzheimer, menstrual pain, improve fertility, lack of appetite, hypertension, cure fever and colds.

**Keywords:** *Swietenia mahagoni*, Mahogany, limonoids, swietenolide, antidiabetic, antibacterial.





## ***SPILANTHES ACMELLA*: AN ENDANGERED MEDICINAL PLANT - AN OVERVIEW OF ITS TRADITIONAL, PHYTOCHEMICAL AND THERAPEUTIC PROPERTIES**

*Sachin Shrivastav\*, Emdad Hossain*

*Pharmacy College, Itaura, Chandeshwar, Azamgarh 276001, Uttar Pradesh*

### **Abstract**

Under the family *Asteraceae*, *Spilanthes acmella*, is a well known medicinal plant having high medicinal usage with an increasing high demand worldwide. It is widely distributed in tropical and subtropical regions of the world. It is commonly known as anti-toothache plant. Different types of bioactive compounds have been isolated from different parts of the plant from time to time. In different reports it was found very effective as anti-pyretic, anti-diuretic, anti-inflammatory, anti-oxidant, immunomodulatory, anti-cancer, hepatoprotective, anti-toothache and anti-AIDS. The aim of the present work was to highlight the ethanobotanical knowledge of the plant used for ayurvedic preparations as therapeutic agent. Present work also described the endangered status of the plant and its possible conservation strategies through *in-vitro* regeneration practices. The present work also aimed to compile up to date and comprehensive information of *Spilanthes acmella* on its traditional, phytochemical, therapeutic uses.







# SELECTED ABSTRACTS





## APPLICATION OF ULTRASONICATION: FOOD AND PHARMACEUTICALS

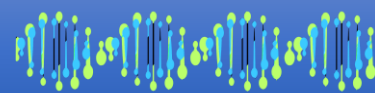
*Preety Gautam\*, Anubhav Anand, Manjul P. Singh*

*School of Pharmacy, BBD University, Faizabad Road, Lucknow. 226028*

Product development by Particle Design Techniques such as Spherical crystallization, Extrusion Spheronization, Melt solidification, Spray drying, Solution atomization, crystallization by means of ultrasonic waves or energy is used to modify the physicochemical, micromeritics and biopharmaceutical properties of the drug. Application of ultrasonic energy to molten mass called Sonocrystallization increases the kinetic energy of molecule and number of collisions causing faster crystallization of drug in less than 30 seconds. It is a newer particle engineering technique which yielded agglomerates comprising of very fine plates and needles of drug and has shown high surface area and solubility. Due to crystal habit changes in drug, the compression properties also change. In the pharmaceutical industry, ultrasound energy was introduced to increase the solubility of sparingly soluble drugs, modification of crystallization yields to micro and nano-size crystals, increase in bioavailability. Wide spread applicability as non-thermal technology in heat-sensitive foods because it retains sensory nutritional and functional characteristic along with enhanced self-life, microbial safety and carrying away of bacterial biofilms and also in phytopharmaceutical industries to extract essential oils, antioxidants (flavonoids), natural pigments (anthocyanin) and crude oil desulfurization. Ultrasonic pretreatment changes the physical and functional attribute of protein such as gelation, foamability, emulsification, and solubility. On the basis of above-mentioned applications, it can be concluded that the ultrasonic technology is used as non-toxic, eco-friendly application in different fields of science and technology.

**Keywords:** Ultrasonic energy, Phyto pharmaceutical, Food technology, Sonocrystallization, Solubility, Bioavailability





## FORMULATION DEVELOPMENT AND EVALUATION OF DISPERSIBLE TABLETS CONTAINING POLY HERBAL COMBINATION OF AQUEOUS ROOT EXTRACTS

*Harikesh Maurya\*, Tirath Kumar*

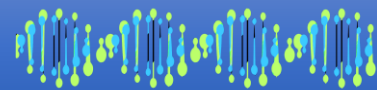
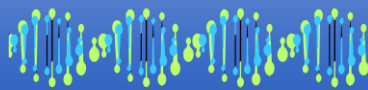
*Dept. of Pharmaceutical Science, Bhimtal Campus, Kumaun University, Nainital, India*

### ABSTRACT

Herbal plants possess various complex chemical substances as secondary metabolites which have curative properties in human ailments. The study deals with formulation and evaluation of poly herbal dispersible tablets prepared from aqueous extract of the selected plant possess antiglomerulonephritis properties. A solid pharmaceutical dosage formulation using a novel dry plant roots extract using various excipients viz.,  $\beta$ -cyclo dextrin, Crosspovidone, Na<sup>+</sup> Starch glycolate, Crosscarmellose Na<sup>+</sup>, Microcrystalline cellulose, Sodium Saccharin, Mg. Sterate and Talc by direct compression method. The micromeritic properties were determined for all the physical mixtures. The results of angle of repose, Carr's Index and Hausner ratio indicated that the powder mixtures possess good flow properties. The physical properties of tablet were determined and all the samples of the test product complied with the official requirements of uniformity. The drug content was found to be close to 98.80% in all formulations. The absorption curve of Formulation F8 showed excellent absorption at  $\lambda_{\max}$  283nm in 0.1N HCl. It was found that the release rate of drug increased from 65.50% to 98.05% (F8) in 2 hours observation as the percentage of Crosscarmellose Na<sup>+</sup> was increased from 15mg to 25mg. The optimized formulation F8 was subjected for accelerated stability studies for about 3 months at 25°C/60% RH, 30°C/60% RH and 40°C/75% RH and the results were reproducible.

**Keywords:** Antiglomerulonephritis, Poly herbal dispersible tablets, Micromeritic properties





## RECENT ADVANCES OF SOME HETEROAROMATIC DERIVATIVES OF CHROMEN-2-ONE

*Priyanka Dixit*

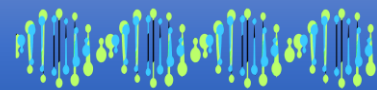
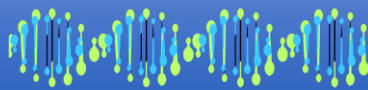
*School of Pharmacy, Babu Banarasi Das University*

### ABSTRACT

Chromen-2-one (Coumarin) is the heterocyclic compound formed from benzene and pyrone ring containing oxygen and its derivatives are of wide awareness because of their diverse biological activity and clinical applications. Chromen-2-ones (Coumarins) have been reported to possess anti-inflammatory, anti-diabetic, anticancer, antimicrobial, and antioxidant properties. Benzoxole fused to a chromen-2-one are known for their anticancer activity. A new series of 3-(2-(benzylideneamino) thiazol-4-yl)-2H-chromen-2-ones were evaluated for their potential to inhibit alkaline phosphatase and ecto-5'-nucleotidase. A novel series of (E)-4-(substituted-benzylideneamino)-2H-chromen-2-one derivatives were evaluated for carbonic anhydrase II inhibition and free radical scavenging activity. A novel, new series of coumarin-benzimidazole hybrids had reported for their broad spectrum antimicrobial activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus subtilis* and *Proteus vulgaris*. 4-((Bis(2-chloroethyl)amino)methyl)-2H-chromen-2-ones that were synthesised were found to exhibit a broad spectrum antifungal activity as well as promising activity against *M. tuberculosis* bacterial strains.

Keywords; Coumarin, heteroaromatic derivatives, antimicrobial.





## PHARMACOVIGILANCE AND POST-MARKETING SURVEILLANCE: A NEW OPPORTUNITY FOR PHARMACY STUDENTS

Ankita Dixit Shukla\*, Deepika Singh

School of Pharmacy, BBD University, Faizabad Road, Lucknow, 226028

### Abstract:

Pharmaceuticals are regarded as an evergreen industry. The regulatory framework for conducting clinical trials of drugs is provided under the Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945. Part X-A and Schedule Y of the Rules specifically deal with clinical trial of drugs in India. Drug safety or PV is at the center stage of new drug development as well as PMS of approved drugs and devices. This creates a very vital niche for the PV industry inside the much larger and expanding pharmaceutical business. PV deals with collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, blood products, herbals, vaccines, medical device, traditional and complementary medicines with a view to identify new information about hazards associated with products and preventing harm to patients. One interested in pursuing this career would be called as Drug Safety Associate. Post marketing surveillance is performed after market approval/clinical trials of drugs in India. *A CRO is an organization that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis like: Quintiles, Parexel, Inventiv Health, Icon, etc. KPO is a form of outsourcing in which knowledge and information-related work is carried out by workers in a different company or by a subsidiary of the same organization eg. TCS, Cognizant etc.* This abstract can be helpful for career aspirant pertaining to **PV and PMS**.

**Key words:** Clinical trial, **Pharmacovigilance (PV)**, Post-marketing surveillance (PMS), Contract Research Organization (CRO), Knowledge Process Outsourcing (KPO)





## DO WE KNOW ABOUT FANCONI SYNDROME

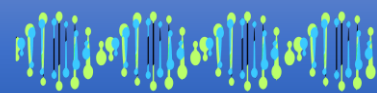
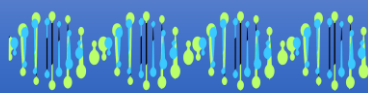
*Aditya Gupta\**, *Mayank Kulshreshtha*  
*School of Pharmacy, BBD University, Lucknow*

### ABSTRACT

Fanconi syndrome is a syndrome of inadequate reabsorption in the proximal renal tubules of the kidney. The syndrome can be caused by various underlying congenital or acquired diseases, by toxicity (for example, from toxic heavy metals), or by adverse drug reactions. It results in various small molecules of metabolism being passed into the urine instead of being reabsorbed from the tubular fluid (for example, glucose, amino acids, uric acid, phosphate, and bicarbonate). Fanconi syndrome affects the proximal tubules, namely, the proximal convoluted tubule (PCT), which is the first part of the tubule to process fluid after it is filtered through the glomerulus, and the proximal straight tubule (pars recta), which leads to the descending limb of the loop of henle. Different forms of Fanconi syndrome can affect different functions of the proximal tubule, and result in different complications. The loss of bicarbonate results in type 2 or proximal renal tubular acidosis. The loss of phosphate results in the bone diseases rickets and osteomalacia (even with adequate vitamin D and calcium levels), because phosphate is necessary for bone development in children and even for ongoing bone metabolism in adults. The end result is a decrease in the ability of the mitochondria to produce ATP. It is possible to acquire this disease later in life. Causes include ingesting expired tetracyclines (where tetracycline changes to form epitetracycline and anhydrotetracycline which damage proximal tubule), and as a side effect of tenofovir in cases of pre-existing renal impairment. In the HIV population, Fanconi syndrome can develop secondary to the use of an antiretroviral regimen containing tenofovir and didanosine. Lead poisoning also leads to Fanconi syndrome.

**Key words;** Fanconi syndrome, loop of henle, respiratory complex.





## NANOSTRUCTURED LIPID CARRIERS (NLC)-BASED GEL FOR THE TOPICAL DELIVERY OF ACECLOFENAC: PREPARATION, CHARACTERIZATION, AND IN VIVO EVALUATION

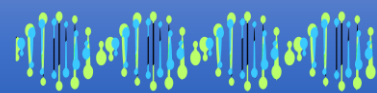
*Aman Agrahari, Vipin Kesharwani, Mr. Dilip Km. Patel, Roohi Kesharwani*

### **Abstract:-**

The aim of this study was to prepare nanostructured lipid carriers (NLC)-based topical gel of aceclofenac for the treatment of inflammation and allied conditions. Stearic acid as the solid lipid, oleic acid as the liquid lipid, pluronic F68 as the surfactant, and phospholipon 90G as the co-surfactant were used. NLCs were prepared by melt-emulsification, low-temperature solidification, and high-speed homogenization methods. Characterization of the NLC dispersion was carried out through particle size analysis, scanning electron microscopy (SEM), differential scanning calorimetry (DSC), and an in vitro release study. The anti-inflammatory effect of the NLC gel was assessed by the rat paw edema technique and compared to marketed aceclofenac gel. The NLC dispersions exhibited d90% between 233 nm and 286 nm. All of the NLC showed high entrapment efficiency ranging from 67% to 82%. The particle size of NLC was further confirmed by the SEM study. The result of DSC showed that aceclofenac was dispersed in NLC in an amorphous state. Both the entrapment and release rate were affected by the percentage of oleic acid, but the method of preparation affected only the entrapment efficiency. The nanoparticulate dispersion was suitably gelled and assessed for in vitro permeation. Finally, NLC-based gels were found to possess superior (almost double) the antiinflammatory activity compared to the marketed product. The anti-inflammatory 750 D. Patel et al.: Sci Pharm. 2012; 80: 749–764 activity of NLC gel showed a rapid onset of action, as well as a prolonged duration of action as compared with the marketed gel.

**Keywords:-** Aceclofenac • Nanostructured lipid carriers (NLC) • Topical gel • Nanoparticle





## NANOEMULSIONS: FORMATION, PROPERTIES AND APPLICATIONS

*Md Amir Ansari, Md Shariq Ansari, Miss Ruby Tabassum, Mr. Dilip K. Patel*

*Chandra Shekhar Singh College of Pharmacy, Kausambi, Allahabad, U.P. INDIA.*

### ABSTRACT

Nanoemulsions are kinetically stable liquid-in-liquid dispersions with droplet sizes on the order of 100 nm. Their small size leads to useful properties such as high surface area per unit volume, robust stability, optically transparent appearance, and tunable rheology. Nanoemulsions are finding application in diverse areas such as drug delivery, food, cosmetics, pharmaceuticals, and material synthesis. Additionally, they serve as model systems to understand nanoscale colloidal dispersions. High and low energy methods are used to prepare nanoemulsions, including high pressure homogenization, ultrasonication, phase inversion temperature and emulsion inversion point, as well as recently developed approaches such as bubble bursting method. In this review article, we summarize the major methods to prepare nanoemulsions, theories to predict droplet size, physical conditions and chemical additives which affect droplet stability, and recent applications.

## DENDRIMER: A NOVEL DRUG DELIVERY SYSTEM

*Ankit kushwaha<sup>1</sup>\*, Md shariq Ansari, Mr. Dilip Km. Patel, Miss Ruby Tabassum*

### Abstract:-

Dendrimers are novel artificial compound systems having improved physical and chemical properties owing to their distinctive three-dimensional design. Dendrimers have a well-defined size, shape, relative molecular mass and monodispersity. These are compatible with drug moieties further as bioactive molecules like polymer, Lipoamin, and different polyanions. The cavities within the nerve fiber structure may be changed to include hydrophobic and deliquescent medicine. The terminal teams are changed to connect antibodies and bioactive substances for targeting purpose at the side of providing miscibility, reactivity, and solubility. Currently, dendrimers are of nice interest for delivering drug molecules via totally different routes as a nanocarrier. Toxicity issues related to cationic dendrimers are overcome by PEGylation, that neutralizes the charge on them. This review contains varied structural aspects and properties of dendrimers at the side of their pharmaceutical application as a possible novel drug delivery carrier.

Keywords: Dendrimers, PAMAM, monodispersity, nanocarriers, targeted, PEGylation.







## SUSPENSION SYSTEMS: A REVIEW

*Md Asif, Sanskriti Tripath<sup>1</sup> Ruby Tabassum, Dilip K. Patel*

*Chandra Shekhar Singh College of Pharmacy, Kausambi, Allahabad, U.P. INDIA.*

### ABSTRACT

Abstract - Suspension systems don't tend to get much publicity, but they're probably the most crucial factor in the day-to-day enjoyment of your car. Automakers are always tweaking and refining their designs in search of that elusive ideal: a perfect ride coupled with race-worthy handling. We haven't quite gotten there yet, but the latest systems are better than ever at reconciling the competing goals of comfort and performance. Like most other components on a vehicle, manufacturers have taken many different approaches when it comes to suspension design. Luxury cars are engineered for a comfortable ride, while sports cars need to corner at high speed. Trucks, on the other hand, need to carry heavy loads and may travel off the pavement.

**Key Words:** Active Suspensions, Vehicle System, Intelligent Control, Modernisation of Suspensions, Adaptive Control System





## ROLE OF NATURAL KILLER T CELLS IN MODULATION OF DENDRITIC CELL RESPONSE TO *LEISHMANIA DONOVANI* INFECTION

Deepika Singh\*, Ankita Dixit Shukla

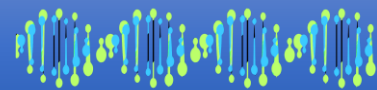
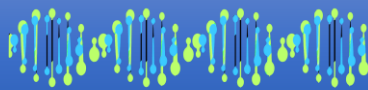
School of Pharmacy, BBD University, Faizabad Road, Lucknow

### ABSTRACT:

iNKT cells play an essential role in regulation of immune responses. The importance of the interaction between natural killer T (NKT) cells and dendritic cells (DCs) in the expansion of antiviral and antitumor immune responses is well-documented; however, limited information on DC-NKT cell interaction during parasitic infections is available. We found that the addition of freshly isolated, iNKT cells significantly promoted the activation of DCs that were preinfected with *Leishmania donovani* promastigotes and that these activated DCs, in turn, stimulated NK cell activation mostly via cell contact-dependent mechanisms. Alpha-Galactosylceramide ( $\alpha$ -GalCer) is a glycolipid with potent antitumor properties that binds to CD1d molecules and activates mouse V $\alpha$ 14 and human V $\alpha$ 24 NKT cells. Sorted iNKT cells have definitive role in Leishmaniasis and helps in elimination of the infection. However, the major concerns associated with these cells are that the concentration of iNKT cells decreases during visceral leishmaniasis, particularly in lymphoid organs. iNKT cell may able to reduce parasite by augmenting immune mediators. V $\alpha$ 14 natural killer T (iNKT) cells activated by alpha-galactosylceramide (GalCer) secrete a large amount of cytokines. We demonstrated that the iNKT cells activated by  $\alpha$ GalCer augmented IFN- $\gamma$  induced NO production. iNKT-cell responses to the glycolipid antigen  $\alpha$ -galactosylceramide ( $\alpha$ -GalCer) were dampened by prior autoreactive activation. iNKT cells were observed with a capacity to reduce not only drug sensitive *L.donovani* parasite in infected DCs but also drug resistant (miltefosine) *L.donovani*. Additionally iNKT cells helped in restoration and drug response.

**Key Words:** iNKT (invariant Natural Killer T Cell),  $\alpha$ - Galcer, DC (Dendritic Cell)





## DRUG INDUCED FEVER: RECENT CASES FROM THE PUBLISHED REPORTS

*Hemlata, Amrita Yadav*

*School of Pharmacy, BBD University Lucknow*

### ABSTRACT

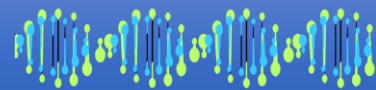
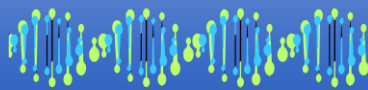
Homeostasis is a key concept. It maintains body system in a normal range, in the presence of toxins homeostasis would be disrupted and body becomes sick. Average body temperature is about 37°Celsius and temperatures above 38°Celsius are considered to be a fever. Drug fever is conventionally defined as a fever above 38°C occurring after drug administration, that ceases within 72 hours. Fever can be the sole manifestation of an adverse drug reaction in 3 to 5% of cases. The risk of developing drug fever increases with the number of drugs prescribed. Development of drug fever is based on structure and function of causative agents. The recognition of drug fever is clinically important. Failure to recognize the etiologic relationship between a drug and fever, often has undesired consequences including extra testing, unnecessary therapy and longer hospital stays. The diagnosis of drug fever is challenging and is particularly difficult when the patient is receiving the drug to treat a disease which is presents with a fever

Recent cases may involve drug induced fever by Peperacillin-Tazobactum in a patient with HIV infection, Drug induced rashes with Eosinophilia and systemic symptoms (DRESS) by Cefotaxime, Tigecycline induced drug fever and Leukemoid reaction.

Early diagnosis may reduce inappropriate, potentially harmful, expensive diagnostic and therapeutic interventions. Rechallenge with the offending agent will usually cause recurrence of fever within a few hours, confirming the diagnosis. The published report on drug induced fever may assist in making the diagnosis easier.

**Keywords:** Homeostasis, Drug induced Fever, Diagnosis, Recent cases, DRESS.





## **FUTURE ASPECTS OF PHARMACOVIGILANCE IN INDIA**

*Aditya Dubey, Vipin Kesharwani, Ravi Kesh Singh, Ruby Tabassum*

*Chandra Shekhar Singh College of Pharmacy, Koilaha, Puramufti, U.P India*

### **ABSTRACT:**

Pharmacovigilance is related to protection of public health and adverse drug reaction. A properly working pharmacovigilance system is essential if medicines are to be used safely. Polypharmacy is also associated with negative consequences, such as increased risk of mortality. Specific aim of pharmacovigilance programmers are to contribute to the regulatory assessment of benefit, harm, effectiveness, and risk of medicines, encouraging their safe, rational and more effective (including cost effective) use. It helps pharmaceutical companies to monitor their medicines for risk and to devise and implement effective risk management. Bank funded National Pharmacovigilance Program for India was made operational. The objective of NPP were to involve a large number of healthcare professionals in the process, inculcate the culture of reporting ADRS and to be a land mark for global drug monitoring. NPP has made recommendation in the WHO document titled "Safety Monitoring of Medicinal Products Guidelines for Setting up and running a Pharmacovigilance Centre. A regulation is required to implement the system of reporting adverse events of drugs introduced in the Indian market by pharmaceutical companies. The government has to play an important role in ensuring the availability of safe medicines to the public. The DCGI should act quickly to improve pharmacovigilance so as to integrate Good Pharmacovigilance Practice into the processes and procedures to help ensure regulatory compliance and enhance clinical trial safety and post marketing surveillance.

**Keywords:** Pharmacovigilance, National Pharmacovigilance Program, Clinical Trial





## IMPORTANCE OF ANTIAGINGS IN COSMETICS

*Jitendra Km.Sharma, Vipin Kesharwani, Md.Shariq Ansari*

### **Abstract:**

Antiaging is emerging class of cosmetics which combine the benefit of anti aging ingredients with the elegance skin feel and delivery system of cosmetics antioxidants, anti cellulites and anti microbial have been use in maintaining and enhancing human beauty. Anti aging ingredients also help to reduce the fine lines, increasing the moisture level and reduces wrinkles and puffness to keep the skin in good condition. New delivery system is a more effective solution for the skin aging resulting from photoaging. New vehicle like liposome and nanoparticles is a new generation for antioxidants with enhanced bioavailability and very stable activity. Our objective is to review present state of the art knowledge pertaining to mechanisms involved in skin aging, factor responsible for aging and various new ingredients use to treat aging defect.

**Key words:-** Antiagings, Nanoparticles, Antioxidants, Bioavailability.

## IMPORTANCE OF PHARMACEUTICAL EXCIPIENTS IN DOSAGE FORM

*Kaseem Ahmad, Sanskriti Tripathi, Ruby Tabassum, Dilip K. Patel*

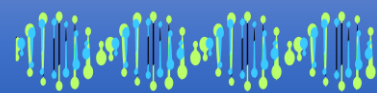
*Chandra Shekhar Singh College of Pharmacy, Kausambi, Allahabad, U.P. INDIA.*

### **ABSTRACT**

Excipients play an important role in formulating a dosage form. These are the ingredients which along with Active Pharmaceutical Ingredients make up the dosage forms. Excipients act as protective agents, bulking agents and can also be used to improve bioavailability of drugs in some instances, the following review discusses the various types and sources of excipients along with their uses, and these can be used for different activities. Specific excipients are best suited for a particular dosage form; the selection criterion for excipients and various interactions that an excipient can undergo during its course of stay in formulation has been discussed in this review. Some excipient interactions can be detrimental and need to be avoided. This has been detailed out in the interaction section. Excipients as like other active pharmaceutical ingredients need to be stabilized and standardized; the following review gives brief information about standardization and stabilization process alongwith the safety evaluation parameters of the excipients.

**Keywords:** excipient, Interactions, co-processed excipients, Standardization





## RP-HPLC: AN EFFECTIVE TOOL IN PHARMACEUTICAL SCIENCES

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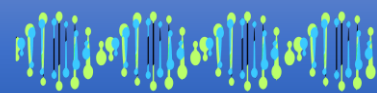
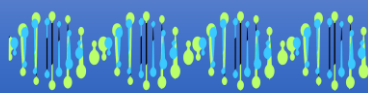
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### Abstract

Reversed-phase high-performance liquid chromatography (RP-HPLC) involves the separation of molecules on the basis of hydrophobicity. The separation depends on the hydrophobic binding of the solute molecule from the mobile phase to the immobilized hydrophobic ligands attached to the stationary phase, i.e., the sorbent. Reversed-phase HPLC is very widely applicable for small molecule analyses (M.Wt. < 2000 Da). A C18 or Octadecylsilane (ODS) column is usually the first choice for method development. Reversed-phase HPLC is a good choice for peptide and protein separations when short chain alkyl stationary phases are used. Here, analysis of compounds with a molecular weight above 2000 Daltons is possible. The separation of amines requires more attention but can be easily accomplished by the use of additives, pH control, or the use of specially treated columns. Reversed phase HPLC successfully separates both polar and nonpolar neutral molecules with molecular weights below 2000 Daltons. It is widely used in the pharmaceutical industry for separation of compounds such as vitamins, steroids,  $\beta$ -blockers. In the food and beverage industry for analysis of sweeteners, food additives and carbohydrates. In the chemical industry is used for analysis of polymer additives. In the field of environmental monitoring for analysis of pesticides and herbicides in clinical analysis for the determination of catecholamines. Today, because it is more reproducible and has broad applicability, reversed-phase chromatography is used for approximately 75% of all HPLC methods.

**Key words;** RP-HPLC, column, catecholamines





## HISTORY OF ANTIBIOTICS AND EVALUATION OF RESISTANCE

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### ABSTRACT

The discovery of penicillin in 1928, by Alexander Fleming marked a mile stone in modern medicine. Thus the “Antibiotic Revolution” shared million of line during Second World War. Subsequently, this passed a way for the advent of new antibiotics against, dread full infections. The evaluations of an antibiotic resistance in the bacteria are primarily due to the dr selection pressure, which involves use of drugs both in human and animals. It is of epidemiological concern as the resistance may spread locally, regionally or globally. Emergence of “Superbugs”, (Bacteria highly resistant to antimicrobial agents) has severally threatened therapeutic options in the last few decades. The battle against these pathogens is an ultimate challenge.

**Keywords:** Antibiotics, Beta-lactams, Cabapenems.

## EMERGING IMPLICATIONS OF NANOTECHNOLOGY ON CANCER THERAPY: A REVIEW

*Sanskriti Tripathi, Md Shariq Ansari, Ruby Tabassum, Dilip K. Patel*

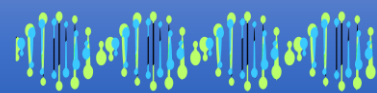
*<sup>1</sup>Chandra Shekhar Singh College of Pharmacy, Kausambi, Allahabad, U.P. INDIA*

### ABSTRACT:

Nanotechnology is apace developing a subdivision of technology that affects several fields. It offers an unprecedented, paradigm-changing chance to create important advances in cancer medical aid. It will assist to own a more robust designation with less harmful substance as optical nanoparticles and ICG molecules. It’sincontestable however applied science will facilitate solve one in every of the foremost difficult and long issues in medication, that is a way to eliminate cancer while not harming traditional body tissue. A recent trend in engineering and technology has a diode to the event of the many new nanoscale devices, together with quantum dots, nanoshells, gold nanoparticles, magnet nanoparticles, and carbon nanotubes. the essential approach of the review processes rising implications of those platforms style & development of nanoparticle-based medicine for cancer medical aid.

**Keywords:** Optical nanoparticles, ICG molecules, nanotubes, nanoshells, quantum dots.





## AN UPDATE ON TREATMENT OF PARKINSON'S DISEASE

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*School of Pharmacy, BBD University, Lucknow*

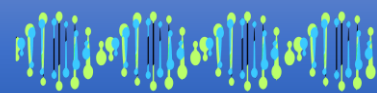
### ABSTRACT

Although levodopa remains the most effective symptomatic drug for Parkinson's disease (PD), its use is limited by the emergence of motor fluctuations and dyskinesias, particularly in young-onset patients. Dopamine agonists, catechol-O-methyltransferase inhibitors and other anti-parkinsonian drugs have been found to diminish or prevent these complications and possibly to exert disease-modifying effects. Neurologists are faced with many challenges in caring for patients with Parkinson's disease (PD). This chronic, long-term illness that affects at least one million people in the United States requires a coordinated healthcare partnership between the physician and the patient. The importance of early diagnosis is essential to delaying disease progression and early diagnosis and intervention may be aided by recent advances in biomarkers, genomics, and imaging. A misdiagnosis or late diagnosis will lead to deteriorating patient health. Additionally, physicians should incorporate current guidelines into their treatment strategies, and awareness of the reasoning behind these guidelines is critical for appropriate use. The U.S. Food and Drug administration approved a drug called Duopa in 2015. This medication is made up of carbidopa and levodopa. However, it's administered through a feeding tube that delivers the medication in a gel form directly to the small intestine. Duopa is for patients with more advanced Parkinson's who still respond to carbidopa-levodopa, but who have a lot of fluctuations in their response. Because Duopa is continually infused, blood levels of the two drugs remain constant. Dopamine agonists include pramipexole (Mirapex), ropinirole (Requip) and rotigotine (given as a patch, Neupro). A short-acting injectable dopamine agonist, apomorphine (Apokyn), is used for quick relief.

**Keywords;** Parkinson's disease, Duopa, Dopamine agonist.







## TOXICITY AND SAFETY RELATED TO NANOTECHNOLOGY

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### ABSTRACT-

The emerging field of nanotechnology has created risk for environment and human health. Nanoparticles are not a recent discovery. It has existed for many years. Today synthesis of nanoparticles takes place for many applications in various field of science, technology, medicine, colloid technologies, diagnostics, drug delivery, health impacts, food, personal care applications etc. In spite of this, toxicology of nanoparticles is poorly understood as there are no sufficient methods to test nanoparticles for health, safety and environmental impacts, especially in the size range lower than 50nm. Thus the branch of nanotoxicology deals with the study relating to the toxicity of the nano materials, as it is essential to know the toxicity of nano material before using it for a variety of applications. “Nanosafety” is a broad term and a lack of specific objectives can lead to ineffective use of resources.

**Key Words:** Nanosafety, nanoparticles, nanotoxicity, health and risk, environmental impact.

## LIPID-POLYMER HYBRID NANOCARRIERS AS DRUG DELIVERY PLATFORM

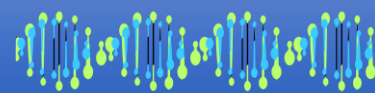
*Vipin Kesharwani, Mohd. Asad Farooqi, Dilip Km. Patel*

Chandra Shekhar Singh College of Pharmacy, Koilaha, Kaushambi, U.P. INDIA

In the pharmaceutical sciences, the most popular branch is pharmaceutical nanotechnology are become highly developed in a previous year. The nanoparticles have significant application in drug delivery, diagnostic of disease and their treatment. The lipid and polymeric nanoparticles are two most promising class of Nanocarriers including Liposomes, Solid Lipid Nanoparticles and polymeric micelles, are approved for clinical use but have some limitations. The lipid nanoparticles have some drawback like insufficient drug loading, drug leakage, and physical and chemical instability during storage. Polymeric nanoparticles have some limitation like use of toxic organic solvents in the production process and polymer degradation. Thus, to overcome the limitation of Nanocarriers, develop a new carrier system known as lipid-polymer hybrid nanoparticle (LPHNPs). The polymeric core (inner parts) encapsulate both hydrophilic and hydrophobic drugs; the lipid shells (outer parts) coating the external surface of polymer core, which form barriers to prevent drug leakage, allowing the prolonged and controlled release action hence are a most promising delivery platform. The outer phospholipids layer act as bioactive and biomimetic molecules hence has a high targeting ability. These LPHNPs are prepared by two step and single step method and have various application in Cancer treatment. Brain drug delivery, multiple drug delivery (pro-drug) delivery of Diagnostic imaging agent and siRNA.

**Keyword:** Diagnostic, Hydrophobic, Lipophilic, Biomimetic





## A REVIEW ON HERBAL DRUGS FOR THE TREATMENT OF DIABETES

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### ABSTRACT

Diabetes mellitus is both insulin-dependent (IDDM) and non-insulin dependent (NIDDM) type of commonest endocrine disorder that affects more than 100 million people worldwide (6% of the population). Diabetes mellitus has not known permanent cure and is highly prevalent worldwide. In traditional medicine and Ayurveda it is correlated with disease called Madhumeh. Traditional Medicines derived from medicinal plants are used by about 60% of the world's population. This review focuses on Indian Herbal drugs and plants used in the treatment of diabetes, especially in India. Diabetes 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. Though there are various approaches to reduce the ill effects of diabetes and its secondary complications, herbal formulations are preferred due to lesser side effects and low cost. A list of medicinal plants with proven antidiabetic and related beneficial effects and of herbal drugs used in treatment of diabetes is compiled. These include *Allium sativum*, *Eugenia jambolana*, *Momordica charantia*, *Ocimum sanctum*, *Phyllanthus amarus*, *Pterocarpus marsupium*, *Tinospora cordifolia*, *Trigonella foenum graecum* and *Withania somnifera*. One of the etiologic factors implicated in the development of diabetes and its complications is the damage induced by free radicals and hence antidiabetic compound with antioxidant properties would be more beneficial. Therefore information on antioxidant effects of these medicinal plants is also included.





## IMPORTANCE OF RP HPLC IN ANALYTICAL METHOD DEVELOPMENT

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### Abstract

Chromatography, although primarily a separation technique, is mostly employed in chemical analysis in which High-performance liquid chromatography (HPLC) is an extremely versatile technique where analytes are separated by passage through a column packed with micrometer-sized particles. Now a day reversed-phase chromatography is the most commonly used separation technique in HPLC. The reasons for this include the simplicity, versatility, and scope of the reversed-phase method as it is able to handle compounds of a diverse polarity and molecular mass. Reversed phase chromatography has found both analytical and preparative applications in the area of biochemical separation and purification. Molecules that possess some degree of hydrophobic character, such as proteins, peptides and nucleic acids, can be separated by reversed phase chromatography with excellent recovery and resolution. This review covers the importance of RP-HPLC in analytical method development and their strategies along with brief knowledge of critical chromatographic parameters need to be optimized for an efficient method development.

**Key word:** HPLC, Phase Chromatography, micrometer.

## ULTRA PERFORMANCE LIQUID CHROMATOGRAPHY

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### Abstract

UPLC is a rising chromatographic separation technique whose packing materials have smaller particle size lesser than  $2.5\mu\text{m}$  which improves the speed, resolution and sensitivity of analysis. When many scientists experienced separation barriers with conventional HPLC, UPLC extended and expanded the utility of chromatography. The main advantage is a reduction of analysis time which also reduces solvent consumption. The analysis time, solvent consumption and analysis cost are very important factors in many analytical laboratories. The time spent for optimizing new methods can also be greatly reduced. This results in many analyses in a day and quick results which is of very importance to the industries and research laboratories. UPLC principle is same as that of HPLC that is based on Van Deemter equation but decrease in particle size has increased efficiency at increased flow rates.

**Key word:-** UPLC, HPLC, Chromatography.





## RECENT DEVELOPMENTS ON ANTIMYCOBACTERIAL AGENTS

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### Abstract

With characteristic mycolyl-arabinogalactan-peptidoglycan complex cell wall, the mycobacteria are a group of aerobic, non-motile and acid fast bacteria. Tuberculosis and leprosy are the diseases which are caused by the genus mycobacterium. Tuberculosis is defined as the infection with *Mycobacterium tuberculosis* complex and was declared a global health emergency principally because of the appearance of multidrug-resistant strains and the associated risk of infection in immune-compromised population. The chronic infectious disease caused by *Mycobacterium leprae* results in leprosy. There is an urgent clinical need for novel, potent and safe anti-mycobacterial drugs. Natural products have been used since antiquity for treating diverse complaints and novel pharmacophores are discovered every year. Plants are also the source of an exquisite variety of antimicrobials that can lead to useful antimycobacterial agents in the future. Recently, thiophene and thiazoles derivatives have been found to have antimycobacterial potential. Some 1H-1,2,3-triazoles bases compounds have also displayed the antimycobacterial activity.

**Key words:** Leishmaniasis, visceral, drug, derivative

## DRUGS FOR THE TREATMENT OF LEISHMANIASIS

*Anjali Kumari and Parmesh K. Dwivedi*

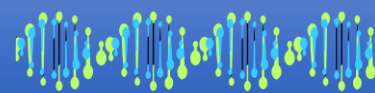
*Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow campus*

### Abstract

Leishmaniasis, which is spread by the bite of certain types of sandflies may be divided into cutaneous, mucocutaneous and visceral types. This Neglected tropical disease (NTD) is common in some parts of Asia, Africa, South and Central America and southern Europe. Various drugs which are used for the treatment of this disease belonging to class macrolide, pentavalent antimonials, benzamidine, phosphorylcholine etc. Amphotericin B is often used in visceral leishmaniasis while pentamidine may be an option for both visceral leishmaniasis and cutaneous leishmaniasis. Miltefosine, sodium stibogluconate and meglumine antimoniate are used to treat visceral, mucocutaneous, and cutaneous leishmaniasis. An antibiotic, paromomycin is used to treat a number of infections including leishmaniasis. In addition to this, for the treatment of *L. major* and *L. tropica* infections, fluconazole or itraconazole are given orally.

**Key words:** Leishmaniasis, visceral, drug





## RECENT DEVELOPMENT ON ANTIDIABETIC NATURAL PRODUCTS

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*Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow campus*

### Abstract

Among the different forms of diabetes such as type-1, type-2 and gestational diabetes, the patient with type-2 diabetes are increasing day by day. Although, there are various established drugs but they do not fulfill all the requirements of patients and hence there is still demand for new anti-diabetic drugs. In recent years, much researches have been focused on antidiabetic natural products. In this regard, the antidiabetic potential of andrographolide from *Andrographis paniculata* (Acanthaceae) has been established. The significant antidiabetic activities has been shown by the methanolic extract of *Picralima nitida* (Apocynaceae) and the hydroethanolic extract of *Sonchus oleraceus* (Asteraceae). Studies on phlorizin revealed that it has promising potential for the treatment for type 2 diabetes. In this way plants and other natural sources have been useful in search and development of drugs for treating the diabetic patients.

**Key words:** Antidiabetic, natural product, drug

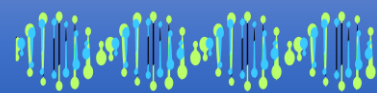
## A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL ASPECTS OF MYRICA ESCULENTA

*Dinesh Kumar\*, Kamendra Kr. Maurya and Vivek Kr. Gupta.*

*Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

*Myrica esculenta* (Myricaceae) commonly known as box berry or *kaphal* is an important Indian medicinal plant. It is found in foothill tracks of Eastern Himalayas, Meghalaya, Nepal, China and Pakistan. Phytochemical studies of the different parts of plant revealed the presence of various bioactive phytoconstituents such as phenolic compounds, alkaloids, glycosides, triterpenoids and volatile oils. The plant is also reported to have innumerable significant pharmacological activities like analgesic, anxiolytic, antiallergic, antidiabetic, antimicrobial, antihypertensive, antiulcer, antioxidant and antiinflammatory evaluated by using various animal models. The objective of the present review article is to compile all the relevant published information regarding phytochemistry and therapeutic potential of *M. esculenta*.





## **PHYTOCHEMICAL PHYTOPHARMACOLOGICAL POTENTIAL OF *MORUS ALBA*: A REVIEW**

*Adesh\*, Inamullah, Kamendra Maurya and Vivek Gupta.*

*Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

Medicinal plants of Moraceae family have been well-recognized traditionally due to their versatile applications in various fields including agriculture, cosmetic and food as well as in pharmaceutical industries.. The present review was aimed to summarize and critically discuss the biomedical implications of *Morus* species, their bioactive compounds, and phytochemicals. Bioactivity guided fractionation of these medicinal plants revealed that different types of bioactive phytochemicals and secondary metabolites such as steroids, saponins, alkaloids, glycosides and phenolic compounds including terpenoids, flavonoids, anthocyanins and tannins were present. The critical analysis of the literature revealed that the aqueous, methanolic, and ethanolic extracts of *Morus* species and their bioactive compounds exhibit remarkable anti-oxidative, anti-diabetic, anti-stress, nephroprotective, antimicrobial, anti-mutagenic, anticancer, anxiolytic, hepatoprotective, anthelmintic, antimicrobial, immune-modulatory and cholesterol lowering effects.

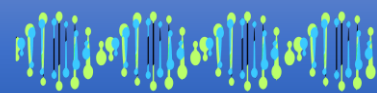
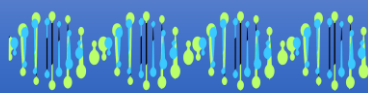
## **PHARMACEUTICAL LIPOSOMAL DRUG DELIVERY: A REVIEW OF NEW DELIVERY SYSTEMS**

*Sujeet\*, D. N. Singh, Kamendra Maurya and Vivek Gupta.*

*Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

In the past 15 years, some major breakthroughs in liposome technology have fueled the rapid development of new pharmaceutical liposomal applications. In order to optimize the delivery of factors for maximum efficacy, novel methods have been proposed to increase the permeation rate of drugs temporarily and deliver the desired target compound in a time regulated and locally restricted manner to the target site New approaches to construct improved liposomes for therapeutic delivery have addressed, on one end, biophysical parameters Advances and challenges of liposome assisted drug delivery which can be manipulated by altering the constituent bilayer phospholipids to better tailor the liposome to the required application.





## PHARMACOSOMES: A NOVEL CARRIER FOR TARGETED AND CONTROLLED VESICULAR DRUG DELIVERY SYSTEM

*Hemant Mishra\*, Anand Patel, Kamlendra Maurya and Vivek Gupta.  
Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

Vesicular drug delivery system showed application in targeted and controlled drug delivery and transport the active agent to the tissue through biological barriers. Novel vesicular drug delivery carrier intend to delivery the drug at a rate directed by the need of body during the period of treatment and channel the active moiety to the site of action providing target. Pharmacosomes are one of the most promising approaches for this system to increase the bioavailability of drug substance, improve drug stability, and prolong the existence of the drug in systemic circulation and target drugs to specific site in the body. Pharmacosomes are amphiphilic, colloidal dispersion prepared from drug lipid conjugates with or without additional surfactant. Targeted pharmacosomal drug delivery system is very useful in cancer therapy because such pharmacosomes should selectively localize anticancer drug at the tumour site, thus reducing the toxicity of the drug to normal cell and improving their therapeutic activity. The great advantages of pharmacosomes are it may be minimize drug degradation and diminished the toxicity (GIT).

## PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF GYMNEMA SYLVESTRE

*Vibhor Jain\*, Mayank Tiwari, Kamlendra Maurya and Vivek Gupta.  
Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

The present review is a research update on *Gymnema sylvestre*, a rare herb with significant medicinal attributes with an overview of its ethnobotanical uses, phytochemistry dealing with an in-depth study of its phytochemicals, and their bioactivities. It also explores the facts and prospects of its development into a modern and efficient therapeutic, contemporary with the present trends of pharmacology and drug development. Furthermore, it holds significant prospects in major health problems like cardiovascular disorders, obesity, osteoporosis, and asthma besides being a popular medication for number of other health ailments. The herb finds significant application in various food preparations for control of obesity and blood cholesterol levels besides regulation of sugar homeostasis. The herbal preparations of *G. sylvestre* are presently used in tea bags, health tablets and supplements, beverages, and confectioneries.





## **E-MARKETING IN THE PHARMACEUTICAL INDUSTRY**

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Digital has become an important part of the everyday life. All the sectors have been adapting to the digital era at a faster rate. However other than the website, the pharma industry has not quite been able to adopt digital marketing. In this era more pharmaceutical companies utilize social media sites or ecommerce sites as digital marketing platform. This enables online purchase of products by the customers. Some organisations are trying to understand the true value of digital while others are integrating it into the wider marketing strategy. However all the companies cannot sell products online as they manufacture prescription drugs, which cannot be sold online. For example, Pfizer is active and responsive to the customers via social networking platforms. YouTube, Facebook and Twitter were used to communicate with customers. Johnson and Johnson was one of the first companies to launch a YouTube channel. Quantum Pharmaceuticals and The Specials Lab, North East based pharmaceutical companies offer online ordering of special medicines promoting e-commerce and digital marketing.

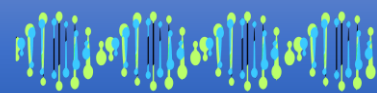
## **ROLES OF PHARMACIST IN PHARMACOVIGILANCE**

*Saif khan\*, Brajnandan kishor, Kamlendra Maurya and Vivek Gupta.  
Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

World Health Organization (WHO) defines Pharmacovigilance as the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problems. Pharmacovigilance plays an important role in ensuring patients drugs safety. Adverse Drug Reaction (ADR) is defined according to WHO as any response to a drug which is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or the modification of physiological function. Complete information of unintended and severe adverse events could be finding through the Pharmacovigilance. It could not be done through clinical trials which are conducted in in-vivo method. Pharmacists are not mere preparing or dispensing of drugs. The professional practice reaches far beyond serving community. Pharmacists have an important responsibility in monitoring the on-going safety of medicines as part of their professional practice. Pharmacist role in pharmacovigilance varies from country to country, but the professional responsibility is the same regardless of jurisdiction. Pharmacists can create a trusted environment by counselling patients to reduce medication errors, improve safety and quality of care.







### **ME-TOO DRUGS: IS THERE A PROBLEM?**

*Deepankar\*, D. N. Singh, Kamlendra Maurya and Vivek Gupta.*

*Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

This brief note presents an economic perspective on “me-too” drugs (sometimes also called “follow-on” drugs). Me-too drugs are products which largely duplicate the action of existing drugs. Several recent books (such as Angell (2004), Avorn (2004) and Goozner (2004)) have heaped criticism on the drug industry for the increasing extent to which investment appears to be focused on developing drugs which have a similar mechanism of action to pre-existing drugs. Others, such as Calfee (2000) and diMasi and Paquette (2004) have defended me-too drugs, as providing more therapeutic options and enhancing competition. diMasi and Paquette have also observed that many me-too drugs enter development long before the first drug in a new class is approved, so that in many cases me-too drugs are the result of parallel development rather than of imitation. The key problem with me-too drugs is that, to the extent that they are similar to pre-existing drugs, they diminish the incentives for innovation in pioneering drugs without adding therapeutic value. Me-too drugs also absorb R&D resources, which is wasteful if they are undifferentiated from pre-existing drugs. On the other hand, the more differentiated me-too drugs are from pioneering drugs, the greater their potential benefits, and the less they harm the incentives for pioneering research.

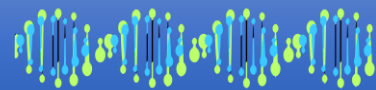
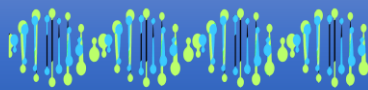
### **PHARMACEUTICAL INDUSTRY IN INDIA**

*Ashish srivastava\*, Pawan Kushwaha, Kamlendra Maurya and Vivek Gupta.*

*Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

The Indian pharmaceuticals market is the third largest in terms of volume and thirteenth largest in terms of value, and it accounts for 20 per cent in the volume terms and 1.4 per cent in value terms of the Global Pharmaceutical Industry as per a report by Equity Master. India is the largest provider of generic drugs globally with the Indian generics accounting for 20 per cent of global exports in terms of volume. Of late, consolidation has become an important characteristic of the Indian pharmaceutical market as the industry is highly fragmented. India enjoys an important position in the global pharmaceuticals sector. The country also has a large pool of scientists and engineers who have the potential to steer the industry ahead to an even higher level. Presently over 80 per cent of the antiretroviral drugs used globally to combat AIDS (Acquired Immuno Deficiency Syndrome) are supplied by Indian pharmaceutical firms.





## **THE ROLE OF THE PHARMACIST IN THE HEALTH CARE SYSTEM**

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*Department of Pharmacy, Sagar Institute of Technology & Mang. Barabanki*

The role of the pharmacist has been changing over the past two decades. The pharmacist is no longer just a supplier of medicines and a concocter of medicinal products, but also a team member involved in the provision of health care whether in the hospital, the community pharmacy, the laboratory, the industry or in academic institutions. 1 For the purposes of this definition, medicines include herbal and traditional products. Pharmaceutical care is growing in importance with the challenges of self-care. For pharmacists, their greater involvement in self-care means greater responsibility towards their customers and an increased need for accountability. The increase in self-care is due to a number of factors. These factors include: socioeconomic factors; lifestyle; ready access to drugs; the increased potential to manage certain illnesses through self-care; public health and environmental factors; greater availability of medicinal products; and demographic and epidemiological factors.





## JAPANESE ENCEPHALITIS: A BIG PROBLEM FOR GORAKHPUR, INDIA

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Azad institute of Pharmacy & Research, Lucknow, UP*

### ABSTRACT

Japanese Encephalitis (JE) is a common mosquito born flaviviral encephalitis. It is one of leading form of viral encephalitis. *JE estimate 50,000 cases; 15,000 deaths per year.* Its first case was found in Japan in 1871 and major epidemic have been reported in 1924 over 6,000 cases. In India, Uttar Pradesh, Gorakhpur major causes in 1978 with 1,002 cases and 297 deaths reported. Till 2007 with 103,389 cases and 33,729 death. Approx 597,542,000 lives in India and about 1500 to 4000 cases are reported per year.

Japanese encephalitis virus (JEV) causes Japanese encephalitis which is a leading form of viral encephalitis in Asia and part of India. With around 50,000 cases and 10,000 death per year in children below 15 year of age. The JEV has shown a tendency to extend to other geographic regions. Fatality averages 30% and a high percentage of survivors are left with permanent neuropsychiatric sequel. Currently there is no cure for JEV and treatment is mainly supportive. Patients are infective but should avoid further mosquito bites. A number of antiviral agents have been shown to improve the outcome of JEV. In this review the current knowledge of epidemiology and the pathogenesis of this deadly disease have been summarized.

### Keywords:

Epidemiology; Pathogenesis; vector born disease; Epidemics





## DRUG DEVELOPMENT PROCESS

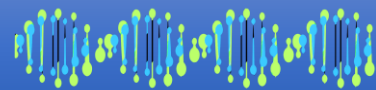
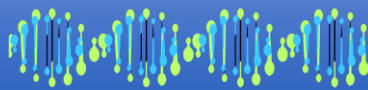
*Anil Kumar Chauhan, Rakesh Sharma, Syed Usman Tayyab, Neelkanth M. Pujari  
Lucknow Institute of Pharmacy, Lucknow (U.P.)*

### ABSTRACT

The development of a drug from an initial idea to its entry into the market is a very complex process which can take around 5-10 years and cost \$1.7 billion. The idea for a new development can come from a variety of sources which include the current necessities of the market, new emerging diseases, academic and clinical research, commercial sector, etc. Once a target for discovery has been chosen, the pharmaceutical industries or the associated academic centres work on the early processes to identify the chemical molecules with suitable characteristics to make the targeted drugs. Typically, researchers discover new drugs through: New research into a disease process that encourages the scientists to discover a new product to stop or reverse the effects of the disease. Many tests of molecular compounds to find possible beneficial effects against any of a large number of disease. Existing treatments that have unanticipated effects. New technologies, such as those that provide new ways to target medical products to specific sites within the body or to manipulate genetic material. At this stage, thousands of compounds may be potential candidates for development as a medical treatment. After early testing, however, only a small number of compounds look promising and call for further study. Once researchers identify a promising compound for development, they conduct experiments to gather information regarding their absorption, distribution, metabolism, excreted, mechanisms of action, dosage, route of administration, side effects (toxicity), effect on different gender, race, or ethnicity, interactions with other drugs and effectiveness as compared with similar drug.

**Key words:** drug design, development, research, clinical trial





## PHARMACIST: BACKBONE OF PHARMAUETICAL INDUSTRY

*Awadhesh Singh, Anupam Sharma, Rakesh Sharma, Neelkanth M. Pujari*

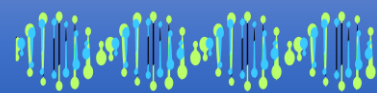
*Lucknow Institute of Pharmacy, Lucknow (U.P.)*

### ABSTRACT:

The pharmaceutical industry is an important component of health care systems throughout the world; it is comprised of many public and private organizations that discover, develop, manufacture and market medicines for human and animal health. The pharmaceutical industry is based primarily upon the scientific research and development (R&D) of medicines that prevent or treat diseases and disorders. Drug substances exhibit a wide range of pharmacological activity and toxicological properties. Modern scientific and technological advances are accelerating the discovery and development of innovative pharmaceuticals with improved therapeutic activity and reduced side effects. Molecular biologists, medicinal chemists and pharmacists are improving the benefits of drugs through increased potency and specificity. Many dynamic scientific, social and economic factors affect the pharmaceutical industry. Some pharmaceutical companies operate in both national and multinational markets. Therefore, their activities are subject to legislation, regulation and policies relating to drug development and approval, manufacturing and quality control, marketing and sales. Academic, government and industry scientists, practicing physicians and pharmacists, as well as the public, influence the pharmaceutical industry. The pharmaceutical industry is largely driven by scientific discovery and development, in conjunction with toxicological and clinical experience (show the poster). Major differences exist between large organizations which engage in a broad range of drug discovery and development, manufacturing and quality control, marketing and sales and smaller organizations which focus on a specific aspect.

**Keywords:** *R&D, pharmaceutical industry, pharmacy practice*





## OVERVIEW ON PARACETAMOL

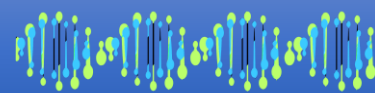
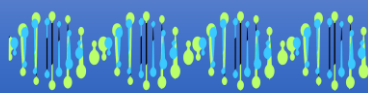
*Bidiya Ambedkar, Anupam Sharma, Rakesh Sharma, Neelkanth M. Pujari  
Lucknow Institute of Pharmacy, Lucknow (U.P.)*

### ABSTRACT:

Paracetamol is used to treat mild to moderate pain from (headaches menstrual periods toothaches backaches osteoarthritis, or cold/flu aches and pains) and reduce fever. The drug should not be taken more than recommended. If giving acetaminophen to child, be sure use a product that is meant for children. Do not take this medication forever for more than 3 days unless directed by your doctor. This drug usually has no side effects. A very serious allergic reaction to this drug is rare. These medications may interact and cause very harmful effects. However, it does not reduce swelling likes the NSAIDs do. It is often sold in combination with other drugs, such as in many cold medications. Paracetamol is available as a generic medication with trade names including Tylenol and panadol. After being taken by mouth it is rapidly absorbed by the gastrointestinal tract. Paracetamol consist of a benzene ring core, substituted by one hydroxyl group and the nitrogen atom of an amide group in the para pattern. Paracetamol is extremely toxic to cats and lethal to snakes but it is as effective as aspirin in musculoskeletal pain in dogs.

**Keywords:** paracetamol, acetaminophen, medication, drugs





## GREEN COFFEE

*Deepika Gupta<sup>1</sup>, Bhavana Dubey<sup>1</sup>, Neelkanth M. Pujari<sup>2</sup>*

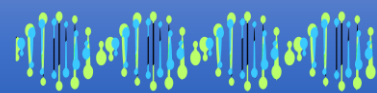
*<sup>1</sup>Department of Pharmacy, Saroj Institute of Technology & Management, Lucknow*

*<sup>2</sup>Lucknow Institute of Pharmacy, Lucknow (U.P.)*

Green coffee obtained from the different species of the coffee plant. There are two very well known species Arabia and the Robusta. It contains two most important substances are Caffeine and chlorogenic acid. Several studies have shown that caffeine can boost metabolism by up to 3-11%. Chlorogenic acid is believed to be responsible for the weight loss effects. Unfortunately most of Chlorogenic acid is removed when coffee is roasted. Some human studies it found that chlorogenic acid can reduce the absorption of carbohydrate from the digestive tract which lower the blood sugar and insulin spikes. Other studies (in mice and rats) was shows that Chlorogenic acid can reduce body weight reduce fat absorbed from the diet reduce fat function of the fat burning hormone Adiponectin. It has also been shown to drastically improve cholesterol and triglyceride level in rats. These are important risk factors for heart disease.

**Keywords:** Green coffee, Chlorogenic acid, Caffeine, Adiponectin





## NOVEL APPROACHES FOR THE DELIVERY OF BIOLOGICS TO THE CNS

*Namrata Shukla, Richa Tiwari, Rakesh Sharma, Neelkanth M. Pujari*

This topic describes novel approach and formulation in the delivery of Biologics of the CNS. We begin by discussing the increasing global burden of CNS disorders as well as providing an overview of the current market share of pharmaceuticals for CNS indication. We then briefly review the structure and function of blood brain barrier (BBB) and discuss a market survey of U.S. food and Drug Administration (FDA)-approved CNS drugs, followed by a review of the current clinically available strategies, both physical and chemical for overcoming the BBB. We conclude by discussing recently developed direction of CNS delivery of Biologics that rely on natural transport pathway. Vector-mediated delivery system, Stem cell and nanomaterial

**Keywords:** *Blood brain barrier, drug disorder, Neurological disorder*







## COMBATING ANTIBIOTIC RESISTANCE, NEED FOR HEALTH

*Neelam Gupta, Anupam Sharma, Neelkanth M. Pujari, Taiyab Usman  
Lucknow Institute of Pharmacy, Lucknow (U.P.)*

### ABSTRACT

Antibiotic resistance has been called one of the world's most pressing public health problems. Almost every type of bacteria has become stronger and less responsive to antibiotic treatment when it is really needed. These antibiotic-resistant bacteria can quickly spread to family members, schoolmates, and co-workers; threatening the community with a new strain of infection disease that is more difficult to cure and more expensive to treat. There are several reasons for the development of antibiotic-resistant bacteria. One of the most important is antibiotic overuse. Antibiotic use promotes development of antibiotic-resistant. Every time a person takes antibiotics, sensitive bacteria are killed, but resistant germs may be left to grow and multiply. Repeated and improper uses of antibiotic are primary cause of the increase in Drug - Resistant Bacteria. While antibiotic should be used to treat bacterial infection, they are not effective against viral infection like the common cold, sore throats, and the flu. These illnesses are usually caused by viruses, not by bacteria and antibiotics don't work against viruses. But the doctors are knowingly involved in such kind of practice just to make their patients happy, to get faster results than ordering tests to confirm the cause. We will have to stop the antibiotic resistance by avoiding the overuse and misuse and taking antibiotics safely like (only for bacterial infection, don't save some of your antibiotic for the next time you get sick, take an antibiotic exactly as the healthcare provider tells you). Smart use of antibiotics is the key to controlling the spread of resistance.

**Key words:** antibiotic, overuse, resistance





## HEART DISEASE IN WOMEN

*\*Neha Rawat, Anupam Sharma, Richa Tewari, Neelkanth M. Pujari  
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### Abstract

In every year since 1984, cardiovascular disease has claimed the lives of more females than males. More than 450,000 women succumb to heart disease annually, and 250,000 die of coronary artery disease. The perception that heart disease is a man's disease and that women are more likely to die of breast cancer is alarming. Although women develop heart disease about 10 years later than men, they are likely to fare worse after a heart attack. The poorer outcomes are due, in part, to the failure to identify heart attack symptoms. Approximately 35% of heart attacks in women are believed to go unnoticed or unreported. However, because of increased age, women are more likely to have co-morbid diseases such as diabetes and hypertension. In women, not only is "tightness" or discomfort in the chest a warning sign, but in addition, nausea and dizziness are common indicators of myocardial ischemia. Other symptoms include breathlessness, perspiration, a sensation of fluttering in the heart, and fullness in the chest. In comparison to men, women are less likely to undergo tertiary care interventions such as cardiac catheterization, angioplasty, thrombolytic therapy, and bypass surgery; to participate in cardiac rehabilitation; and to return to work full-time after myocardial infarction. The most common heart attack symptom in women is some type of pain, pressure or discomfort in the chest. Women are more likely than men to have heart attack symptoms unrelated to chest pain, such as: Neck, jaw, shoulder, upper back or abdominal discomfort and shortness of breath.

**Key words:** chest pain, ischemia, breathlessness





## ALCOHOLISM

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### ABSTRACT

Alcoholism, also known as alcohol use disorder (AUD), is a broad term for any drinking of alcohol that results in mental or physical health problems. In a medical context, alcoholism is conditions when a person drinks large amounts over a long time period, acquiring and drinking alcohol takes up a great deal of time, alcohol is strongly desired, usage results in social and health problems. Alcohol use can affect all parts of the body, but it particularly affects the brain, heart, liver, pancreas, and immune system. This can result in mental illness, an irregular heartbeat, cirrhosis of the liver, and an increase in the risk of cancer, among other diseases. Women are generally more sensitive than men to the harmful physical and mental effects of alcohol. Environmental factors and genetics are two components that are associated with alcoholism, with about half the risk attributed to each. Environmental factors include social, cultural, and behavioral influences. High stress levels, anxiety, as well as inexpensive cost and easy accessibility to alcohol increase the risk. Prevention of alcoholism may be attempted by regulating and limiting the sale of alcohol, taxing alcohol to increase its cost, and providing inexpensive treatment. Due to medical problems that can occur during withdrawal, alcohol detoxification should be carefully controlled. Mental illness or other addictions may complicate treatment. The medications acamprosate, disulfiram, or naltrexone may also be used to help prevent further drinking.

**Keywords:** addiction, alcoholic, disulfiram





## OVERVIEW ON THE NOSOCOMIAL INFECTIONS AND THEIR PREVENTION

*Neha Rawat, Anupam Sharma, Richa Tewari, Neelkanth M. Pujari*

*Lucknow Institute of Pharmacy, Lucknow (U.P.)*

### Abstract

A hospital-acquired infection (HAI), also known as a nosocomial infection, is an infection that is acquired in a hospital or other health care facility. To emphasize both hospital and nonhospital settings, it is sometimes instead called a health care–associated infection (HAI or HCA). Such an infection can be acquired in hospital, nursing home, rehabilitation facility, outpatient clinic, or other clinical settings. Infection is spread to the susceptible patient in the clinical setting by various means. Health care staff can spread infection, in addition to contaminated equipment, bed linens, or air droplets. The infection can originate from the outside environment, another infected patient, staff that may be infected, or in some cases, the source of the infection cannot be determined. In some cases the microorganism originates from the patient's own skin microbiota, becoming opportunistic after surgery or other procedures that compromise the protective skin barrier. Though the patient may have contacted the infection from their own skin, the infection is still considered nosocomial since it develops in the health care setting. The most common preventions of nosocomial infection are, before surgery cleaning and washing hand carefully and use mask, globs. There are other key policies important in the control of infection including policies that will reduce the infection risk from use of catheters, tubes, cannulas, and those regarding the prudent use of antibiotics. However, infection control is a complex problem. For example, HAI risks are greatly increased by extensive movement of patients in the hospital, by high bed occupancy, and by an absence of facilities to isolate infected patients.

**Key words:** HAI, spread, environment, cleanliness





## DRUG OVERDOSE

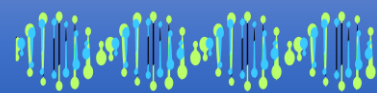
*\*Sunil Kumar Chauhan, Rakesh Sharma, Anupam Sharma, Neelkanth M. Pujari  
Lucknow Institute of Pharmacy, Lucknow (U.P.)*

### Abstract

The term drug overdose (or simply OD) describes the ingestion or application of a drug or other substance in quantities greater than are recommended or generally practiced. An overdose may result in a toxic state or death. Overdoses aren't exclusive to street drugs. Prescription and over-the-counter drugs intended to heal and help us, when used in the wrong way, can be dangerous and addictive— even lethal. Still, this doesn't count out illegal street drugs, as many people do abuse them with seriously negative side effects. Mainly pain reliever drugs are cause overdosing, symptoms of pain reliever such as constipation, pinpoint pupils, nausea, vomiting, intestinal tract or stomach spasms, weak pulse, slow breathing, low blood pressure and arises other symptoms. Symptoms of opioid overdoses include slow breathing, heart rate and pulse. Opioid overdoses can also cause pinpoint pupils, and blue lips and nails due to low levels of oxygen in the blood. Patients often abuse legal medications worldwide. Yearly overdose deaths, and the drugs involved are more than 64,000 deaths estimated in 2016, the sharpest increase occurred among deaths related to fentanyl and fentanyl analogs (synthetic opioids) with over 20,000 deaths. The Centers for Disease Control and Prevention (CDC) estimates that U.S. programs for drug users and their care givers prescribing take-home doses of naloxone and training on its utilization are estimated to have prevented 10,000 opioid overdose deaths. Stabilization of the victim's airway, breathing, and circulation (ABCs) is the initial treatment of an overdose. Specific antidotes are available for certain overdoses. Foreexample, Naloxone is the antidote for opiates such as heroin or morphine. Similarly, benzodiazepine overdoses may be effectively reversed with flumazenil.

**Keywords:** Drug abuse, overdose, drug poisoning, prevention





## ALZHEIMER'S DISEASE

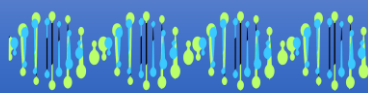
*Sweta Shukla, Richa Tiwari, Rakesh Sharma, Neelkanth M. Pujari*

### ABSTRACT

Alzheimer's disease is a degenerative brain disease and the most common cause of dementia. Dementia is a syndrome a group of symptoms—that has a number of causes. The characteristic symptoms of dementia are difficulties with memory, language, Special Report examines how the use of biomarkers may influence the AD diagnostic process and estimates of prevalence and incidence of the disease. An estimated 5.5 million Americans have Alzheimer's dementia. By mid-century, the number of people living with Alzheimer's dementia in the United States is projected to grow to 13.8 million, fueled in large part by the aging baby boom generation. Today, someone in the country develops Alzheimer's dementia every 66 seconds. By 2050, one new case of Alzheimer's dementia is expected to develop every 33 seconds, resulting in nearly 1 million new cases per year. In 2014, official death certificates recorded 93,541 deaths from AD, making AD the sixth leading cause of death in the United States and the fifth leading cause of death in Americans age 65 years. Between 2000 and 2014, deaths resulting from stroke, heart disease, and prostate cancer decreased 21%, 14%, and 9%, respectively, whereas deaths from AD increased 89%. The actual number of deaths to which AD contributes is likely much larger than the number of deaths from AD recorded on death certificates. In 2017, an estimated 700,000 Americans age 65 years will have AD when they die, and many of them will die because of the complications caused by AD. In 2016, more than 15 million family members and other unpaid caregivers provided an estimated 18.2 billion hours of care to people with Alzheimer's or other. Total payments in 2017 for health care, long-term care, and hospice services for people age 65 years with dementia are estimated to be \$259 billion. In recent years, efforts to develop and validate AD biomarkers, including those detectable with brain imaging and in the blood and cerebrospinal fluid, have intensified. Such efforts could transform the practice of diagnosing AD from one that focuses on cognitive and functional symptoms to one that incorporates biomarkers.

**Keywords:** alzheimer's disease; alzheimer's dementia; dementia; diagnostic criteria





## JAPANESE ENCEPHALITIS

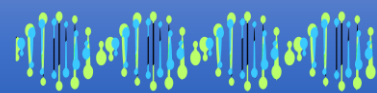
*'Palak Agrawal'*

*'Saroj Institute of Technology And Management'*

Japanese encephalitis is a neurologic infection with a broad range of manifestations. It is caused by the JEV, a flavivirus. It is a mosquito-borne viral infection. It is spread by bites of culicine mosquitoes, most often *Culex tritaeniorhynchus*. People in rural areas where the virus is common are at highest risk. It is more likely to affect children, because adults in areas where it is endemic generally become immune as they get older. Less than 1 percent of people infected with the virus develop symptoms. However, according to the WHO, it is fatal for 30 percent of those who do develop symptoms. It is most common in Japan and Southeast Asia. Vietnam, Cambodia, Myanmar, India, Nepal, and Malaysia still experiences epidemics occasionally. A person with JE will probably have no symptoms at all, but if there are symptoms, they will appear 5 to 15 days after being infected. JE is an inflammation of the brain which can cause fever, headache, confusion, seizures, and, in some cases, death. Humans can get the disease when they are bitten by a mosquito that carries the virus. This virus cannot be transmitted from one person to another. After attachment of the JEV to a host cell membrane, disruption may lead to entry of the virus into the cell itself. The virus initially propagates at the site of the bite and in regional lymph nodes. JEV-specific IgM capture ELISA on cerebrospinal fluid (CSF) is the standard diagnostic test for JE. There is a safe and effective vaccine that can prevent infection. The vaccine is given as a 2-dose series, with the doses spaced 28 days apart. Children younger than 3 years of age get a smaller dose than patients who are 3 or older. Anyone who has had a severe allergic reaction to a dose of JE vaccine should not get another dose. JEV likely represents the first mosquito-transmitted viral pathogen to affect neural stem cells.

**Keywords-** JE: Japanese Encephalitis, JEV: Japanese encephalitis virus,





## SYNTHESIS & BIOLOGICAL EVALUATION OF BENZIMIDAZOLE FLUOROQUINOLONES DERIVATIVE AS ANTIMICROBIAL AGENTS

Bhavana Dubey \*

\* *Pharmaceutical chemistry Research Laboratory, Department of Pharmacy, Saroj Institute of Technology & Management, Lucknow-226002, India*

### ABSTRACT

Increasing multidrug-resistant pathogens have become a serious problem, particularly during the last decade. A more controlled usage of these drugs may be a way to partially counterbalance these challenges. However, the design of new agents active against resistant organism remains the critical importance. Benzimidazole is a heterocyclic aromatic organic compound. This bicyclic compound consists of the fusion of benzene and imidazole. Benzimidazole in an extension of the well elaborated imidazole system, has been used as carbon skeleton for N- heterocyclic carbenes. In recent years, fluoroquinolones research has focused on achieving several goals, including (1) enhanced potency against gram-positive cocci, notably *Streptococcus pneumoniae*, and anaerobes, while (2) maintaining potency against gram-negative pathogens, (3) optimizing pharmacokinetics and pharmacodynamics (PK/PD), and (4) minimizing potential adverse drug reactions through recognition and avoidance of structural configurations that have characterized earlier, reactive compounds. In this project we synthesis the different Fluoroquinolones Benzimidazole Hybrids as antimicrobial agent. Fluoroquinolones are broad-spectrum antibiotics that play an important role in treatment of serious bacterial infections, especially hospital-acquired infection and other in which resistance to older antibacterial classes is suspected. Because the use of broad-spectrum antibiotics encourages the spread of multidrug resistant strains so these benzimidazole hybrids includes Ciprofloxacin, Gatifloxacin and Norfloxacin Fluoroquinolones are used with secondary amine like dimethylamine, pyrrolidine, piperazine, piperidine to make active Mannich bases. These Mannich bases hybrids were identified and confirmed by FT-IR, NMR and elemental analysis. The antimicrobial assay of these synthesized analogues was tested against *H. pylori*, *E. coli* (ATCC 35218), *P. auroginosa* (ATCC 2485), *S. typhi* (MTCC 3216), *B. subtilis* (MTCC 2423), *B. threogensis*, *S. aureus* (MTCC 1430) *MRSA* and *A. niger* and were found to be active.

**Keywords** Benzimidazole, antimicrobial agent, fluoroquinolones, H.pylori, E. coli







## ACNE

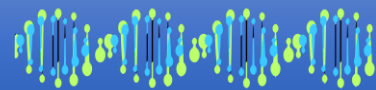
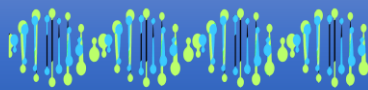
*Ram Janam Maurya\*, Ravi Prakash Yadav, Dinesh Kumar Shakya and Ashutosh Kumar*

### ABSTRACT

Acne, also known as acne vulgaris, is a long-term skin disease that occurs when hair follicles are clogged with dead skin cells and oil from the skin. It is characterized by blackheads or whiteheads, pimples, oily skin, and possible scarring. It primarily affects areas of the skin with a relatively high number of oil glands, including the face, upper part of the chest, and back. The resulting appearance can lead to anxiety, reduced self-esteem and, in extreme cases, depression or thoughts of suicide. Genetics is thought to be the primary cause of acne in 80% of cases. The role of diet and cigarette smoking is unclear, and neither cleanliness nor exposure to sunlight appear to play a part. During puberty, in both sexes, acne is often brought on by an increase in hormones such as testosterone. A frequent factor is excessive growth of the bacterium *Propionibacterium acnes*, which is normally present on the skin.

**Keywords** Acne, anxiety, cigarette smoking, *Propionibacterium acnes*.





## ADAPTOGEN'S

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*Saroj Institute of Technology & Management , Lucknow*

### ABSTRACT

The adaptogens or adaptogenic substances which refer to a pharmacological concept where by administration results in stabilization of physiological process and promotion of homeostasis which decrease sensitivity to stress. The concept was created in 1947 to describe a substance that may increase resistance to stress. The mechanisms of action of adaptogens are specifically related to stress-protective activity and increased adaptability of the organism.

Adaptogens exhibits beneficial effects against chronic inflammation Atherosclerosis , Neurodegenerative cognitive impairment metabolic disorder , cancer , and other aging related diseases. "Adaptogens are also considered metabolic regulator which increase the ability of an organism to adopt to environmental factor and to avoid damage from such factors"

**Keywords** Homeostasis , Stress , Adaptability , Atherosclerosis





## ANAEMIA

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### ABSTRACT

Anemia means that you have fewer red blood cell than normal or you have less hemoglobin than normal in each red blood cell. In other case a reduce amount of oxygen in the bloodstream. Symptoms of anemia are tiredness, feeling faint and becoming easily breathless and headaches, altered taste, and ringing in the ears and the people look pale. Lack of iron is called iron deficiency anemia. Pregnancy or child growth a person need more iron than usually. During menstrual period the amount of iron that we eat may not be enough to replace the amount that you lose from heavy periods. Some intestinal diseases are also there like colic disease in which there is a poor absorption in our body. A simple blood test can measure the amount of hemoglobin in our blood and count the number of red blood cells per milliliter. Sometimes the underlying cause is obvious, for example, anemia is common in pregnancy and in women who have heavy menstrual periods. In these situations, no further tests may be needed and treatment with iron tablets may be advised.

**Keywords-** anemia, hemoglobin, coeliac disease





## PREPARATION AND EVALUATION OF MICROSPHERES CONTAINING ESSENTIAL OIL

*Archana*

### ABSTRACT

Essential oil has been reported to possess an antimicrobial (Antifungal and antibacterial) action. However, its application in topical preparations is not possible due to its rapid volatility and skin irritation. The objective of this study was therefore to reduce the rate of evaporation of the oil and skin irritation via microencapsulation. Microspheres were prepared using emulsion method and the microspheres were hardened with a cross-linking agent, NaOH. The effects of three variables, stirring rate, amount of cross-linking agent, and Drug – Polymer ratio on entrapment efficiency were studied. The microspheres under the optimized conditions provided Entrapment Efficiency of 78.3%. Based on the FT-IR and DSC reveals that the developed microspheres contained the chemical ingredients and functional groups of the wall material (chitosan) and the core active ingredient (Essential oil). The overall results confirm the development of microspheres containing essential oil and there was some interaction between drug and polymer and the drug was uniformly dispersed in polymer matrices at molecular level. Therefore, it could be concluded that microencapsulation of essential oil can prolong the anti-microbial and anti-fungal action for at least 10<sup>th</sup> hr thus minimizing the direct contact of oil to the skin thereby reducing the skin irritation property of oil and indicating their potential in improving patient acceptance and topical delivery of essential oil.

**Keywords-** DSC (Differential scanning calorimetric), FT-IR (Fourier transform infrared spectroscopy), SEM (Scanning electron microscopy).





## INFLUENZA VIRUS(H4N2)

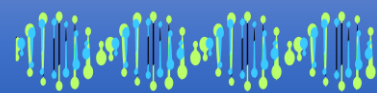
*Ashish Kumar Gupta*

*Saroj Institute of Technology And Management Lucknow*

A type of Influenza virus  $h_4N_2$  is called as I virus, a novel virus invented or manmade virus. This type of influenza virus rarely infect human being. It is mostly observed to affect the birds and animals. It is labeled as 2 strands of hemagglutinin (H) and 4 strands of neuraminidase (N). H antigens vary from H1 to H18 and N antigens varies from N1 to N11, totally these 18 H and 11 N various combinations give rise to different influenza virus based on chemical characteristics. The I virus ( $h_4N_2$  influenza virus) basic characteristic is changing physiology.  $H_4N_2$  influenza virus develops through 3 stages. In the first stage, anterior pituitary glands grow very fast and the epithelial cells forming mature glands. In the second stage epithelial cells will become flatter and lumen enlarges abnormally. Influence of adreno cortical hormones, full secretory. The third stage or final stage of  $H_4N_2$  influenza virus is the development stage where resting glands in the formed ducts. It will be like a Mammary tumor virus (MTV).

Keyword:- Hemagglutinin, neuraminidase, Mammary tumor virus.





## AWARENESS FROM SMOKING

*Saumya Shukla\* and Pratima Sen*

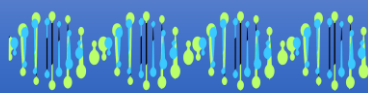
*\* Pharmaceutical Chemistry Research Laboratory, Department of Pharmacy, Saroj Institute of Technology & Management, Lucknow-226002, India*

### ABSTRACT

Smoking is associated with increased risk of cardiovascular and chronic respiratory disease, stroke and cancers of many organs of the body such as mouth, larynx, lungs, kidneys, cervix and pancreas. There are significant negative impacts of smoking on health-care system and society causing huge direct health-care expenditures and indirect costs in the form of loss of productivity and income for families. Smokers live approximately 10 years lesser than non-smokers, and smoking cessation efforts can reduce 97% risk of death associated with continuing smoking before the age of 30 years. Adolescents are vulnerable to starting smoking and becoming addicted to nicotine because they go through rapid hormonal and cognitive changes during their adolescence and they are influenced by cultural, social, families and behavioral factors. The factors that lead adolescents to start smoking include advertising of cigarettes, stress, low self-esteem, poor academic performance and occurrence of smoking among parents and other members, friends. According to the WHO, 6 million people die because of tobacco smoking and an estimated 600,000 individuals lose their lives due to second hand smoke globally each year. Increasing the awareness about the harmful effects of tobacco consumption on health should be incorporated in smoking campaigns and programs. The academic environment in schools can help reduce tobacco use among adolescents.

**KEY WORDS:** Smoking, Tobacco, Adolescence, Health-care, Awareness.





## LUNG CANCER

*Nancy Anand*

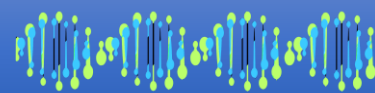
*Saraj Institute of Technology & Management , Lucknow*

### **ABSTRACT:**

Lung cancer is the top cancer killer and smoking remain the leading preventable cause of death in the US. Furthermore ,major disparities in smoking and lung cancer exist by education,income and race. While tobacco control polices are the most effective strategies to prevent lung cancers,lung cancer computed tomography CT screening has also been shown to reduce lung cancer risk among heavy current and former smokers. the cancer intervention and surveillance modling network CISNET lung group develop and applies population models for lung cancer, quantifying the impact of tobacco cobtrol and CT screening on the lung cancer and all cause mortality.

**KEYWORD:-** Tobacco, Smoking,Ct-Screening,Cisnet





## ISOLATION OF THE BIOACTIVE COMPOUNDS FROM INDIAN MEDICINAL PLANT *ECLIPTA ALBA*

Saumya Shukla\*

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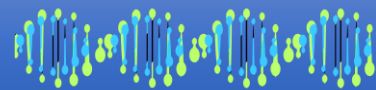
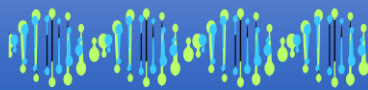
### ABSTRACTS

*Eclipta alba* (Linn) Hassk. (Asteraceae) commonly known as 'Bhingraj' has been used in Indian traditional systems of medicine and also by traditional healers since ancient times, especially in the southern region of India for the treatment of cancer. Aerial parts of *Eclipta alba* are used traditionally for the treatment of several diseases of liver, skin and stomach. *Eclipta alba* contains wide range of active principles which includes coumestans, alkaloids, flavonoids, glycosides, polyacetylenes, and triterpenoids, stigmaterol, a-terthienylmethanol, wedelolactone, demethylwedelolactone and demethylwedelolactone-7-glucoside. It is a good source of thiophene derivatives which are effective against cancer cells. From *Eclipta alba*, trithiophene derivative was isolated by column chromatography followed by characterization of isolated compounds by UV, IR, NMR and Mass spectroscopy.

**Keywords** *Eclipta alba*, demethylwedelolactone, thiophene derivatives, chromatography.







## EBOLA VIRUS

*Sakshi Gupta*

*Saroj Institute of Technology & Management , Lucknow*

### ABSTRACT:-

Ebola virus is transmitted to people as a result of direct contact with body fluid containing virus of an infected patient. The incubation period usually lasts 5 to 7 days approximately 95% of a patient appear signs within 21 days after exposure. Typical features include fever, profound weakness, diarrhea, abdominal pain, cramping, nausea, and vomiting for 3 to 5 days and may be persisting for up to a week. Laboratory complications including elevated amino transferase levels, marked lymphocytopenia, and thrombocytopenia may have occurred. Hemorrhagic fever occurs in less than half patients and it takes place most commonly in the gastrointestinal tract.

One is a chimpanzee adenovirus vector vaccine, other vaccines involve replication defective adenovirus serotype 5 and recombinant vesicular stomatitis virus.

**KEYWORDS:-** Diarrhea , cramping , lymphocytopenia, thrombocytopenia.





## **ZIKA VIRUS**

*Sourabh Kumar Patel*

*Saroj Institute of Technology & Management , Lucknow*

### **ABSTRACT:-**

The history of zika virus disease serves as a paradigm of a typical emerging viral infection zika virus disease mosquito borne flavivirus was first isolated in 1947 in the zika forest of uganda. The same virus was isolated from jungle-dwelling mosquitoes.

Zika virus was imported to northern brazil possibly during the world soccer championship that was hosted by brazil in june through july 2014.

A cluster of severe fetal malformations microcephaly and ocular defects was noted in 2015 in the northeast of Brazil and intrauterine infection with zika virus were confirmed. The dramatic change in zikavirus photogenicity upon its introduction to Brazil has remained an enigma.

**KEYWORDS:-** Flavi virus , Photogenicity, Jungle-dwelling mosquito- oes, Intrauterine infection





## WHAT IS A BRAIN STEM STROKE?

*Surya prakash\**

*Saroj Institute of Technology And Management Lucknow*

A stroke occurs when blood supply to the brain is interrupted. The way a stroke affects the brain depends on which part of the brain suffers damage, and to what degree. Sitting just above the spinal cord, the brain stem controls your breathing, heartbeat, and blood pressure. It also controls your speech, swallowing, hearing, and eye movements. Impulses sent by other parts of the brain travel through the brain stem on their way to various body parts. We're dependent on brain stem function for survival. A brain stem stroke threatens vital bodily functions, making it a life.

Other conditions that increase your risk of stroke include:

- high blood pressure
- high cholesterol
- diabetes
- cardiovascular disease
- certain blood disorders
- pregnancy
- cancer





## THALASSEMIA

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### ABSTRACT

Thalassemia is an inherited blood disorder caused when the body doesn't make enough of a protein called hemoglobin, an important part of red blood cells. Thalassemia is a treatable disorder that can be well managed with blood transfusions and chelation therapy. Vaccines can help protect us against a number of serious diseases. If anyone is receiving blood transfusions as part of the treatment, it is important that the person should be vaccinated against hepatitis A and B. These are viruses that can be spread through blood. Its severeness can be profiled by its treatment. The more severe the thalassemia, the less hemoglobin the body has. One way to treat anemia is to provide the body with more red blood cells to carry oxygen. This can be done through a blood transfusion. It is a procedure in which you receive blood through a small plastic tube inserted into one of our blood vessels. People suffering from thalassemia major need regular blood transfusions because their body makes such low amounts of hemoglobin. People with thalassemia inter media may need blood transfusions sometimes, such as when they have an infection or an illness. People with thalassemia minor usually do not need blood transfusions because they either do not have anemia. A person with thalassemia will need to receive medical care on a regular basis from a hematologist.

**Key words;** - Thalassemia, Hemoglobin, Blood transfusions, Hematologist, Vaccine.





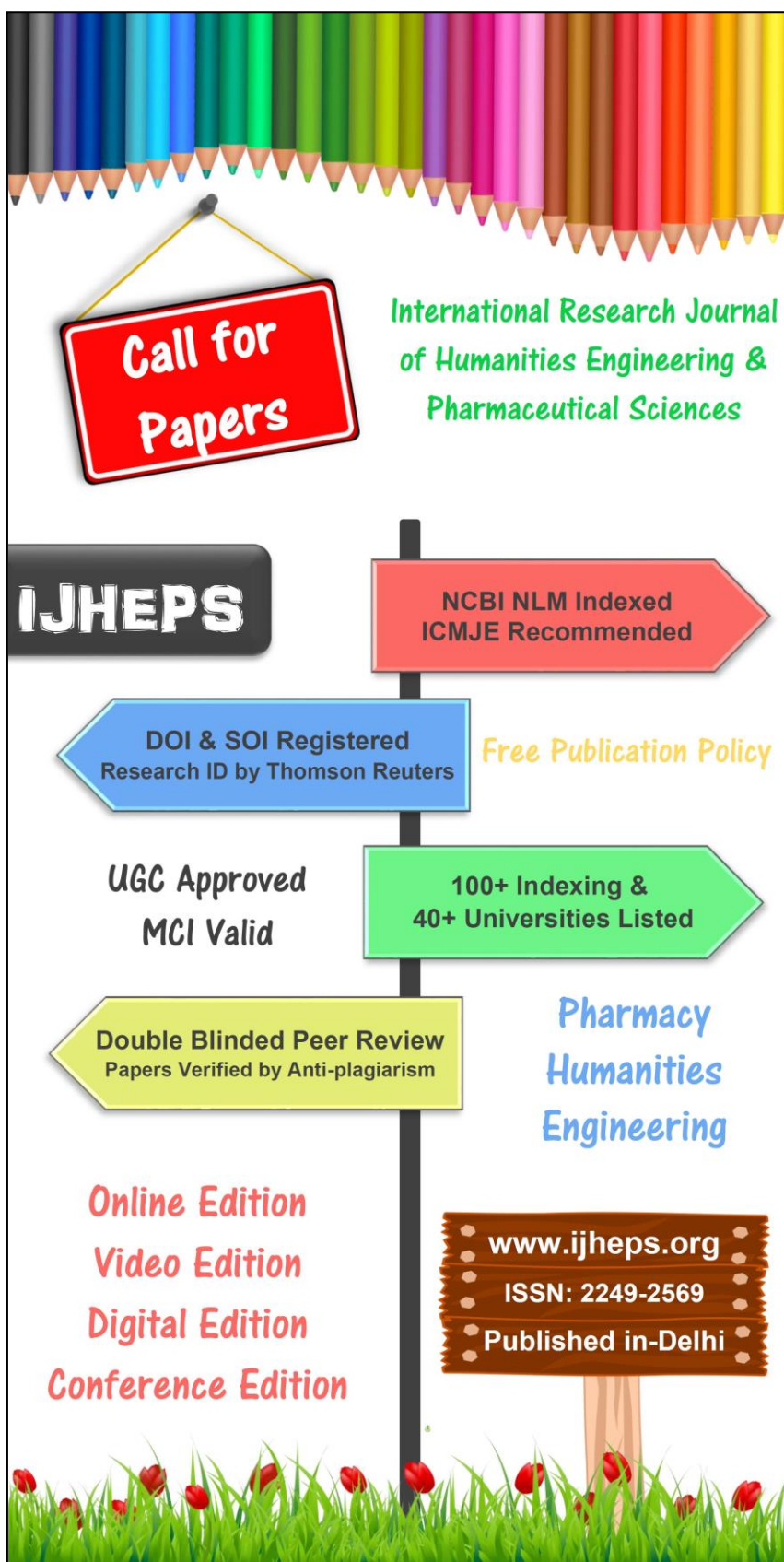
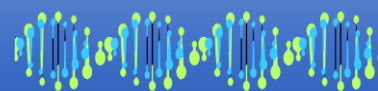
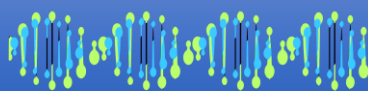
## ANALYTICAL METHODS FOR QUALITY CONTROL OF HERBAL PRODUCTS

*Ansari Alhaza Mohammed Arif, Arvind Kumar Sirvastava  
United Institute of Pharmacy Naini Allahabad*

The herbal products are complex mixtures that originate from biological sources. Recently, Growth and popularity of herbal products have taken in healthcare. The physical and chemical characters are used to evaluate quality of herbs and quality standards. Each Countries (Such as:- India, Japan, Korea, China, USA etc.) has its own guidelines to assess the quality control of herbal products. The techniques used in quality control of herbal products are Thin Layer Chromatography {TLC}, High Performance Liquid Chromatography {HPLC}, Gas Chromatography {GC}, Mass Spectrometry {MS} and Infrared Spectrometry {IR}. The fingerprint analysis has been internationally accepted as one of the efficient methods to control the quality of herbal products. Chemical fingerprints obtained by chromatographic thenique. The current scenario is that botanical parameters like sensory or organoleptic evolution, histological observations and measurements are in discuss.

**Key Words :** Chromatography, Herbal products, Quality Control





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