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FUNCTIONALIZED LIPID-POLYMER HYBRID NANOPARTICLES MEDIATED TARGETED DRUG DELIVERY

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Abstract:

For many decades, the interest in modifying drug delivery system has been a prominent thrust of pharmaceutical research. Nanotechnologies have been enormously used in the last two decades to facilitate the delivery of therapeutics and imaging agents for various medical application[1]. Polymeric nanoparticles (PNs) and liposomes mainly represent two primary delivery of nanocarrier capable of encapsulating and delivering a variety of drug classes. But these nanoparticles face certain challenges in targeting drug delivery due to poor solubility, lesser stability resulting in early disintegration of the drug in the blood stream and lesser systemic circulation half-life. They too have lesser drug loading capacity and early drug release problems[2]. These factors remain to limit their application to a certain extend. To overcome these limitations, both PNs and liposomes have been combined to develop a newer novel platform, named "Lipid-Polymer Hybrid nanoparticles (LPHNs)" that combines the positive attributes of liposomes and PNs excluding their shortcomings[3]. These LPHNs have a hydrophobic polymeric core where poorly soluble drugs can be encapsulated, a hydrophilic polymeric shell to enhance nanoparticles stability and systemic circulation half life, a lipid monolayer to promote drug retention inside the polymeric core, thereby enhancing drug encapsulating efficiency, increasing drug loading yield and controlling drug release. In this review, special types of LPHNs structures are discussed in details introducing the synthesis and surface functionalization techniques of the LPHNs followed by a typical characterization of the particles approaching targeted drug delivery by LPHNs, summarizing the current and the potential medical application of these new hybrid nanoparticles.

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Keywords: Nanotechnology, lipid-polymer hybrid nanoparticles, drug targeting, surface functionalization.

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IN- SILICO APPROACH TOWARDS LEAD IDENTIFICATION FROM PHYTOCONSTITUENTS OF *HOMALOMENA AROMATICA* SCHOTT. AGAINST *ENTAMOEBA HISTOLYTICA*.

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Abstract:

Background: It is being reported that 40 to 50 million people suffer from amoebiasis worldwide which is estimated to cause more than 100,000 deaths per year (Abhyankar et al. 2012). Metronidazole, the drug of choice in amoebiasis caused by *E. histolytica* is reportedly cytotoxic with sporadic cases of resistance. The rhizome of *H. aromatica* is used by different tribes of north-east India to treat stomach ailments (Majumdar & Datta 2007).
Objective: The objective of the present study is to identify lead compounds from *H. aromatica* against amoebiasis caused by *E. histolytica* with the help of *in-silico* screening technique.
Methods: The phytoconstituents of *H. aromatica* were docked on thioredoxin reductase, cysteine synthase, glyceraldehyde-3-phosphate dehydrogenase and ornithine decarboxylase proteins of *E. histolytica* using Biovia Discovery Studio 2017 R2 (DS 2017 R2). Toxicity profiling of the molecules were performed by toxicity prediction protocol of DS 2017 R2. Docking weighted network pharmacology approach was performed by application of Cytoscape V3.4.0 software to draw a relationship between the phytoconstituents and proteins. The best networked phytoconstituents were further analysed by Density functional theory (DFT) analysis to identify the lead compounds (Smoot et al. 2011).
Results and Discussions: Based on the docking weighted network pharmacology approach and DFT results 3,7-dimethylocta-1,6-dien-3-yl acetate, α-methyl-α-(4-methyl-3-pentenyl)-oriranemethanol and 7-octadiene-2,6-diol-2,6-dimethyl were identified as lead compounds.
Conclusion: Three compounds were identified as lead compounds. Structural modifications could possibly bring out potent drug molecules by

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considering the phytoconstituents in the present study. This *in silico* study would provide ample opportunities for further research.

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DENDRIMERS AS NANOBIOPOLYMER IN DRUG DELIVERY APPLICATION

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Abstract:

Biopolymers are polymers that are produced from living organisms is important to control particle size, charge, morphology of surface and release rate of loaded molecules to use biopolymer-based nanoparticles for drug/gene delivery [1]. Biopolymers provide a plethora of applications in medicines, food and petroleum industries, because of its low toxicity, biodegradability, high bioactivity, stability and appropriate mechanical properties. To obtain nanocarriers for therapeutic purposes, a variety of biomaterials and preparation process has been attempted [2]. Dendrimers are new classes of nanobiopolymeric materials have a well defined size, shape, molecular weight and monodispersity. Currently, dendrimers are great interest for delivering drug molecules via different routes. The nanoscopic size and recognition abilities make dendrimers as ideal building blocks for self-assembly and self-organization systems. The inside cavities of the dendrimers can be able to incorporate both hydrophobic or hydrophilic drugs and the terminal groups are modified to attach to antibodies, bioactive substances for targeting purposes [3]. This review summarizes the various structural aspects and properties of dendrimers along with their pharmaceutical application as a potential drug delivery carrier.

Keywords: *Biopolymers, nanotechnology, dendrimers, drug targeting.*

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NANOSTRUCTURED LIPID CARRIERS IN TOPICAL AND TRANSDERMAL APPLICATION

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Abstract:

Transdermal drug delivery is one the most important alternative to parental administration. The biggest challenge in percutaneous absorption is to overcome the stratum corneum barriers and maintain skin integrity at the same time [1,2]. Nanostructured lipid carriers (NLCs) have attracted broad interests for transdermal drug delivery because of its capability of film formation, skin hydration and control occlusion. NLCs contains both solid and liquids lipids, at room temperature the structure of NLCs provides better penetration for loaded drug and enhance the percutaneous permeation/absorption. NLCs are colloidal carriers which are more advanced as compared to polymeric, carbon-based, metal-based nanoparticles in case of drug loading, targeted drug delivery and less expensive etc [3]. This review reports the various preparation methods of NLCs, transdermal drug delivery mechanism, benefits and important aspects of NLCs in topical and transdermal drug delivery.

Keywords: *Transdermal drug delivery, Topical drug delivery, NLCs.*

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NANOTOXICOLOGICAL CLASSIFICATION: A REVIEW

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Abstract:

Background: Nanotechnology is an emerging area applied to design novel carriers for drug delivery(Ae et al., 2008), which has changed the concept and prospects of drug delivery technology.However, the industry mostly focuses on formulation development and marketing of products without much consideration of possible potential toxicological effects on human health and environment.

Objective: The purpose of this review is to study and highlight toxicity issues and classification of nanoparticles based on their toxicity.

Methods: Extensive literature survey was carried to identify the key factors for nanomaterial classifications and the findings are summarized from the available literature.

Results and Discussion: Nanoparticulate drug delivery systems include liposomes, nanoemulsions, nanocrystals and polymeric lipid nanoparticles. These particles may necessarily possess side effects with the immune system. The presence of impurities and oxidative stress in nanomaterials produce toxicological effects. Nanoparticles are classified based on persistency in three classes – no or low risk; medium risks; high risk and on the basis of size these are classified into four classes (Keck & Müller, 2013). The classification based on size also considers the biodegradability of nanoparticles(Janrao, Gadhave, Banerjee, & Gaikwad, 2014). However, predictability of delayed toxicity in case of nano sized pharmaceuticals is questionable. This also calls for urgent attention from the pharmaceutical researchers.

Conclusions: The classification system serves as a guideline in pharmaceutical formulation development and also provides guidance for risk assessment and management associated with human, animal and environment. Monitoring and maintaining properly the associated parameters, nanoparticles would prove to be a boon to therapy.

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Keywords: Nanotechnology; Nanotoxicity; Oxidative stress.

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ETHOSOMES: A NOVEL VESICULAR SYSTEMS TO ENHANCED TRANSDERMAL DELIVERY

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Abstract:

The aim is to focus on the applicability of ethosomes (lipid based vesicular system) on transdermal drug delivery system, their mechanism, factors affecting their permeation and penetration efficiency, methods of preparation and evaluation parameters. Ethosomes are lipid based carriers and may be denoted as modified liposomes, which were first reported by Touitou *et al*., 2000. Ethosomes have similar structure like that of liposomes i.e. it exhibit a bilayer of lipid but differ with the presence of a high concentration of ethanol. They are noninvasive, soft and flexible vesicles in which an active agent can be incorporated to deliver through the skin. The size range of ethosomes varies from few nanometers to micrometers depending on the methods of preparation and application (Chourasia et al. 2011). It can well entrap hydrophilic, lipophilic and amphiphilic compounds. Active agents can be delivered to the deeper layer of the skin i.e. to the dermal layer overcoming the natural barriers of the skin. It increased the permeability which may be due to the synergistic mechanism between ethanol, phospholipids and the skin lipids. Ethanol increases the fluidity of the lipids of both the ethosomes and skin, provide a soft flexible vesicles for easy penetration through the skin. The ethosomes fuse with the skin lipids and release the drug along the penetration pathway (Limsuwan & Amnuaikit 2012, Sarwa et al. 2014, Touitou et al. 2000).

Keywords: Lipid based vesicular system; Ethosomes; Transdermal drug delivery system; Ethanol.

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HYBRID 4-AMINOQUINOLINE 1,3,5-TRIAZINE: SYNTHESIS AND *IN-VITRO* ANTIMALARIAL EVALUATION

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Abstract:
Background: Malaria is one of the world's greatest global public health challenges. It is most prevalent in sub-African, Asian, and South American countries, and it mostly affects children under the age of five and pregnant women [1]. The emergence of chloroquine resistance, particularly in *P. falciparum* has dramatically reduced the chemotherapeutic options [2].
Objectives: The present research work deals with the design and synthesis of hybrid 4-aminoquinoline 1,3,5- triazine as antimalarial agents.
Methods: Novel hybrid molecules were synthesized by simple neucleophilic substitution reaction. Antimalarial activity of synthesized compound was evaluated against chloroquine-sensitive (3D-7) strains of *P. falciparum* using chloroquine as standard drug.
Results: The present study disclosed that title compounds were synthesized and their chemical structures were confirmed by FT-IR, ^{13}C-NMR, ^{1}H-NMR, Mass, and elemental analysis. Among the synthesized compounds only isopropylamine substitution on triazine showed low antimalarial activity and Cyclohexyal ethylamine substitution on triazine show mild to moderate activity (***% dead rings + schizonts)*** using chloroquine as standard drug.
Conclusion: The present study revealed that hybrid derivative may be utilized as lead molecules for antimalarial activity.
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ANTIBACTERIAL SCREENING OF SOME MEDICINAL PLANTS OF ASSAM USED IN TRADITIONAL MEDICINES

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Abstract:

Background: Screening of plants for medicinal activity is the first and most essential step in the search for new medicinal compounds under any drug discovery and development programmes.
Objective: Design of the present study was made aiming to the screen the antibacterial activity of three plants used traditionally in Assam by measuring the zones of inhibition on bacteria.
Methods: Antibacterial activity evaluation of three indigenous plants of Assam used in traditional treatment of bacterial infection was carried out by preparing methanolic extract against three gram positives and three gram-negative bacterial strains as per the standard disc diffusion method[1] using ciprofloxacin injection IP, 25µg/ml as the standard control drug. The evaluation was carried out by using test solutions with a concentration of 100µg/ml of the methanolic extracts of *Musa balbisiana[2,3], Moringa oleifera* [4] *and Calotropis procer [5].*
Results & Discussion: *Among the extracts, Moringa oleifera* extract showed good activity against only *Pseudomonas aeruginosa* while *Musa balbisiana* extract showed very good activity against two strains, *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Calotropis procera* showed very good activity against two bacterial strains, *Micrococcus luteus* and *Bacillus subtilis* at the tested concentration.
Conclusion: So, this type of study will help to establish newer plants having an antimicrobial property which will be cost effective as they are present into our nature. The ultimate result of such study will establish a new benchmark in the field of antimicrobial agents which will open so many aspects for future study to develop a new product with lesser toxicity, greater efficacy and less adverse drug reaction.

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EVALUATION OF *IN VITRO* ANTIOXIDANT ACTIVITY OF DIFFERENT FRACTIONS OF METHANOLIC EXTRACT OF LEAVES OF *ANNONA RETICULATA* LINN.

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Abstract:

Background: *Annona reticulata* Linn. (Bullock's heart) is a versatile tree and its fruits are edible. Parts of *A. reticulata* are used as source of medicine and also for industrial products[1]. It possesses several medicinal properties such as anthelmintic, analgesic, anti-inflammatory, antipyretic, wound healing and cytotoxic effects[2].

Objective: The present study has been designed to determine the anti-oxidant activity of four different fractions of methanolic extracts of leaves of *Annona reticulata* Linn.

Methods: Antioxidant activity of different fractions of methanolic extract of leaves of *Annona reticulata* Linn. eluted by column chromatography was studied for its free radical scavenging property on different in vitro models e. g. - 1, 1-diphenyl-2picryl hydrazyl (DPPH) method, nitric oxide method and hydrogen peroxide method [3,4,5].

Results: The fractions showed good dose dependant free radical scavenging property in all the models. DPPH, H_2O_2 and Nitric oxide scavenging effect of different fractions of leaf extracts of *Annona reticulata* i.e. F1, F2, F3 and F4 were found to be dose dependant with maximum inhibition at highest concentration 400µg/ml. Fraction -**F2** is found to have most potent anti-oxidant activity in all three in vitro methods. IC50 value DPPH,H_2O2 and nitric-oxide inhibition of fraction -F2 are 70.09%, 68.04% and 68.04%. Fractions- **F1** and **F3** also showing remarkable anti-oxidant activity.

Conclusion: Hence *Annona reticulata* leaf extracts have been found to show promising effect against DPPH, hydrogen peroxide and nitric-oxide Ascorbic acid was used as standard.

Keywords: Antioxidant, *Annona reticulata*, Methanolic ,Free radical scavenging and ascorbic acid.

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LIPID-BASED NANOCARRIERS FOR ORAL DRUG DELIVERY SYSTEM

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Abstract:

Though oral drug delivery is the most convenient way of drug administration but issues like poor solubility, stability and bioavailability of many drugs have cause a tremendous challenge in achieving therapeutic levels through the GI tract. Lipid-based drug delivery system has become one of the most emerging techniques in the field of medicine where the drugs are formulated with the goal of enhancing bioavailability. Lipid-based nanostructured drug delivery system includes Solid Lipid Nanoparticles, Nanostructured Lipid Carriers, Liposomes have emerged as potential carriers of drug, especially for lipophilic compounds in order to improve gastrointestinal absorption, oral bioavailability and therapeutic effectiveness. Solid lipid nanoparticles, newer generation lipid nanoparticle, nanostructured lipid carriers are hugely studied for their capability as oral drug carriers. Homogenisation technique is one of the reliable processes for the preparation of lipid-based nanoparticles. Lipid-based nanostructures have come up with many benefits including prolonged and sustained drug release, stability enhancement and protection of drug from gastrointestinal degradation. Recent advances have led to efficacious and profitable commercialization of lipid-based formulation of wide variety of drugs like anti-tumour agents, antiviral, antibacterial, antifungal and antimicrobial. Some of the marketed oral nanocarrier based formulations include Cyclosporin, Estradiol, Heparin, Docetaxel, Lovastatin, Paclitaxel, Timolol (1-5). This paper highlights diverse lipid based nano drug delivery system for oral drug delivery using nanostructured systems for bioavailability enhancement of various drugs belonging to the BCS class II to IV. It also highlights different formulations, formulation and characterisation technique of different lipid based nanocarriers.

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Keywords: Lipid nanocarrier, Oral drug delivery, Sustained drug release, Gastrointestinal absorption, Bioavailability enhancement.

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SOLID DISPERSION: AN INNOVATIVE STRATEGY FOR IMPROVEMENT OF BIOAVAILABILITY OF POORLY WATER SOLUBLE DRUGS

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Abstract:

With the advent of combinatorial chemistry and high throughput screening, drugs emerging in drug discovery process are lipophilic and poorly water soluble. Among all the newly discovered chemical entities, about 40-45% drugs fail to reach market due to their poor water solubility [1]. The dissolution rate could be the rate-limiting process in the absorption of a drug from a solid dosage form of relatively insoluble drugs [2]. Therefore, the poor solubility behavior of drugs remains one of the major challenges for the formulation scientist, as this leads to low absorption and low bioavailability resulting in limited efficacy [3]. There are various formulation strategies to overcome this solubility issue, however, solid dispersion technique offers a promising method and forms an excellent formulation alternative for such drugs. Solid dispersion molecularly disperses the drug in carrier and thus improves solubility and dissolution rate and hence the bioavailability of the drug by reducing particle size, improving wettability and forming amorphous particles [4]. Formulation of solid dispersion in water soluble carrier has become more researched topic over the past four decades for solubility and relative bioavailability enhancement [5]. This review reports recent advances in the solid dispersion technology and outlines the problems and their solutions for the development of better formulations.

Keywords: Molecular dispersion, solubility enhancement, dissolution, carrier

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SURFACE FUNCTIONALIZATION TO IMPROVE THE THERAPEUTIC EFFICACY OF NANOCARRIERS FOR ANTICANCER DRUG TARGETING

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Abstract:

Pharmaceutical nanotechnology promises new routes to medical diagnosis, treatment and drug targeting. There are many promising therapeutic nanocarriers are already available for cancer treatment like polymeric, lipid-based, metal-based, carbon-based etc. But such kind of nanocarriers having some drawbacks like early drug release, non-specific drug distribution in normal cells, poor circulation time, low dissolution resulting to poor bioavailability and rapid drug uptake, ultimately less therapeutic effect [1]. The main aim in the surface functionalization of the nanocarriers is to successfully warrant these delivery affiliated obstacles and carry drugs to the desired sites of therapeutic action while reducing detrimental side effects. The surface of the nanoparticles is more crucial than those of the core because the surface shell layer rapidly touches with organs and body fluids. In spite of this cancerous cells having highly complex and harsh environment, thus nanoparticles should be protected for effectual drug delivery to cancer resistant cell [2]. Generally, the surface of nanoparticles is coated with hydrophilic polymeric materials to give prolong circulation time and/or coupled with targeting ligands for site-specific delivery. Therefore, considerable innovation and effort have been given to the study and creation of nanoparticle surfaces to improve the therapeutic efficacy for anticancer drug targeting [3]. This paper highlights the recent studies on the nanoparticles surface engineering, explore the influence of chemistry in the fabrication of nanoparticle surfaces and the biomedical applications of these particulate systems in cancer therapy.

Keywords: *Nanocarriers, surface functionalization, anticancer drug targeting.*

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NOVEL LIPID-POLYMER HYBRID (LPH) NANOCARRIER BASED TREATMENT WITH CURCUMIN FOR ENHANCED MANAGEMENT OF PSORIASIS

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Abstract:

Background: Psoriasis is an auto immune disorder of the skin characterized by relapsing episodes of inflammatory lesions and hyperkeratotic plaques. The currently available treatment for psoriasis includes topical therapy, phototherapy and systemic therapy which are unsafe, ineffective and unable to completely cure it [1].
Objective: In this study Lipid-Polymer Hybrid (LPH) nanocarrier for delivery of curcumin was investigated for the enhanced management of Psoriasis.
Methods: Single emulsion solvent evaporation technique [2] was used for preparation of LPH nanocarrier loaded with curcumin (Cu-LPH) using ethylcellulose, stearic acid, curcumin, ethanol and 1% aqueous Tween 80 solution. Cu-LPH nanocarriers were characterized by particle size, polydispersity index, zeta potential, entrapment efficiency, SEM, TEM, DSC, drug release etc. Lyophilised Cu-LPH powder was loaded in gel comprising Carbopol 940, glycerine, methylparaben and triethanolamine to investigate *in-vitro* skin permeation study and *in-vivo* anti-psoriatic effect on Imiquimod (IMQ) induced psoriatic rat model [3].
Results and Discussion: The optimized Cu-LPH nanocarrier had particle size of 209.9 nm, zeta potential -28.3 mV, entrapment efficiency 87.4 ± 0.99% and maximum drug release was found 55.37 ± 1.40% upto 24 hours at pH 4.5. FT-IR, DSC and XRD studies confirmed that there was no interaction between drug and excipients. The topical Carbopol gel of Cu-LPH showed pH of 5.53±0.32, spreadability 206±14.52 g.cm/sec. The *in-vitro* skin permeation study of the gel showed sustained release behavior. Histopathological and TEM analysis of skin treated with gel showed significant anti-psoriatic effect of Cu-LPH nanocarrier compared to

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Betamethsone Valerate cream due to efficient accumulation of Cu-LPH nanocarrier in the skin.

Conclusion: The study showed that novel Cu-LPH nanocarrier based treatment could enhance the management of psoriasis.

Keywords: *Lipid-polymer hybrid, nanocarrier, curcumin, psoriasis, IMQ induced anti-psoriatic rat model.*

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NOVEL NANOMEDICAL FORMULATION FOR TARGETED CHEMOTHERAPY AND DIAGNOSIS

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Abstract:
Cancer is the second worldwide cause of death, caused by damage or mutation of cells due to environmental or inherited factors. Cancer continues to be one of the most difficult global healthcare problems. Although there is a large number of drugs that can be used in cancer treatment, the problem is selectively killing all the cancer cells while reducing collateral toxicity to healthy cells. There are several biological barriers to effective drug delivery in cancer such as renal, hepatic, or immune clearance [1]. Nanoparticles loaded with anti-cancer drugs can be designed to overcome these biological barriers to improve efficacy while reducing mortality [2]. Nanomedicine offers numerous advantages over conventional drug delivery approaches and is particularly the hot topic in research and diagnosis of anti-cancer drugs [3]. Nanoparticles (NPs) have many unique criteria that enable them to be incorporated in anticancer therapy [4]. Recent advances in nanotechnology have contributed to the development of engineered nanoscale structures for anticancer drug therapy [5]. This research review reports the various nanocarriers developed for anticancer targeted chemotherapy and diagnosis of various nanomedical formulation.

Keywords: Cancer, nanoparticles, nanomedicines, targeted chemotherapy.

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TRANSDERMAL DRUG DELIVERY CARRIERS BASED ON NANOTECHNOLOGY

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Abstract:

Transdermal Drug Delivery System (TDDS) is an alternative to conventional delivery by lowering the problems associated with the oral and parenteral administration of drugs. Major challenges in the transdermal drug delivery are to overcome the layer of stratum corneum [1]. Various types of conventional drug delivery carries are already available like patches, cream, gel, ointment etc. but such kind of carriers having numerous limitations including large particle size, unable to penetrate the stratum corneum barrier leading to poor solubility, systemic absorption, poor bioavailability and less therapeutic effectiveness [2]. Therefore, novel transdermal drug delivery systems are urgently required to overcome this disputed point or challenges. Currently, nanotechnology in an outstanding and dynamic approach to transdermal applications by enhanceing the skin penetration of low molecular weight, hydrophilic drug and macromolecules. Nanocarriers like dendrimers, SLNs, NLCs, lipid-polymer hybrid NPs, silver NPs are made of polymers, lipids, metals have been favorably used to increase penetration of drugs, control drug release and deliver the drug to specific areas of skin *in vivo* [3]. Here, we review the current state of nanoparticle-enabled skin delivery systems with special emphasis on targeting skin diseases.

Keywords: *Nanotechnology, stratum corneum, skin diseases, drug targeting.*

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SYNTHESIS AND CHARACTERIZATION OF ACETYLATED JACKFRUIT (*ARTOCARPUS HETEROPHYLLUS*) SEED STARCH AS A CONTROLLED RELEASE POLYMER

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Abstract:
Background: Chemical modifications of starch are usually done to enhance or repress the inherent property of these native starches or to impact new properties to meet the requirements for NDDS [1].
Objective: The objectives of the present work is to synthesize and characterization of acetylated jackfruit (*Artocarpus heterophyllus*) seed starch as a controlled release polymer.
Methods: Starch was isolated from the jackfruit seeds using water extraction method and was evaluated. The isolated starch was acetylated with acetic anhydride (12% w/v). The acetylated starch was characterized for degree of substitution (DS), swelling index, FTIR, DSC, and acute toxicity study. Further Ibuprofen loaded acetylated jack fruit starch microsphere were prepared by quasi-emulsion solvent diffusion method [2] and characterized by SEM, FTIR, DSC and in-vitro drug release study.
Results and Discussion: The jackfruit seed starch was successfully isolated and acetylated starch was prepared with degree of substitution (DS) of 1.23. The DSC and FTIR study confirmed the formation of acetylated starch. The acute toxicity study confirmed the safety of the acetylated starch at 2000 mg/kg body weight of mice. Particle size of microsphere was found to be 540±3.95 µm, entrapment efficiency 80.00 ± 2.95% w/w. In-vitro release study of microsphere showed controlled release profile of the model drug Ibuprofen following zero order kinetics.
Conclusion: These results conclude that acetylated starch may be used as a controlled release polymeric carrier.

Keywords: *Jackfruit seed starch, Acetylated starch, Controlled release, Ibuprofen, Zero order kinetics.*

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TOXICITY AND CHALLENGES OF NANOPHARMACEUTICALS

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Abstract:

Background: Nanotechnology is widely utilized as a carrier in drug delivery to administer the drugs via ingestion, inhalation, injection and surface exposure to patients. There is inadequate knowledge regarding the toxicity of nanoformulations on human health and the environment (Vega-Villa et al., 2008), therefore, there is an urgent need to investigate the toxicological profiles of nanoformulations.

Objective: The objective of this review is to analyze the cellular toxicity of nanoformulations so that comprehensive information can be generated for development of formulations. It also aimed to highlight the current progress in the toxicity of nanoformulations with biomolecular signaling and biological kinetics of biological systems.

Methods: In view of this, extensive literature survey was carried out to understand the cause, mechanism, control and prevention of toxicity in living systems. Data retrieved from databases were analysed and interpreted to draw conclusion.

Results and Discussions: The nanosize alters surface characteristics and binding affinities with biological macromolecules (Sharma, 2015). It may affect the cell membrane, function of mitochondria, pro-oxidant/antioxidant status, enzyme leakage, DNA and other biochemical processes on therapeutic applications which may result in cell death (El-Ansary & Al-Daihan, 2009; Fu, Xia, Hwang, & Ray, 2014). The biomolecular signaling and biological kinetics of biological systems are correlated with shape, size, surface charge, composition and chemical functionality in both cell culture and animal experiments (Albanese, Tang, & Chan, 2012).

Conclusions: Nanoformulations changes the solubility, stability, biomolecular signaling and pharmacokinetics of the drug. The long-term utilization necessitates caution; the nanomaterials should be properly evaluated for toxicity and should be disposed properly to prevent accidental

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health hazards and environmental impacts. Finally, regulatory authorities should take responsibility for the approval of safe and effective use of formulations.

Keywords: DNA; Health hazard; Nanotechnology; Regulatory authorities.

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A REVIEW ON SITE SPECIFIC TRANSDERMAL DELIVERY OF COLCHICINE AND DICLOFENAC SODIUM FOR MANAGEMENT OF GOUTY PAIN

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Abstract:

Background: Gout is complex form of chronic arthritis disease where monosodium urate monohydrate (MSU) deposits in synovial fluid and other body tissues. Corticosteroids, uricosuric agents, Colchicine and non-steroidal anti-inflammatory drugs (NSAID's) are administered via systemic route to treat gout. Colchicine is an alkaloid obtained from the plants *Colchicum autumnale* (Family- Liliaceae) (Ashok, Satyappa, & Ashok, 2017).The oral administration of Colchicine and Diclofenac Sodium has a gastrointestinal side effects,in addition, Colchicine causes bone marrow depression (Singh, Utreja, Tiwary, & Jain, 2009).To overcome the difficulties novel drug delivery systems for instance Transdermal drug delivery system (TDDS) was introduced to administer the drug to patients.

Objective: The objective of the present review is to highlight the developments in dermal permeability and site specific local delivery of combined transdermal patch of Colchicine and Diclofenac Sodium.

Methods:In this perspective,literature survey was carried out to analysis the mechanisms and factors that influences permeation of drug through skin from applied transdermal patch for better local drug availability and enhancement of patient compliances.

Results and Discussion: The literature suggested that the drug administered via transdermal route increases bioavailability of drug by localized site specific release from the dosage form. In addition, it also ameliorate the patient compliance and minimizes systemic toxicities (Kumar, Ashish, & Satish, 2012).The enhancement of permeation results better release of Colchicine and Diclofenac Sodium from applied transdermal patch (Soujanya et al., 2014). Several approaches have been reported for improved

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drug release such as uses of permeation enhancers like Eucalyptus oil, menthol etc.

Conclusion: The transdermal route is a promising novel delivery route for controlled delivery of drugs. Therefore, it can be considered as a better option for delivery of Colchicine and Diclofenac Sodium and similar combinations, so far as the release and toxicity are concerned.

Keywords: Gout, Novel Drug Delivery systems, Site specific, Transdermal.

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INVESTIGATION OF ANTIMALARIAL POTENCY OF FLAVONOID COMPOUNDS FROM *CITRUS* SPECIES BY *IN SILICO* MULTI-TARGET SCREENING APPROACH

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Abstract:

Background: Flavonoid is a very important class of plant secondary metabolites having significant therapeutic potentials including antimalarial activity (Rudrapal *et al* 2017). *Citrus* species is very much rich with flavonoid compounds and different parts from some of these plants are used to prepare antimalarial herbal remedy in different regions of the world. Hence antimalarial activity prediction by *in silico* approach for some flavonoid compounds present in the juice of different *Citrus* species was carried out.

Objectives: To prepare a ligand library using flavonoid compounds present in the juice of different *Citrus* plants and to carry out *in silico* multi-target screening against some vital targets of *Plasmodium falciparum*.

Methods: The flavonoid compounds were collected from previously published research articles and the library was prepared using Discovery Studio 2017 R2 software (DS software) (Gattuso*et al* 2007). Three vital targets *Pf*DHOH, *Pf*DHFR-TS and *Pf*ATP4 of the parasite, which were found to be very promising for target based antimalarial drug development, were selected to carry out the study using DS software (Chaparro *et al* 2018).Then networking based interaction analysis was performed to find out the compounds having a higher binding affinity towards the maximum targets (Gogoi *et al* 2017). Finally, the best compounds wereanalyzed for ADMET, toxicity prediction and drug-likeness using the DS and Data Warrior software.

Results & discussions: 3 compounds for *Pf*DHOH, 22 compounds for *Pf*DHFR and 36 compounds for *Pf*ATP4 were found to have good docking score in comparison to their respective standard ligands. In networking

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analysis, 21 compounds were found to have good binding interaction with two target proteins*Pf*DHFR-TS &*Pf*ATP4, and 3 compounds have binding interaction with *Pf*ATP4 &*Pf*DHOH. Out of these 24 compounds 19 were survived in toxicity analysis and they were further analysed for ADMET properties where only one compound has satisfied the criteria properly and two compounds have satisfied partially.

Conclusions: This study helps to validate the use of traditional herbal remedy from Citrus plants and direct to check the potency of the compounds in wet lab methods. Further, it will also help the researchers/scientists to design some new derivatives or analogs of the active flavonoid compounds for better efficacy, safety and with an improved pharmacokinetic profile.

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DEVELOPMENT AND IN-VITRO CHARACTERIZATION OF BRAIN TARGETED NANOSTRUCTURED LIPID CARRIERS (NLCS) USING DESIGN OF EXPERIMENT

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Abstract:

Background: Human Immunodeficiency Virus (HIV) not only infects immune systems, it also injures both central and peripheral nervous systems including the microglia, culminating in a wide spectrum of neuropsychiatric disorders. This neuropsychiatric disorder in HIV infected patient is called NeuroAIDS (Das *et al* 2016). Tenofovir Disoproxil Fumarate (TDF) is a potent acyclic nucleotide antiretroviral drug that suffers low brain permeability due to efflux by P-glycoproteins present in Blood Brain Barrier (BBB) (Zhang *et al* 2011).
Objectives: The objective of the present study was to develop and evaluate TDF loaded NLCs to target into the brain via intranasal administration.
Methods: TDF loaded NLCs were developed by using design of experiment *i.e.* by the application of response surface methodology. NLCs were prepared using modified emulsion solvent diffusion method with biodegradable Compritol ATO 888, Oleic acid, Pluronic F-68 and Tween-80. NLCs were optimized using Response Surface Central Composite Design taking lipid to drug ratio, manufacturing phase pH and sonication time as independent variables. NLCs were evaluated for particle size, zeta potential, drug entrapment efficiency, drug loading, *in vitro* drug release in Phosphate buffer (PB) pH 6.4, pH 7.4 and artificial cerebrospinal fluid (ACSF), *ex vivo* nasal permeation via pig nasal mucosa, cytotoxicity and histopathology.
Results & Discussions: Mean diameter of optimized NLCs was found to be 132±1.1nm. Spherical shape and size were confirmed using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). *In vitro* release studies showed 54.89±2.75% in PB pH 6.4, 56.09±2.75% in PB

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pH 7.4 and 58.36±1.93% in ACSF over 48 h. *Ex vivo* permeation study showed 57.19±0.97% permeation over 48 h. The cell viability assay showed a safety profile of the NLCs with the treated concentration. The NLCs showed very minor histopathological changes on pig nasal mucosa.

Conclusions: Overall, the results suggest that the NLCs have potential as drug delivery vehicle to the brain via intranasal route.

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EXTRACTION AND CHARACTERIZATION OF PECTIN FROM PEEL OF BANANA CULTIVATED IN MIZORAM

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Abstract:

Background: Pectin is a complex polysaccharides mainly present in the primary cell wall of plants. Pectin has a wide application as the food ingredients and also drug delivery system as it is biocompatible and biodegradable. The quality of pectin can be highly affected by various factors like the sources, region of cultivation, temperature, extraction process etc. (Sardani 2017)
Objective: The present works focus on the extraction and characterization of pectin from banana peel obtained in Mizoram.
Method: In the present study, pectin extraction was done with citric acid solution (0.5N) and ethanol was used as a precipitating agent. Pectin was isolated by centrifugation at 5000rpm for 30mins and dried in the oven at 60˚C for 24hrs (Castillo-Israel et al. 2015). The extracted pectin was characterized for the % yield, ash value, equivalent weight, moisture content, total anhydrouranic acid, methoxyl content and the degree of esterification. (Khamsucharit et al. 2017)
Results and Discussions: From the experimentation results, the percentage yield, total ash content, moisture content, equivalent weight, methoxyl content, anhydrouranic acid, and degree of esterification were found to be 2.04%, 2.76%, 7.81%, 666.66 mg/mol, 6.51%, 38.16% and 96.85% respectively which shows that the extracted pectin from the banana peel was suitable for industrial applications.
Conclusion: The present study investigated on the extraction efficiency and characterization of pectin from peels of banana cultivated in Mizoram. The extracted pectin was brownish white in colour. From the characterization results, we can conclude that Pectin was successfully isolated and the extracted pectin can be further utilized for food industry as well as a carrier for drug delivery system.

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Key Words: Extraction, Banana peel, pectin, degree of esterification

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A PHYTOPHARMACOLOGICAL REVIEW ON THE *MORUS ALBA* LINN.

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Abstract:

Background: *Morus alba* Linn. commonly known as mulberry of the family Moraceae, have been known since long for promoting health benefits and is used in traditional systems of medicine. The natives of India use the leaves of plant to treat cough, asthma, bronchitis, eye infection, headache, dizziness, vertigo, tooth infections [1]. The Chinese people have been using the leaves, bark and branches of mulberry as medicine to protect the liver, improve eyesight, strengthen joints, diuretic and lower blood pressure [2]. **Objectives:** The present review was undertaken to provide snapshot on the available phytoconstituents, traditional claims and validated pharmacological activities. **Methods:** Articles were retrieved from the pubmed, scopus, web of science and google scholar from March 2018 to August 2018, and the information for the study was selected based on the traditional use of medicinal plants, phytochemical and pharmacological activity reported on mulberry [3]. **Results & Discussion:** This compilation was helpful for the development of the validated monograph of this potential medicinal plant and provides insight into the nutraceutical importance of the plant and their parts. **Conclusion:** This review trigger to the development of the nutraceutical as well as therapeutic lead for betterment of public health in cost effective manner.

Key Words: Mulberry, Traditional Medicine, Nutraceutical.

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DEVELOPMENT OF HERBAL CHEWABLE TABLETS BASED ON *CURCUMA LONGA*, *FOENICULUM VULGARY* AND *CURCUMA AMADA*

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Abstract:

Background: *Curcuma longa*, *Foeniculum vulgary* and *Curcuma amada* are one of the most celebrated herbs in the Indian system of traditional medicine. Here an attempt was made to convert this plant parts into chewable tablets to improve its palatability, shelf life and fixation of proper therapeutic dose.
Objectives: To develop digestive herbal chewable tablets based on *Curcuma longa*, *Foeniculum vulgary* and *Curcuma amada.*
Methodology: In the present research work, orally chewable tablets by using Turmeric (*Curcuma longa)*, Fennel seed (*Foeniculum vulgary)* and Mango ginger (*Curcuma amad)* were prepared by direct compression method and wet granulation method (Nagaich et al. 2014; Kashikar and Patkar, 2011). Here, powders were prepared initially and it was mixed with additives and preservatives followed by direct compression. Granules were prepared from this mixture by adding binding agent, finally compressed **into tablets (Farheen and Bhardwaj, 2014).**
Results and Discussion: The physico-chemical analyses of turmeric and fennel seed were found to be- Foreign matter- Nil, Moisture content-11.53% and 2.9%, pH-6.46 and 5.69, respectively. Organoleptic properties such as taste, shape, thickness, diameter and pre-formulation studies showed significant improvement of tablets prepared by wet granulation in comparison to direct compression method. In the pre-compression studies, the granules and powder thus prepared were evaluated. Angle of repose of powder and granules were found to be 32.56 ± 3.56^{o} and 28.065 ± 0.46^{o}, respectively. Thus it can be said that the granules prepared by wet

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granulation had excellent flow property. The bulk density value for powder and granules were found to be 0.57±0.03 g/cm^3 and 0.39±0.01 g/cm^3, respectively. The tapped density value was found to be 0.68±0.05 g/cm^3 in powdered form and 0.46±0.3 g/cm^3 in granules. The Hausner's ratio for powder and granules were found to be 1.18±0.05 and 1.17±0.04, respectively. As the value of % compressibility for powder was found to be 15.5±2.8%, which indicates good flow ability. These values were compared with the study performed by Nagaich et al. 2014, and it was observed that granules formulation of tablet has advantage over its counterpart. In the preformulation study, it was observed that all the parameters checked for the ingredients were within standard range.

Conclusion: The prepared digestive herbal chewable tablets based on *Curcuma longa*, *Foeniculum vulgary* and *Curcuma amada* were of good quality. The developed formulation of herbal chewable tablet can be a better alternative to other dosage forms in order to meet consumer preferences.

Key Words: Chewable tablet*, Curcuma longa, Foeniculum vulgary*, *Curcuma amada,* Direct compression method, Wet granulation method.

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A REVIEW ON DIVERSE BIOLOGICAL ACTIVITY OF 1, 3, 5-TRIAZINE ANALOGS

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Abstract:

Background: The synthesis of nitrogen atom bearing aromatic heterocyclic ring structure compounds has been drawing attention in the area of medicinal chemistry due to high degree of binding affinity of numerous biological receptors. Among them, triazine analogues occupy a prominent position owing a wide range of biological functions. The isomers of triazine are recognized from each other by the positions of their nitrogen atoms and addressed as 1,2,3-triazine, 1,2,4-triazine, and 1,3,5-triazine respectively (Singla, Luxami, & Paul, 2015).

Objective: In this review, the diverse biological activities of various heterocyclics containing 1, 3, 5- triazine core are highlighted.

Method: In this prospect a broad literature survey was carried to study the existing 1, 3, 5- triazine core containing compounds and their medicinal applications.

Results and Discussion: As 1, 3, 5-triazines are weak base and have much weaker resonance energy than benzene, therefore a series of compounds have been synthesized via nucleophilic substitution reaction of 2, 4, 6-trisubstituted-1, 3, 5-triazines with numerous nucleophilic reagents like primary and secondary amine. Substituted 1, 3, 5-triazine derivatives have exhibited wide spectrum biological activity for instance anti-histaminics, antioxidant, anti-cancer, antiviral, fungicidal, bactericidal, anti-tubercular, antimicrobial and antimalarial agents in medicinal chemistry (Basedia, Dubey, & Shrivastava, 2011; Kumar et al., 2017). Triazine derivatives are also utilized as herbicidal, insecticidal, dyes, lubricants and analytical reagents in other pharmaceutical field (Basedia et al., 2011; Singla et al., 2015).

Conclusions: 1, 3, 5- Triazine analogues have occupied a unique position in the field of medicinal chemistry owing to their high potency and low

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toxicity. Thus triazine analogues can be useful for design and development of novel drug.

Key Words: Heterocyclic ring; Isomer; Nucleophilic substitution.

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NANOSTRUCTURED LIPID CARRIERS: AN EMERGING SOLID LIPID DRUG CARRIER

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Abstract:

Background: Nanostructured lipid carriers (NLC), the new generation of lipid nanocarriers are attracting major attention as novel colloidal drug carriers. NLCs are drug delivery systems composed of both solid and liquid lipids as a core matrix *(Fang et al. 2013).* The solid matrix of the lipid nanoparticle contains a nano-oil section in which drug solubility is higher, thus increasing the total drug loading capacity *(Khan et al. 2015).* The NLCs owing to their advantages like increased solubility, improved permeability and bioavailability, reduced adverse effects, prolonged half-life and their tissue targeted delivery over conventional carriers have attracted increasing attention in recent years *(Fang et al. 2013)*.

Objective: The main objective of this review is to shed light on the general overview of NLCs, its preparation method, mechanism of drug release, formulation aspects, their applications and future perspectives.

Methods: The review has been carried out by extensive literature survey from different sources like Google, PubMed, ScienceDirect etc.

Results and Discussions: From the extensive literature survey, it has been found that NLC is prepared by binding a liquid with a solid lipid and thus shows a high loading capacity for active compound by creating a less ordered solid lipid matrix and ultimately achieving higher particle drug loading. The mechanism of drug release for lipid particles occurs by diffusion and simultaneously by lipid particle degradation in the body. Sometimes, this mechanism of drug release might be desirable to have a controlled fast release giving beyond diffusion and degradation *(Magdalene et al. 2005).*

Conclusion: From this review, it can be concluded that NLCs seem to be suitable delivery systems intended for topical, oral, pulmonary, ocular,

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parenteral administration of drugs and it can be expected that more drug products will be formulated as NLC because of the obvious advantages.

Key Words: Nanostructured lipid carrier, solid lipid, liquid lipid, bioavailability, targeted delivery

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MICROEMULSIONS: FOR ENHANCEMENT OF SOLUBILITY AND BIOAVAILABILITY OF DRUGS

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Abstract:

Background: Microemulsions are thermodynamically stable transparent or translucent, optically isotropic colloidal dispersions having low viscosity and fine droplets size (<200nm) *(Sane et al 2013)*. These are the self-micro emulsifying drug delivery systems which are composed of high amount of surfactant and co-surfactant mixtures along with oil and water *(Solanki et al 2012).* Recently these formulations are widely used to improve the absorption of drug by improving dissolution of poorly soluble drugs.
Objective: The aim of this review is to give an overview on microemulsion. In this present review we will study about the various advantages and disadvantages of microemulsion along with its preparation, classification, characterization and some examples of drugs which are given in the form of microemulsion for increasing its solubility and bioavailability with its future prospective.
Method: The review was carried out by extensive literature survey on microemulsions from various sources like PubMed, ScienceDirect and Google.
Results & Discussion- These formulations are prepared by using water titration method, varying the concentration of oil, water and surfactant and co-surfactant mixtures. Advantages of microemulsion include spontaneous formation, thermodynamic stability and high solubilization capacity of lipophilic and hydrophilic compounds *(Jha et al 2011)*. According to various studies Microemulsions positively influence drug absorption in a number of ways, such as protecting the incorporated drugs from oxidation, enzymatic degradation, enhancing membrane permeability and lymphatic transport *(Tang et al 2013).*
Conclusion- In conclusion, microemulsions are an effective and promising delivery system to enhance the bioavailability of poorly water-soluble drugs.

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Key Words: Microemulsion, thermodynamic stability, surfactant, co-surfactant.

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IN VITRO ANTIUROLITHIATIC ACTIVITY OF ZINC OXIDE NANOPARTICLES SYNTHESIZED USING BIOSURFACTANT ISOLATED FROM *BACILLUS VALLISMORTIS* MDU6 STRAIN

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Abstract:

Background: Urolithiasis is one of the painful urologic disorders that occur in approximately 12% of the global population. During the last several years, various chemical methods have been used for synthesis of a variety of metal nanoparticles. Most of these methods pose severe environmental problems and biological risks; therefore the present study reports a biological route for synthesis of zinc oxide nanoparticles (ZnO NPs) using biosurfactant isolated from *Bacillus vallismortis* strain MDU6.

Objective: ZnO NPs was synthesized using biosurfactant isolated from *Bacillus vallismortis* strain MDU6 and their *in vitro* antiurolithiatic property was studied using single diffusion gel growth technique.

Methods: An efficient biosurfactant producing bacterial strain *Bacillus vallismortis* MDU6 was isolated from an oil logging area in Dibrugarh district of Assam, India. The isolated biosurfactant was used to synthesize ZnO NPs. The ZnO NPs were characterised using UV-vis absorption spectroscopy, Powder-XRD and TEM analysis. The ZnO NPs were used for the *in vitro* growth inhibition of struvite crystals using the single diffusion gel growth technique.

Results and discussions: Formation of stable ZnO NPs gave mostly nanostar shaped with a particle size ranging from 50-300 nm. The UV–vis spectra presented a characteristic absorbance peak at 360 nm for synthesized ZnO NPs. The XRD spectrum showed that ZnO NPs are crystalline in nature and have typical hexagonal type polycrystals. Furthermore, the ZnO NPs showed growth-inhibition properties of struvite crystals.

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Conclusion: The inhibition of crystal growth by different concentrations of the ZnO NPs was promising and rapid, indicating the potential of the ZnO NPs for further urolithiatic studies.

Keywords: urolithiasis, biosurfactant, nanoparticles, struvite.

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WAFERS: A NOVEL DRUG DELIVERY SYSTEM

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Abstract:

Background: Wafers are paper thin polymer films used as carriers for pharmaceutical active ingredient. It is a solid dosage form, which dissolves in a short period of time when placed in the mouth without drinking water or chewing and also possess mucoadhesive properties depending upon the polymer being used while formulating the wafer *(Ramesh et al. 2016)*.
Objective: The objective is to exploit the mucoadhesive property of wafer in oral mucosal tissue or wound site.
Methods: The review has been carried out with extensive literature study and survey from PubMed and Science direct.
Results and Discussions: The literature study revealed that wafer when placed in oral mucosal tissue or wound site, it instantly gets wet by saliva or wound exudates respectively, thus, gets hydrated and adheres onto the site of application within seconds and forms highly viscous gels from glassy, porous solids *(Matthews. et. al. 2004)* that remain in situ for prolonged periods of time to release sustained amounts of the drug *(Labovitiadi et. al. 2012).* It shows high dissolution rate, lesser extent of hepatic first pass metabolism *(Labovitiadi et. al. 2012)*, sustained release of drugs *(Bromberg et. al. 2000)* and possess no risk of choking.
Conclusion: Based on the study it is concluded that wafer has created new possibilities for action profiles and has number of advantages over other dosage forms. It can be further exploited for formulating fast dissolving oral drug delivery systems and in situ implantable.

Key Words: Polymer film, Oral drug delivery, Mucoadhesive drug delivery, Sustained release

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NATURAL SKIN PERMEATION ENHANCERS FOR TRANSDERMAL DRUG DELIVERY

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Abstract:

Background: The drug delivery by oral route is so far most convenient route of drug delivery but now a days considerable interest has been increased in delivery of drugs through skin to the systemic circulation. However, the stratum corneum acts as the formidable barrier to drug penetration thereby reducing bio-availability [1]. One long-standing approach for improving transdermal drug delivery uses penetration enhancers that can reversibly compromise the skin's barrier function and consequently allow the entry of poorly penetrating molecules into the membrane and through to the systemic circulation[2].

Objective: The present review aims to screen various natural sources of permeation enhancers that can be employed for transdermal permeation of drugs and includes classification, feasibility and application of various natural penetration enhancers for TDDS.

Methods: By keeping this particular topic in interest, the extensive literature review has been done from different journals and search engines like Google, PubMed, ScienceDirect. The information and data from these sources are collected, compiled and presented.

Results and Discussions: The literature review revealed that among natural penetration enhancers various terpenes, fixed oils, essential oils, fatty acids has been incorporated in several transdermal formulations for delivery of anti-hypertensives, NSAIDs, antidiabetics [3, 4, 5]. They penetrate skin via different mechanisms: (1) disintegration of the highly ordered intercellular lipid structure between corneocytes in stratum corneum, (2) interaction with intercellular domain of protein, which induces their conformational modification, (3) increase the partitioning of a drug [6].

Conclusion: After extensive literature review it has been found that a large number of natural sources of penetration enhancers have been discussed but

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still a lot of studies and research need to be done to explore the sources of natural penetration enhancers for effective delivery of drug via transdermal route.

Key Words: Permeation enhancers, Stratum corneum, Transdermal drug delivery system.

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TOWARD *PLASMODIUM FALCIPARUM* PI(4)KIIIB INHIBITOR DESIGN

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Abstract:

Background: Malaria is one of the most devastating infectious diseases which have infected hundreds of millions of people worldwide. Although several anti-malarial drugs are in clinical use, there is an urgent need for new drugs acting through novel mechanisms of action due to rapid development of resistance. A lipid kinase, phosphatidylinositol-4-OH kinase (PI(4)K) type IIIβ has been recently identified as the target of imidazopyrazines. However, due to the absence of a crystal structure of *Pf*PI(4)KIIIβ, the process of *in-silico* drug development has not been possible.

Objective: Here, we have modeled the *plasmodial* PI(4)KIIIβ using homology modeling approach. The model has been validated and further, stabilized using molecular dynamics (MD) simulations.

Methods: A total of 178 compounds were retrieved from PubChem database. These compounds were screened on the basis of hERG liability and toxicity. Molecular docking calculations were performed using two softwares to study the interaction of the selected molecules with the model protein. Molecular dynamics simulations were performed to study the stability of the protein-ligand complexes.

Results & Discussions: Docking studies helped us to identify a few molecules with better binding modes. The dynamical movement of five selected molecules were studied and the protein-ligand interactions were analysed. Our results showed that out of the five molecules, three compounds are stable within the binding cavity of the protein and have the potential to inhibit the *Pf*PI(4)KIIIβ (Rajkhowa *et al* 2017).

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Conclusion: Our work provides a strategy for the design of specific inhibitors that could potentially target *plasmodial* PI(4)KIIIβ and would prove to be instrumental in eradicating malaria.

Key Words: PfPI(4)KIIIβ, hERG, docking, molecular dynamics, ADMET.

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IN-VITRO ANTIMYCOBACTERIAL ACTIVITY OF THE RHIZOMES OF *CURCUMA CAESIA* ROXB. AND *CURCUMA ZEDOARIA* ROSCOE USING GOAT URINE AS MENSTRUM

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Abstract:

Background: There is an urgent need for the introduction of new effective, affordable anti-tubercular (anti-TB) agents with little toxicity to replace those currently in use to which mycobacterial resistance has occurred (Newton et al. 2002). In Indian Traditional System of Medicine, Goat urine is believed to have therapeutic value and is also reported its use in the treatment of tuberculosis (Padmanabhan and Sujana, 2008). On the basis of reported traditional uses for the treatment of TB and/or leprosy, extract of the rhizomes of *Curcuma caesia* Roxb. and*Curcuma zedoaria* Roscoe were selected.

Objectives: The objective of this experiment is to extract the rhizome of these two plants using raw and photo-activated goat urine as menstrum and to carry out *in-vitro* anti-mycobacterial activity of the extracts against *Mycobacterium smegmatis* (MC^2155) by disc-diffusion method.

Methods: The rhizomes were collected from in and around Dibrugarh and were dried at room temperature after cleaning and slicing. Goat urine was collected in glass containers and part of the collected urine was photo activated. The dried rhizomes of both the plant species were extracted using raw and photo activated goat urine as menstrum by maceration process. The extracts were evaporated at 70-80^{o}C. *In vitro* anti-mycobacterial activity of the plant extracts was carried out by disc diffusion method.

Results and Discussion: The anti-mycobaterial activity of the photo-activated goat urine extracts of both the plantswas higher than that of the raw goat urine extracts. It is due to the fact thatduring photo-activation, biogenic

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volatile inorganic and organic compounds such as carbon-di-oxide, ammonia, methane, methanol, propanol, acetone, and some metabolic secondary nitrogenous products are formed (Upadhyay, Dwivedi and Ahmad, 2010). Photo-activated urine becomes highly acidic in comparison to fresh urine for which there was an increase in the anti-mycobacterial activity (Hu et al. 2007).

Conclusion: Among all, the extracts obtained using photo activated goat urine showed higher activity than the extracts obtained using raw goat urine. Goat urine also exhibited anti-mycobacterial activity, but not as much as the extracts. Thus, it is proved that the extracts and goat urine have anti-mycobacterial activity and extracting with goat urine thus have improvedactivity.

Key words: Mycobacteria; Goat urine; Northeast; Disc diffusion; Maceration

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ISOLATION AND CHARACTERIZATION OF A TERPENOIDAL COMPOUND FROM *CURCUMA CAESIA* ROXB.

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Abstract:

Background: *Curcuma caesia* Roxb., (Family: Zingiberaceae) is a perennial aromatic herb with bluish-black coloured rhizome that has a bitter taste with pungent smell, commonly known as *'Black Turmeric'* and locally known as '*Kolaa Haladhee*' (in Assamese language). This ethnomedicinal plant is indigenous to northeast India (Das and Zaman 2013; Sahu, Kenwat and Chandrakar 2016) and some parts of hilly regions of east and west Godavari, some districts of Andhra Pradesh, central parts of India and in other Asian countries.Traditionally, the rhizomes are beneficial as a carminative, antiemetic, anti-diarrheal, as a diuretic, in treatment of leucoderma, piles, bronchitis, asthma, abdominal pains, menstrual disorder, wounds, eczema, psoriasis, jaundice, inflammations, blood purification, etc. (Sharma, Chhangte and Dolui 2001; Dolui et al. 2004; Jamir, Sharma andDolui 1999). Besides, this plant also has major amount of useful phytoconstituents like terpenoids and polyphenols. Molecular level based study has been carried out with the plant phyto-constituents and DNA isolates of *Curcuma caesia* with a variety of species of the same genus (Tag , Das and Loyi 2007; Angel, Vimala and Nambisan 2012; Paul et al. 2016).

Objective: The aim of this study was to isolate pure sesquiterpenoid from the rhizomes of *Curcuma caesia*.

Methodology: The dried powdered rhizomes of *Curcuma caesia* Roxb. (Zingiberaceae) were subjected to extraction with methanol by cold maceration technique. The percentage yield of the crude extract was about 9.5%. Fractionation of methanolic extract was executed by suspending in water and then portioned by different organic solvents (hexane, ethyl acetate and methanol) successively by using a separating funnel and concentrated using a rota evaporator. The three different hexane, ethyl acetate and methanolic fractions were tested for *in-vitro* ABTS and DPPH free radical

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scavenging activities (Reenu et al. 2015; Krishnaraj, Manibhushanrao and Mathivanan 2010; Bharathi 2014;Ghosh et al. 2013). Amongst all the three fractions, ethyl acetate fraction showed a significantly better activity and hence was subjected to column chromatography for isolation of pure sesquiterpenoid. Total 54 fractions were collected. Thin layer chromatography was performed for each fraction and out of these, fraction 3 was eluted from the solvent system hexane (90%): ethyl acetate (10%) ratio and an elongated needle shaped crystal like compound was obtained.

Results and Discussion: The yield of the compound was 3%. TLC, HPLC, ^{1}H NMR, ^{13}C NMR, ^{2}D NMR and SCXRD analysis were carried out for further structural characterization and identification of the compound. From the TLC report a single purplish coloured spot was obtained and HPLC report illustrated 97% purity. The compound was identified as a sesquiterpenoid with molecular formula $C_{15}H_{18}O_3$ from ^{1}H NMR, ^{13}C NMR, ^{2}D NMR and SCXRD analysis.

Conclusion: These results illustrated that the methanolic extract, which was further fractionated into hexane, ethyl acetate and methanolic portion, yielded a pure crystalline compound known as Zederone which needs to be further explored for various biological activities.

Keywords: Maceration, Fractionation, Antioxidant, Chromatography, SCXRD.

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FORMULATION, CHARACTERIZATION AND EVALUATION OF CURCUMIN LOADED PH-RESPONSIVE NANOPARTICLES

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Abstract:

Background: pH-responsive nanoparticles have made a significant impact on targeted drug delivery, which overcomes the limitations of nanoparticles drug delivery systems (Sun *et al.,* 2013).Curcumin has ability to block proliferation of cancer cells by suppressing the nuclear transcription factor (NF-κB).To avoid its low oral bioavailability, high dosage and poor aqueous solubility, curcumin nanoparticles were prepared by using pH-responsive biocompatible polymer such as chitosan by nanoprecipitation method using poloxamer-407 as stabilizer (Rajan *et al.,* 2016).

Objective: Formulation and characterization of pH-responsive chitosan nanoparticles loaded with curcumin and to evaluate its ability to target the acidic pH in cancer cells.

Methods: pH responsive chitosan nanoparticles loaded with curcumin were prepared by nanoprecipitation method using poloxamer-407 as stabilizer. Optimization of nanoparticles was done using different concentration of poloxamer-407 and chitosan. The prepared nanoparticles were characterized using dynamic light scattering, zeta potential, fourier transform infrared spectroscopy (Anitha *et al.,* 2011), differential scanning calorimetry (Hosseinzadeh *et al.,* 2012), scanning electron microscopy. Drug entrapment efficiency (%) and drug loading (%) was evaluated by direct estimation from the nanoparticles followed by UV-Vis detection of curcumin at 424 nm (Vivek *et al.,* 2013). pH responsiveness of the nanoparticles were evaluated by conducting *in-vitro* drug release study at different pH (4.0, 6.0 and 7.4) (Vivek *et al*. 2013).

Results and Discussions: The optimized nanoparticles were obtained with particle size distribution of 162.82±10.69 nm, zeta potential value of 25.6±9.20 mV and with drug entrapment efficiency of 44.52% and drug

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loading of 2.32%. FT-IR and DSC studies suggest that the drug was dispersed in its amorphous form. *In-vitro* drug release study results revealed that the prepared nanoparticles showed an increased drug release at acidic pH (pH 4.0 and 6.0) as compared to normal physiological pH of 7.4. The release kinetics study confirms the drug release mechanism from the nanoparticles as the anomalous diffusion.

Conclusion: From the characterization of nanoparticles it can be concluded that the formulation can be helpful for targeted drug delivery to cancer cells which has slightly lower pH than normal physiological pH (7.4). However, further studies should be performed to establish these nanoparticles as efficient drug-delivery systems.

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FORMULATION NANOPARTICLES: A PROMISING WAY FOR GENE DELIVERY

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Abstract:

Background: Gene therapy has become a promising therapeutic modality for specific treatment of numerous gene-associated human diseases and also acquired disorders by the process of introducing foreign genomic materials into host cells to elicit a therapeutic benefit. Gene therapy is being considered as a potential medical revolution as compared to conventional drugs which are associated with potential disadvantages. A successful clinical application of gene-based therapy depends on an efficient gene delivery system. Many extensive efforts for range of efficacious vectors, delivery techniques have been attempted to improve the safety and efficiency of gene-based therapies. Viral vectors in gene delivery have several intrinsic drawbacks. Therefore, non-viral approaches as alternative gene transfer vehicles to the popular viral vectors have received significant attention because of their favourable properties [1].

Objective: In view of the increasing importance of gene delivery, it was thought to be worthy to focus mainly on the present applications of Nanoparticles in gene delivery including future prospects.

Methods: Extensive literature survey was carried out through various databases; information has been retrieved and is incorporated here.

Results: Novel nanoparticle approaches like Cationic lipids, Cationic polymers, Gold Nanoparticles, Magnetic nanoparticles, Quantum dots, Silica nanoparticles, Fullerenes, Carbon nanotubes have been proved to be the most promising non-viral vehicles for clinical gene therapy [2]. Multifunctional biopolymer based nanoparticles, PEGylated nanoparticles, cationic polymers, surface modified silica and gold nanoparticles have demonstrated reliability in gene delivery [3].

Conclusion: However, the realization of such therapies is still debatable. Studies showed that nanoparticles have potential to cause pathological

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conditions and in most cases it is unpredictable. Hence, research in this area still requires in depth studies that involve functional assays; in addition, ethical and legal issues should be taken into consideration, since the technology of gene therapy is rapidly advancing and expanding.

Keywords: Gene therapy; Non-viral vector; Viral vectors; Gene delivery; Nanoparticles; Polymer.

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RECENT ADVANCES IN GALACTOSE ENGINEERED NANOCARRIERS FOR THE SITE- SPECIFIC DELIVERY OF ANTICANCER DRUG

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Abstract:

Galactosylated nanocarriers recently become so populer as viable and versatile tools to deliver drugs at a right time with an appropriate rate specifically to their target tissues or cells, which increases their therapeutic benefits while circumventing off-target effects [Lu *et al.* 2009].On the other hand site specific drug delivery for treatment of cancer is expected to enhance therapeutic efficacy with minimized side effects, and here the ligand-receptor recognition serves as a common targeting approach [Wilhelm *et al. 2016*]. For cell-selective binding,carbohydrate which is one of the crucial structures of tumor cell membranes has found to be effective among the various ligands reported so far [Moradi *et al.* 2016]. Glycosylation-mediated cancer targeted drug nanocarriers have received increasing attention in recent years, the main reason behind it is the abundance of lectin receptors on cell surfaces which makes the galactosylated carriers suitable for the targeted delivery of bioactives [Colotta *et al.* 2009]. Additionally, tethering of galactose (GAL) to various carriers, including micelles, liposomes, and nanoparticles (NPs), might also be appropriate for drug delivery [Chabner *et al.* 1998]. Here, we discuss some recent advances in the development of galactosylated nanocarriers for site specific delivery of anticancer drug. We also provide a brief overview of the targeting mechanisms and cell receptor theory involved in the ligand–receptor-mediated delivery of drug carriers.

Keywords: Galactosylated *nanocarriers, off-target effects, cell-selective binding of galactose (GAL), ligand–receptor-mediated delivery.*

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NANOTOXICITY OF POLYMERIC AND SOLID LIPID NANOPARTICLES

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Abstract:

Since the last decade, the use of nanoparticles has considered as a novel drug delivery system for most of the diseased conditions. Recently, Keck and Muller have classified nanoparticles into different classes (I-IV) from absolutely "no "risk to "high" risk [Keck and Muller 2013].Nanotoxicology includes the toxicity studies of nanomaterials for better understanding and assessing the health risks involved in its use. Due to their different physicochemical properties, such as small size, large surface area and flexible chemical composition their use in nanomedicine has gradually increased and thereby they have found to enhance their toxicological side effects [Khanna et al 2015]. The size of Polymeric nanoparticles (PNs) and Solid lipid nanoparticles (SLNs) varies from 50 to 1000 nm and thus can be considered to possess low to high risk in terms of toxicity assessment. Polymeric nanoparticles can be prepared by using biodegradable or non-biodegradable polymer, whereas lipids used in SLN are usually a mixture of lipids and can show polymorphism. The transformation or degradation of these inert polymers and lipids can leads to various toxicological effects [Prasad et al 2014]. In this discussion we tried to put efforts to show the nanotoxicity of PNs and SLNs when they are used for treatment of various diseases. Here we also provide a brief overview on the methods for the assessment of nanotoxicity.

Keywords: Nanoparticles, Nanotoxicity, PNs, SLNs.

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MODELS FOR RISK ASSESSMENT OF NANOPARTICLES

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Abstract:

Nanoparticles are small scale substance with unique properties which are an emerging class of functional materials, application fields range from medical imaging, gene delivery, tissue engineering, new drug delivery technologies to various industrial product [Kroll et al 2009]. Nanoparticles are highly reactive as they posses distinctive physicochemical properties attributed to their extremely small size, and possess extremely high surface-area-to-volume ratio. There may be harmful interactions of nanoparticles with biological systems and the environment due to toxicity caused by high reactivity [Oberdorster et al 2005]. With the ongoing commercialization of nanotechnology products, human exposure to nanoparticles through inhalation, ingestion, and dermal routes will dramatically increase and an evaluation of their potential toxicity is essential. The use of *in vitro* studies has been suggested as a widely acceptable approach to evaluate the toxicity of nanoparticles so as to facilitate a faster risk assessment. In developing and implementing environmental, health, and safety research-based protocols for addressing nano-safety issues much progress has been made in general. However, challenges remain in adequately investigating health effects given i) many different nanomaterial types, ii) various potential routes of exposure, iii) nanomaterial characterization issues, iv) limitations in research methodologies, such as time-course and dose-response issues, and v) inadequate *in vitro* methodologies for *in vivo* standardized, guideline toxicity testing [Warheit 2018]. This article provides an overview on risk assessment methods for nanoparticles, limitations and challenges for nanoparticles *in vitro* test methods.

Keywords:- Nanoparticles, new drug delivery, *in vitro* risk assessment.

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FORMULATION, CHARACTERIZATION AND *IN VIVO* BIODISTRIBUTION STUDY OF RESVERATROL LOADED NANOSTRUCTURED LIPID CARRIERS

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Abstract:

Background: Resveratrol is a poorly water soluble drug[1] used for the treatment of cancer[2]. NLC consist of a mixture of specially blended solid lipid with liquid lipid which lead to a higher loading capacity and controlled drug release of poorly water soluble drug and also suitable for targeted delivery[3].

Objectives: The objectives of the present study were to develop and characterize Resveratrol loaded NLCs and determine its *in vivo* biodistribution patterns.

Methods: The NLCs were prepared by nanoprecipitation method followed by ultra-sonication[4] using acetone and isopropanol as solvent, Nahor oil as liquid lipid, Precirol ATO 5 and Mango lipid as solid lipid and Pluronic F68 as surfactant. The prepared NLCs were characterized by determining particle size, polydispersity index (PDI), Zeta potential, Drug entrapment efficiency, drug loading, *in vitro* drug release in PBS pH 7.4, SEM, TEM, FTIR, DSC and stability study. The *in vivo* biodistribution of developed NLCs were compared with Resveratrol suspension orally in Wister albino rats. The concentrations of Resveratrol in different organs were estimated by Pico drop 100 UV-VIS spectrophotometer.

Results and Discussions: The particle size of the prepared NLCs was found as 181.6 to 415.8 nm. The particle size & spherical shape of the nanoparticles were confirmed by SEM and TEM. The PDI was found at 0.126 to 0.280 indicating the homogeneity of the particles. The entrapment efficiency was found at 61.05% to 92.76% and drug loading 28.96% to 42.94% means the prepared NLCs were suitable for drug incorporation. Zeta

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potential value found as -11.9 mV to -30.8 mV suggesting that prepared NLCs were stable. FTIR and DSC study for drug and polymer compatibility study showed absence of any physicochemical interaction. The *in vitro* drug release showed cumulative drug release up to 94.56%. The *in vivo* bio-distribution study showed that the resveratrol loaded NLCs significantly increased Cmax, AUC and MRT of Resveratrol as compared to resveratrol suspension. The distribution of Resveratrol loaded NLCs in different organs were more than the Resveratrol suspension.

Conclusion: From these studies, it may be concluded that resveratrol loaded NLCs have potential to formulate homogenous nanoparticles, which can enhanced the incorporation of poorly water soluble drugs and also might be effective than conventional Resveratrol for targeted delivery.

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RETROSPECT ON MODIFICATION AND APPLICATION OF NANOTECHNOLOGY IN TREATMENT OF HYPERTENSION

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Abstract:

Hypertension is a cardiovascular disorder characterise by rise in the arterial blood pressure. Although various conventional dosage forms are available in the market to treat hypertension. But these conventional dosage forms facing the problems of high first pass metabolism leading to poor bioavailability and less therapeutic efficacy [1]. To overcome these limitations, numerous nanopharmaceuticals are formulated to minimize the dosing frequency and enhanced the drug bioavailability. Nanopharmaceuticals like nanoemulsions, dendrimers, micelles, liposomes, solid lipid nanoparticles (SLNs), and polymeric nanoparticles have prominent advantage in novel carrier for antihypertensive drug delivery to contribute sustained release action. For instance, pH-sensitive Nisoldipine can protect from intestinal pH by formulating chitosan-based Polymeric nanoparticle or Carvedilol, a poorly water soluble drug can be incorporated into SLNs to enhance the bioavailability [2,3]. This review emphasizes the application of nanotechnology as novel carrier for antihypertensive drug delivery for management of hypertension, effect of polymers modification on drug actions and challenges associate with oral conventional antihypertensive dosage forms.

Keywords: Antihypertensive, Cardiovascular disorders, Nanopharmaceuticals.

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RECENT DEVELOPMENT OF THERAPEUTIC PROTEIN AND PEPTIDE DELIVERY: A REVIEW

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Abstract:

Background: The therapeutic proteins and peptides has become an emerging area of research and represent the fastest expanding share of the market for human medicines (Shadab et al., 2017). It is administered mostly via parenteral route (Patel et al., 2014). However parenteral administration of some therapeutic macromolecules has not been effective because of the short circulatory half-life exhibited by peptides *in vivo*. Hence, they need to be administered frequently resulting in increased cost of treatment as well as decreased patient compliance (Gupta et al., 2013).

Objective: This review summarizes recent developments on currently existing approaches to ameliorate the systemic stability, bioavailability and site specific delivery of peptide and protein therapeutics.

Methods: In this view an extensive literature survey was carried to study the existing novel delivery system of protein and peptide and their challenges associate with conventional dosage forms.

Results and Discussions: Non-invasive routes of administration such as intranasal, pulmonary, transdermal, ocular and oral delivery of peptides have been attempted intensively (Shadab et al., 2017). To improve protein and peptide *in vitro*/*in vivo* stability and performance several approaches are tried such as chemical modification and different carrier systems. Among them, nano-carrier-based delivery system is an appropriate choice of protein and peptides administration in patients owing to their property to protect proteins from degradation by the low pH conditions in stomach or by the proteolytic enzymes in the gastrointestinal tract (Gupta & Sharma, 2009; Gupta et al., 2013).

Conclusion: There is a need to improve delivery of therapeutic proteins through non-invasive means. Also by increasing the biological half-life, less

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frequent dosing through controlled-release drug delivery and improved drug targeting to increase efficacy and reduce side effects.

Key Words: Bioavailability; Therapeutic protein; Peptide delivery; Macromolecule; Site specific drug delivery.

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ROLE OF NANOPARTICLES TO MODERNIZE THE DRUG DELIVERY SYSTEMS

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Abstract:

Nanotechnology could be defined as the technology that has allowed for the control, manipulation, study and manufacture of structures and devices in the "nanometer" size range. Nanomaterials take on novel properties in micellization of biologically active substances with low-molecular-weight surfactants that have low toxicity and high solubilization power towards poorly soluble pharmaceuticals to aid in large number of therapeutic protocols such as gene therapy, drug delivery, and drug targeting [1]. However, nanoparticles are used to reduce toxicity and side effects of drugs but these carrier systems impose various limitations like lack of target specificity, altered effects and diminished potency due to drug metabolism in the body, cytotoxicity of certain anti-carcinogenic pharmacological agents [2]. Biocompatible nanoparticles with optimized physical, chemical and biological properties can serve to overcome the limitations faced in drug delivery systems by understanding the interactions of nanoparticles with the biological environment, cell-surface receptors, drug releasing process and stability of therapeutic agents [3]. These newer generations of drug delivery systems have significant advantages over the other drug delivery systems. This article discusses the need for nanotechnology-based drug delivery systems, their advantages, applications, classification and limitations of such drug delivery.

Keywords: nanotechnology, nanoparticle, micellization, cytotoxicity.

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SODIUM CARBOXYMETHYLATION OF GLUTINOUS RICE STARCH *BUH TUI* OF MIZORAM, INDIA AND ITS CHARACTERIZATION

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Abstract:

Background: Starch is a widely used excipient in many pharmaceutical formulations as a natural polymer and carboxymethylation of starch shows improved physicochemical properties in comparison to that of the native starch (NS) (Nattapulwat *et al.*, 2009). The aim of this study is to isolate starch from the sticky rice variety *Buh Tui* obtained from Mizoram and its carboxymethylation and to compare the physicochemical properties of sodium carboxymethyl *Buh Tui* starch and native *Buh Tui* starch.

Objectives: The objective of the present work is to study the physicochemical and functional properties of *Buh Tui* rice starch and to further synthesize sodium carboxymethyl starch (CMS) by treating with sodium monochloroacetate to obtain a novel functional material.

Methods: The glutinous *Buh Tui* rice starch was isolated by the method (Ashogbon and Akintayo, 2014) following an alkaline (0.1% NaOH) de-proteination method (Pachuau *et al.*, 2017). Sodium carboxymethyl starch (CMS) was synthesized where sodium monocholoroactetate was allowed to react with starch in presence of alkali (8N NaOH) in an alcoholic medium (isopropyl alcohol) at a specific reaction condition (Mohapatra *et al.,* 2018). The samples were identified by using FTIR spectrophotometer (Nicolet iS 10, ThermoScientific) and characterized by the degree of substitution (Eyler *et al.,* 1947).The particle size was determined by light microscope (Primo Star, Zeiss) and the flow properties of the samples were studied by measurement of angle of repose, bulk density, tapped density Carr's index, Hausner ratio and porosity (Pachuau *et al.*, 2017). Further, the moisture content and swelling index (Nattapulwat *et al.*, 2009) was studied for both sodium carboxymethylated *Buh Tui* starch and native *Buh Tui* starch and compared.

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Results & Discussions:

The glutinous rice starch *Buh Tui* was isolated with yield value of 83.39% and identified by FTIR spectra with absorption bands at 1148.82, 1077.08, 996.10 cm^{-1} due to C=O bond stretching and 927.15cm^{-1} due to anhydroglucose ring stretching vibrations and at 3311.19 cm^{-1} due to O-H bonded groups. The yield of the synthesized sodium CMS was found to be 164.3% with the degree of substitution (DS) of 1.87. The FTIR spectra of sodium CMS indicated the modification of the native starch by showing an intense band around 1593.91 cm^{-1}. The swelling index of CMS was highly increased at different temperatures (30, 55, 65, 75^0C) compared to native starch. The flow properties of the sodium CMS were found to be improved in comparison to that of *Buh Tui* rice starch.

Conclusion:

From this study it can be concluded that sodium carboxymethylation of *Buh Tui* rice starch has improved the physicochemical properties like swelling index, flow properties and compressibility of native *Buh Tui* starch. However, results showed that sodium carboxymethyl *Buh Tui* starch can be used as excipient in various pharmaceutical formulations.

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SYNTHESIS AND CHARACTERIZATION OF SODIUM CARBOXYMETHYL STARCH OBTAINED FROM GLUTINOUS RICE VARIETY JA PNAH OF MEGHALAYA

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Abstract:

Background: Sodium carboxymethyl starch possesses unique physicochemical properties when compared to native starch (Nattapulwat et al., 2009). The properties of modified starch promote industrial utilization of starch and starch based products (Khalil et al., 1990). The purpose of this study is to isolate starch from glutinous rice variety Ja pnah of Meghalaya, characterize and synthesize sodium carboxymethyl starch and compare its physicochemical properties with that of native rice starch Ja pnah.

Objectives: The objective of the present work is to isolate and study the physicochemical properties of Ja pnah rice starch and chemical modification with sodium monocholoroacetate to synthesize sodium carboxymethyl starch (SCMS) to obtain a novel functional excipient.

Methods: Glutinous rice Ja pnah was procured from Police Bazar, Meghalaya. Isolation of the starch was done by alkaline de-proteination method (Pachuau et al., 2018). The isolated starch was identified by FTIR spectrophotometer (Nicolet iS 10, ThermoScientific) and characterized by determination of particle size by using light microscope (Primo Star, Zeiss), flow properties, moisture content and swelling index (Pachuau et al., 2017). Sodium carboxymethyl starch (SCMS) was synthesized with slight modification by reaction of sodium monocholoroactetate with starch in presence of alkali (8N NaOH) in an alcoholic medium (250 ml isopropyl alcohol) at a specific reaction condition (Khalil et al., 1990; Mahapatra et al., 2018). The prepared SCMS was identified by FTIR spectrophotometer and characterized by determining the degree of substitution (Eyler et al., 1947; Yanli et al., 2009), particle size, flow properties, moisture content and swelling index (Pachuau et al., 2017). The results obtained were analyzed and compared to that of the native isolated rice starch (Ja pnah).

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Results & Discussions: The glutinous rice starch Ja pnah was isolated and chemically modified to sodium carboxymethyl starch and identified by characteristic absorption band in IR spectra using FTIR and percentage yield of Ja pnah starch and SCMS was found to be 76.39% and 171.5% respectively and both the starches were characterized for their particle size in terms of average radius, average area and average perimeter, tapped density, bulk density, Carr's index, Hausner's ratio, porosity & angle of repose, percentage moisture content in terms of loss on drying and swelling index at various temperatures at 30, 55 65 &750C and compared. From the FTIR spectra for Ja pnah absorption bands at 1149.54, 1077.06, 996.34 cm−1 due CO bond stretching and observed at 928.31cm-1due to the entire anhydroglucose ring stretching vibrations also an extremely broad band due to hydrogen bonded hydroxyl groups appeared at 3283.12 cm−1 and for SCMS carboxyl group was indicated by the presence of an absorption band at 1596.79cm−1. The particle size was found to be decreased and the flow properties of SCMS was found to be improved in terms of tapped density, bulk density, Carr's index, Hausner's ratio, porosity and angle of repose was found to be in the similar range, the moisture content and swelling index has increased after carboxymethylation

Conclusions: From this study it can be concluded that sodium carboxymethyl Ja pnah rice starch has better physicochemical properties like swelling index, flow properties and compressibility starch in comparison to that of native Ja pnah starch. Thus the sodium carboxymethyl starch can be used as a novel functional excipient in various pharmaceutical formulations.

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IN-SILICO DETERMINATION OF PROTEIN MODELS – POSSIBLY TARGETS OF *HELICOBACTER PYLORI* (STRAIN 26695)

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Abstract:

Background: Modelling plays an important role in the determination of the protein tertiary structures in computational biology in order to predict the 3D structures of the proteins to know about the protein structure in details. The targeted protein sequences are searched in the Protein Data Bank and found that some structures are not determined may be due to certain technical difficulties by X-ray crystallography and other techniques.

Objectives: The purpose is to study the detailed functional analysis of the proteins so that possible drug targets could be targeted and used for further analysis in the field of drug discovery.

Methods: The protein sequences of *H.pylori* strain 26695 were modeled using I-TASSER [1] software. The modeled protein sequences were docked using Autodock vina [2] with the compounds of the plant *Centella Asiatica* and the docked complex were further simulated by using GROMACS [3].

Results and Discussions: Out of 1590 protein sequences of *H. pylori* 1407 and 1409 had shown similarity at various levels to the proteins of Homo sapiens and lactobacillus species respectively. Two set consisting of 183 and 181 dissimilar proteins were sorted. On union of these two sets 81 proteins were found to be in the intersection. The protein stability and structural deviation were calculated through the Molecular Dynamics Simulation Analysis. The RMSD, RMSF scores of the modeled proteins were calculated to indicate its reliability.

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Conclusion: Out of the 81 proteins found to be in the intersection, excluding hypothetical proteins sequences only 7 proteins were modeled, docked and simulated.

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A REVIEW ON THE EFFECT OF FLAVONOIDS IN THE TREATMENT OF AMOEBIASIS CAUSED BY *ENTAMOEBA HISTOLYTICA*

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Abstract:

Background: Amoebiasis is caused by commensal protozoan *Entamoeba histolytica* in the human beings. The parasite has two cell cycle stages, the cyst and the trophozoite.The cysts are secreted in the stool from individuals who harbour *E.histolytica*. The trophozoites emerge from the cysts in the intestine and this vegetative form is able to invade the intestinalmucosa and to disseminate to the liver, producing amoebic liverabscess (ALA).The potential resistance of *E. histolytica* towards nitroimidazoles is a matter of concern (Martínez-Castillo et al., 2018).Therefore, natural and safe alternative drugs like flavonoids, which are natural polyphenolic compounds represent a promising strategy for use against drug resistance of *E.histolytica* should be considered in the era of microbial drug resistance against this parasite are needed (Agrawal, 2011).

Objective: The objective of this study is to make a review regarding the use of natural compounds like flavonoids to treat amoebiasis caused by the protozoa, *E.histolytica*.

Methods: In this review, literature survey has been carried out to study about different flavonoids such as, epicatechin, kaempferol and quercetin to check for their amoebicidal effects.

Results and Discussion: Flavonoids cause morphological changes in amoebas like chromatin condensation, cytoskeleton protein re-organization, as well as the up regulation and down regulationof fructose-1, 6-bisphosphate aldolase, glyceraldehydes-phosphate dehydrogenase, andpyruvate: ferredoxin oxidoreductase which are enzymes of the glycolytic pathway (Martínez-Castillo et al., 2018). Even though, specific molecular targets, bioavailability, route and doses of administrationof flavonoids need

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to be determined. Flavonoids are a promising class of natural compounds that should be taken into consideration to overcome the threat of drug resistance for amoebiasis (Agrawal, 2011).

Conclusion: Taking into account the benefits and future prospect of flavonoids in the treatment of *E. histolytica* infection, further studies need to be done to establish flavonoids as a good alternative for the effective treatment of amoebiasis (Agrawal, 2011).

Keywords: Alternative therapy; Parasite; Pathogen; Protozoa; Nitroimidazoles.

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A REVIEW ON NANOTECHNOLOGY USED IN HERBAL FORMULATION FOR CANCER THERAPY

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Abstract:

Background: Nanotechnology has the potential to increase the selectivity and potency of chemical, biological and physical approaches for eliciting cancer cell death while minimizing collateral toxicity to non-malignant cells. Moreover, nano carrier allows more surface area and have potential to increase solubility, enhance bioavailability, improve controlled release and enhance precision targeting. Chemotherapy of modern anti-cancer drugs are reported more adverse effects in the patients in comparison to herbal formulations (Sah et al., 2017). Herbal nano based formulations are emerging as alternative and safe tools for cancer treatments with significant role in inhibiting inflammation, angiogenesis and tumor progression.

Objective: The current review summarizes various nano formulated herbal drug delivery for treatment and prevention of cancer that gaining more attention for improved therapeutic application.

Methods: In this prospect a broad literature survey was carried to study the different nanoformulations of herbal origin that have been used to treat cancer.

Results and Discussions: Nanocarrier based herbal formulations such as phytosomes, herbosomes transferosomes, ethosomes, liposomes etc. were found to be effective, safe and convenient in herbal drug targeting for cancer therapy. They potentially enhance herbal drug solubility and bioavailability (Ajazuddin & Saraf, 2010). Nanoformulations of lipophilic phytoconstituents such as curcumin, resveratrol, encapsulated in liposomes were found to be enhancing bioavailability in cancer therapy. Quercetin-SLN exhibited controlled release *in vitro*, enhanced bioavailability (Bonifácio et al., 2014). Quercetin encapsulated in phytosomes enhanced activity in comparison to plant extract *in vitro* (Sah et al., 2017).

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Conclusions: Nanotechnology is found to be promising and useful tool in designing future herbal medicine with improved bioavailability profile and less toxicity for cancer therapy. Even though, there are many advantages to apply nano formulations for better delivery of herbal drug in cancer, drug targeting remains a challenge and potential nano formulation toxicity needs to be further investigated.

Key Words: Nanotechnology; Herbal formulation; Anti-cancer.

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COMPARATIVE CARDIOPROTECTIVE EFFECT OF *CLERODENDRUM COLEBROOKIANUM* WALP AND *CENTELLA ASIATICA* LEAF EXTRACTS AGAINST CARBON TETRACHLORIDE INDUCED CARDIOTOXICITY IN MALE WISTAR ALBINO RATS.

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Abstract:

Background: Aqueous methanolic leaf extracts of the plants *Clerodendrum colebrookianum* walp and *Centella asiatica* were selected for the cardioprotective study in male wistar rats. As both the plants are supposed to have potent antioxidant activity. There is a dynamic relationship between reactive oxygen species (ROS) and antioxidants in the human body. Lipid peroxidation can be estimated in terms of Thiobarbituric acid reactive species (TBARS) using MDA (Malondialdehyde) as standard. MDA is lipid peroxidation end product (Buge and Aust (1978).
Objectives: Aim of the study was to know radical scavenging activity of aqueous methanolic extracts of both the plants and thereby to determine lipid peroxidation end product on carbon tetrachloride induced cardiotoxic rats.
Methods: Male albino rats of Wistar strain (250-300 g) were used for the study. Animals were divided into 10 groups of six animals each. Both pre-treatment and post treatment study were done at the dose of 300 mg/kg bw and 700 mg/kg bw orally for 16 days respectively followed by preparation of heart homogenate was done. Malondialdehyde, a lipid peroxidation end product in tissue homogenate, was measured according to the method described by Wills (1969) with some modifications (Wills 1969; Devi R *et al* 2005). The data were subjected to statistical analysis.
Results & Discussions: Results signifies less production of MDA while administering higher dose of the plant extracts on carbon tetrachloride induced cardiotoxic rats. For both pre-treatment and post treatment study MDA concentration was maximum for toxic control group and minimum for control group. For the extracts of *C.colebrookianum* and *C.asiatica* at both the dose level 300 mg/kg body weight and 700mg/kg body weight is

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showing significant reduction in MDA production. For *C.colebrookianum* MDA production is less on higher dose and for *C.asiatica* at low dose only MDA production is less.

Conclusions: The observations made in the present study revealed that leaf extracts of *Clerodendrum colebrookianum* walp and *Centella asiatica* Linn inhibits lipid peroxidation mediated cardiotoxicity in wister albino rats.

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