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A REVIEW ON USE OF ARTIFICIAL INTELLIGENCE IN NOVEL HERBAL DRUG DELIVERY SYSTEM

Dr.Swati S Rawat[1], Dr. Sunil S Jaybhaye[2], Ashwini Bahir[3], Komal Kangane[4], Pratik Datta Handke[5]

*[1]Principal, [2]Vice Principal, [3]Asst prof, [4]Asst prof, [5]Student **

Institute of Pharmacy Badnapur

ABSTRACT

The kind of novel herbal formulations such as polymeric nanoparticles, nanocapsules, liposomes, phytosomes, animations, microsphere, transfersomes, and ethosomes has been reported using proactive and plant selections. The novel formulations are described to have remarkable advantages over conventional formulations of plant actives and extracts which include enhancement of solubility, bioavailability, and protection from toxicity, enhancement of pharmacological activity, enhancement of stability, improved tissue macrophages distribution, sustained delivery, and protection from physical and chemical degradation. Phytosome is a patented technology developed by a leading maker of drugs and nutraceuticals, to incorporate standardized plant extracts or water-soluble phytoconstituents into phospholipids to producd lipid-compatible molecular complexes. The herbal drugs can be used in a more upright course with enhanced efficacy by incorporating them into modern dosage forms. This can be accomplished by designing novel drug delivery systems for herbal ingredients. The present review highlights the current condition of the development of novel herbal formulations and summarizes their type of active components, biological activity, and applications of novel formulations.

INTRODUCTION TO ARTIFCIAL INTELLIGENCE (AI)

Artificial Intelligence (AI) is a stream of science related to intelligent machine learning, mainly intelligent computer programs, which provides results in the similar way to human attention process.[1] This process generally comprises obtaining data, developing efficient systems for the uses of obtained data, illustrating definite or approximate conclusions and self-corrections/adjustments.[2] In general, AI is used for analyzing the machine learning to imitate the cognitive tasks of individuals.[2,3] AI technology is exercised to perform more accurate analyses as well as to attain useful interpretation.[3] In this perspective, various useful statistical models as well as computational intelligence are combined in the AI technology.[4] The progress and innovation of AI applications are often associated to the fear of unemployment threat. However, almost all advancements in the applications of AI technology are being celebrated on account of the confidence, which enormously contributes its efficacy to the industry.

Recently, AI technology becomes a very fundamental part of industry for the useful applications in many technical and research fields.[3,4] The emergent initiative of accepting the applications of AI technology in pharmacy including drug discovery, drug delivery formulation development and other healthcare applications have already been shifted from hype to hope.[5,6] The uses of AI models also make possible to predict the in vivo responses, pharmacokinetic parameters of the therapeutics, suitable dosing, etc. [2,7] According to the importance of pharmacokinetic prediction of drugs, the uses of in silico models facilitate their effectiveness and inexpensiveness in the drug research.[8]

INTRODUCTION TO NOVEL HERBAL DRUG DELIVERY SYSTEM

In the past few decades, considerable attention has been concentrated on the evolution of a novel drug delivery system (NDDS) for herbal drugs. Conventional dosage forms, including prolonged-releasedosage forms, are unable to satisfy for both holding the drug component at a distinct rate as per directed by the requirements of the body, all through the period of treatment, as well as directing the phytoconstituents to their desired target site to obtain an utmost therapeutic response. In phytoformulation research, developing nano-sized dosage forms(polymeric nanoparticles and nanocapsules, liposomes, solid lipid nanoparticles, phytosomes, and nanoemulsion) has a number of advantages for herbal drugs, including enhancement of solubility and bioavailability, protection from toxicity, enhancement of pharmacological activity, enhancement of stability, improving tissue macrophage distribution, sustained delivery, and protection from physical and chemical degradation. Thus, the nano-sized NDDSs of herbal drugs have a potential future for enhancing the activity and overcoming problems associated with the plant medicines. Liposomes, which are biodegradable and essentially nontoxic vehicles, can encapsulate both hydrophilic and hydrophobic materials.[9]

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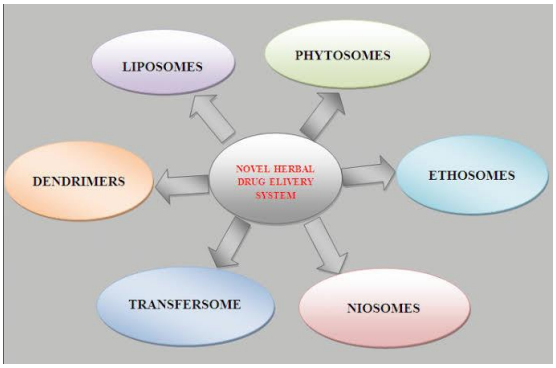
From time immemorial, it has been the endeavor of the doctor and the apothecary to provide patients with the best possible varieties of medications, so that recovery from disease is faster and more complete. The drugs are rendered in a suitable formulation keeping in view the safety, efficacy, and acceptability among other ingredients, and the preparation is usually known as dosage form or drug delivery system. With the progress in all domains of science and engineering, the dosage forms have developed from simple mixtures and pills to highly sophisticated technology, intensive drug delivery systems, which are known as NDDSs.[10] In the past few decades, considerable attention has been concentrated on the evolution of an NDDS for herbal drugs.[11] Herbal drugs are getting more popular in the modern world for their diligence to cure a variety of diseases with less toxic effects and better therapeutic effects. Meanwhile, some limitations of herbal extracts/plant actives such as instability in highly acidic pH and liver metabolism have gone to attain the drug levels below to the therapeutic concentration in the blood resulting in lessor no healing effect.

Incorporation of novel drug delivery technology to herbal or plant actives minimizes the drug degradation or presystemic metabolism and serious side effects by accumulation of drugs to the nontargeted areas and improves the ease of administration in the pediatric and geriatric patients.[12] Conventional dosage forms, including prolonged-release dosage forms, are unable to fulfill the ideal requirements of novel carrierssuch as ability to deliver the drug at a rate directed by the penury of the body and to transmit the active entity of herbal drug to the site of activity. For good bioavailability, natural products must have a sound balance between hydrophilicity (for dissolving into the gastrointestinal fluids) and lipophilicity (to cross lipidic biomembranes). Many phytoconstituents such as polyphenolics have good water solubility, but are poorly absorbed[13] either due to their multiple-ring large-sized particles which cannot be soaked up by simple diffusion or referable to their poor miscibility with oil and other lipids, severely restricting their power to reach across the lipid-rich outer membranes of the enterocytes of the little bowel.[14] Thus, the nano-sized NDDSs of herbal drugs have a potential future for enhancing the natural process and overwhelming problems related with plant medicines.[11] Novel herbal drug carriers cure particular disease by targeting just the affected zone inside a patient's body and transporting the drug to that region. NDDS is advantageous in giving up the herbal drug at predetermined rate and delivery of drug at the site of action which minimizes the toxic effects with an increase in bioavailability of drugs. In novel drug delivery technology, control of the dispersion of the drug is achieved by incorporating the drug in carrier system or in modifying the social organization of the drug at the molecular level. Incorporation of herbal drugs in the delivery system also aids to increase in solubility, enhanced stability, protection from toxicity, enhanced pharmacological activity, improved tissue macrophage distribution, sustained delivery, and protection from physical and chemical degradation. For example, liposomes act as potential vehicles to take anticancer agents by increasing amount of drug in tumor area and decrease the exposure or accumulation of drug in normal cells/tissues, thereby preventing tissue toxicity effects. The phytosomal carriers have been considered for effective delivery of herbal extracts of ginseng (Ginkgo biloba), etc. Direct binding of phosphatidylcholine to herbal extract components led to better absorption characteristics as compared to conventional delivery of herbal infusions. Other vesicular assemblies such as microspheres, animations, and polymeric nanoparticles have been shown beneficial to carry herbal components. The presentreview article is directed to supply an overview of different cases of drug delivery systems incorporating active ingredients and potential advantages of such organizations.[12] In the present study, an effort has been induced to touch on various aspects and applications related to novel herbal drug preparations.

Types of Novel Herbal Drug Delivery Systems:

Several approaches in case of new herbal drug delivery system include different types of expressions such as mouth-dissolving tablets, liposomes, phytosomes, pharmacosomes, museums, nanoparticles, microspheres, transfersomes, ethosomes, transdermal drug delivery system (TDDS), and proniosomes are discussed.



Mouth-Dissolving Tablets

Asoka Lifescience Limited launched Res-Q, the world's first polyherbal mouth-dissolving tablet, fast mouth-dissolving drug. It induces a new drug delivery system that imparts increased efficacy.In theAyurvedicmedicine segment, thisisthe inauguralattempt to make medicines more effective in managing chronic ailments. Res-Q is a polyherbal medicine highly effective for lung problems and other respiratory ailments such as asthma. This unique mouth-dissolving drug delivery system ensures that the drug reaches the blood right away and the first-pass metabolism is bypassed. It dissolves in mouth by mixing with the saliva and get absorbed. This Res-Q provides relief from respiratory distress within 15 min. Hence the product shows a greatresemblance with the efficacy of Sorbitrate,a revolutionarymouth-dissolving drug used in cardiac distress.[15]

Controlled-Release Formulations

A patent describes an orally administrable formulation for the controlled release or stable storage of a granulated herb, comprising a granulated herband a carrier, the formulation release

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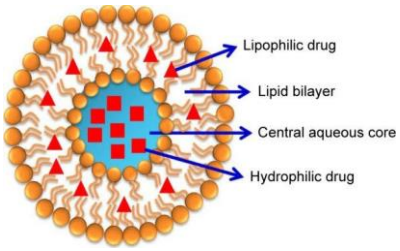
of 75% of the active ingredients between 4 and 18 h after administration. The active elements are selected from the group consisting of hypericin, hyperforin, and echinacosides. The invention seeks to provide improved herbal preparations, whose preparations offer a convenient oral dosage form of herbs for supplying optimum plasma concentrations of the biologically active compounds that facilitates user compliance. The oral-controlled and stable-releasedosage form of granulated herb is in either matrix formulations such as matrix tablets or in multiparticulate formulations such as microcapsules put into two-piece capsules that are performed in order to hold a drug delivery system, which will guarantee a regular supply of the active ingredients for a sustained period.[16]

Another US patent invention is a new stable herbal drug formulation in the form of prolonged-release microgranules containing G. biloba extract as well as the process for building it. Plant extracts have poor flow ability and compressibility properties. Therefore, the expression of such extracts in the kind of sustained-release tablets is difficult, as it requires homogeneous mixtures of extracts with pharmaceutical excipients during all compression straps. Microgranules can be cleared up by a number of different operations, for example, extrusion–spheronization, fluid–air bed process, or a cutting-pan method. Extrusion–spheronization is suitable for pellets with high content of active meaning, but need more equipment. For the manufacture of the granules of the invention, the cutting-pan method is preferred, as it requires only simple equipment and procedure.[17]

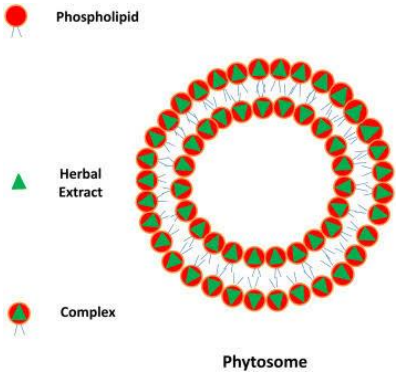
Liposomes



These are microparticulate or colloidal carriers, usually 0.05–5.0 μm in diameter which forms spontaneously whencertain lipids are hydrated in aqueous media.[18] The liposomes are spherical particles that encapsulate a fraction of the solvent, in which they freely pass around or float into their interior. They can carry one, several, or multiple concentric membranes. Liposomes

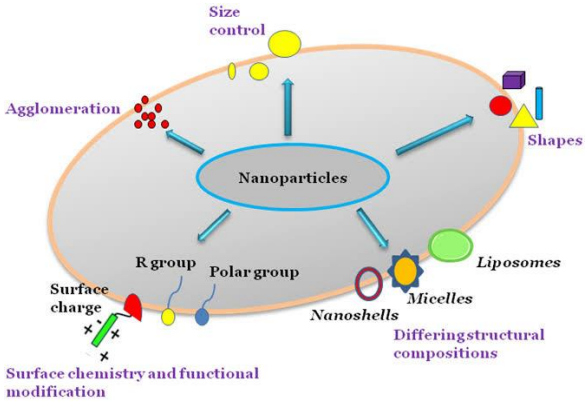
are constructed of polar lipids, which are characterized by having a lipophilic and hydrophilic group of the same molecules. On interaction with water, polar lipids self-layup and form self-organized colloidal particles.[3]Liposome-based drug delivery systems offer the potential to raise the therapeutic index of anticancer agents, by increasing the drug concentration in tumor cells or by lessening the exposure in normal tissues exploiting enhanced permeability and retention effect phenomenon or by utilizing targeting strategies.[19] The primary advantages of using liposomes include (i) the high biocompatibility, (ii) the easiness of preparation, (iii) the chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds, and (iv) the simple modulation of their pharmacokinetic properties by varying the chemical composition of the player components. Few examples of herbal formulations in liposomal drug delivery systems.[20]

Phytosomes:



Most of the bioactive constituents of phytomedicines are flavonoids, which are poorly bioavailable when taken orally. Water-soluble phytoconstituent molecules (mainly polyphenols) can be converted into lipid-compatible molecular complexes, which are called phytosomes. Phytosomes are more bioavailable as compared to simple herbal extracts owing to their enhanced mental ability to skip through the lipid-rich biomembranes and finally arriving to the origin. The lipid-phase substances employed to make phytoconstituents lipid compatible are phospholipids from soy, mainly phosphatidylcholine.[21] Some of herbal formulations in Phytosomal drug delivery systems. Phytosomal complexes were first investigated for cosmetic applications, but mounting evidence of potential for drug delivery has been amassed over the past few years, with beneficial activity in the realms of cardiovascular, anti-inflammatory, hepatoprotective, and anticancer applications.[22] Phytosome complexes show better pharmacokinetics and therapeutic profile than their noncomplexed herbal extract. The phytosome technology has markedly enhanced the bioavailability of selected phytochemicals.[23]

NanoparticlesNanoparticles are efficient delivery systems for the delivery of both hydrophilic and hydrophobic drugs. Nanoparticles are the submicron-sized particles, ranging 10–1000



mm.[12]The major goal behind designing nanoparticle as a delivery arrangement is to control particle size, surface properties, and release of pharmacologically active agents in

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order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen.[24] In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices.[11] The nanospheres have a matrix type structure in which the active ingredient is dispersed throughout(the molecules), whereas the nanocapsules have a polymeric membrane and an active ingredient core. Nanonization possesses many advantages, such as increasing compound solubility, reducing medicinal doses, and improving the

absorbency of herbal medicines compared with the respective crude drugs preparations.[25] The examples of some herbal Naoparticulate drug delivery systems.

Niosomes

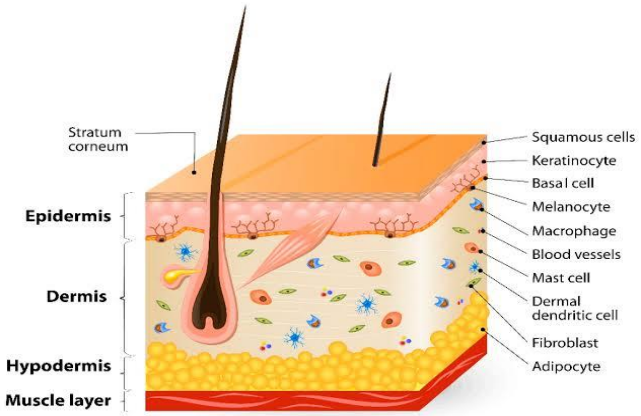
Niosomes are multilamellar vesicles formed from nonionic surfactants of the alkyl or dialkylpolyglycerol ether class and cholesterol. Earlier studies in association with L'Oreal have shown that, in general, niosomes have properties as potential drug carriers similar to liposomes.[26] Niosomes are different from liposomes in that they offer certain advantages over liposomes. Liposomes face problems such as they are expensive, their ingredients such as phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special memory and handling, and purity of natural phospholipids is variable. Niosomes do not have any of these problems.[27]

Proniosomes

Proniosome gel system is step forward to niosome, which can be utilized for various applications in delivery of actives at desired site.[28] Proniosomal gels are the formulations, which on in situ hydration with water from the skin are converted into niosomes.[29] Proniosomes are water-soluble carrier particles that are coated with surfactant and can be hydrated to form niosomal dispersion immediately before use on brief agitation in hot aqueous media.[30] Few examples of proniosomal formulations.[31]

Transdermal Drug Delivery System

TDDS has been an increased stake in the drug administration via the skin for both local therapeutic effects on diseased skin (topical delivery) as comfortably as for systemic delivery of drugs.[32] However, they did not have had such expected success with other drugs. But, immense potential lies in transdermal drug as future smart drug delivery devices.[10] Transdermal delivery system provides the advantage of controlled drug delivery, enhanced bioavailability, reduction in side effects, and easy application. Formulation of transdermal films incorporating herbal drug components such as boswellic acid (Boswellia serrata) and curcumin (Curcuma longa) is one of the first few attempts to utilize Ayurvedic drugs through TDDS, which utilizes skin as a site for continuous drug administration into the systemic circulation. Thus, this delivery system avoids the first-pass metabolism of the drug without the annoyance associated with injection; moreover, the scheme offers a prolonged drug delivery with infrequent dosing via zero-order kinetics and the therapy can be easily fired atanytime. Use of turmeric in TDDS for the local action of the drug at the site of administration can also be regarded as a young version Ayurvedic turmeric poultice orleap.[33]



Microspheres

Microspheres are discrete spherical particles ranging in average particle size from 1 to 50 µ.[33] Microparticulate drug delivery systems are studied and taken on as a reliable one to rescue the drug to the target site with specificity, to assert the desired concentration at the situation of interest without untoward effects. Microencapsulation is a useful method which extends the duration of drug effect significantly and improves patient compliance. Finally, the entire dose and few adverse reactions maybe thinned out since a steady plasma concentration is kept.[34] So far, a series of active ingredients of plants, such as rutin, camptothecin, zedoary oil, tetrandrine, quercetine, and Cynara scolymus extract, has been made into microspheres. In addition, reports on immune microsphere and magnetic microsphere are also usual in recent years. Immune microsphere possesses the immune competence as a consequence of the antibody, and antigen was coated or adsorbed on the polymer microspheres.[35] Some of the herbal Microspheres developed as drug delivery systems.

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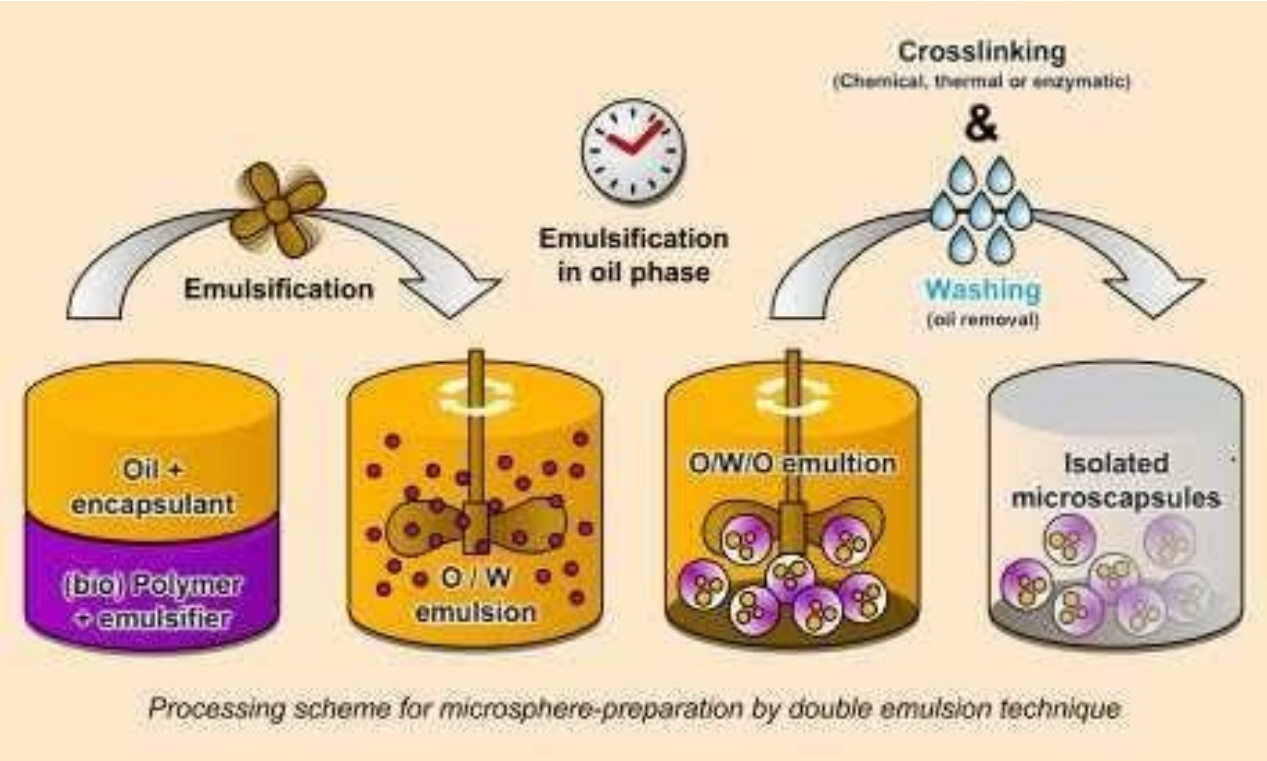

Processing scheme for microsphere-preparation by double emulsion technique

Emulsions

Emulsion refers to a nonhomogeneous dispersion system that is composed of two kinds of liquids unable to dissolve each other, and one of which disperses in the other one in a form of droplets.[36] Broadly speaking, the emulsion is composed of the oil phase, water phase, surfactant, and subsurfactant. Its appearance is translucent to transparent liquid. Emulsion can be split up into ordinary emulsion (0.1–100 μm), microemulsion (10–100 NM), sub-micro-emulsion (100–600 NM), etc. Among them, the microemulsion is also called nanoemulsions, and the sub-micro-emulsion is also called lipid emulsion. As a drug delivery system, emulsion gets distributed in vivo in the targeted areas due to its affinity towards lymphatic fluids. In addition, the drug can be a sustained release in a long time because the drug is packaged in the inner phase and kept off direct touch with the body and tissue fluid.[61] Afterward, along the oily drugs or lipophilic drugs being made into O/W or O/W/O emulsion, the oil droplets are phagocytozed by the macrophage and get a high concentration in the liver, spleen, and kidney in which the quantity of the dissolved drug is truly heavy. While water-soluble drug is produced into W/O or W/O/W emulsion, it can be well contracted in the lymphatic system by intramuscular or subcutaneous injection. The size of the emulsion particle has an impact on its target distribution. Aside from its targeted sustained release, producing the herbal drug into emulsion will also beef up the stability of the hydrolyzed materials, improve the penetrability of drugs to the skin and mucous, and reduce the drugs' stimulus to the tissues. So far, some kinds of herbal drugs, such as camptothecin, Brucea javanica oil, coixenolide oil, and zedoary oil, have been made into emulsion. For example, Kun Z etal.[37] examined the influence of the aluminum emulsion on the human lung adenocarcinoma cell line A549 and protein formulation. Resultsindicated that the aluminum emulsion has a significant inhibition on the growth and proliferation of the A549 in vitro and it showed a time and dose-dependent relationship. Elemenum emulsion is a type of new anticancer drug with great application prospects. Furthermore, it has no marrow inhibition and no damage to the tenderness and liver. A few examples of herbal emulsions.

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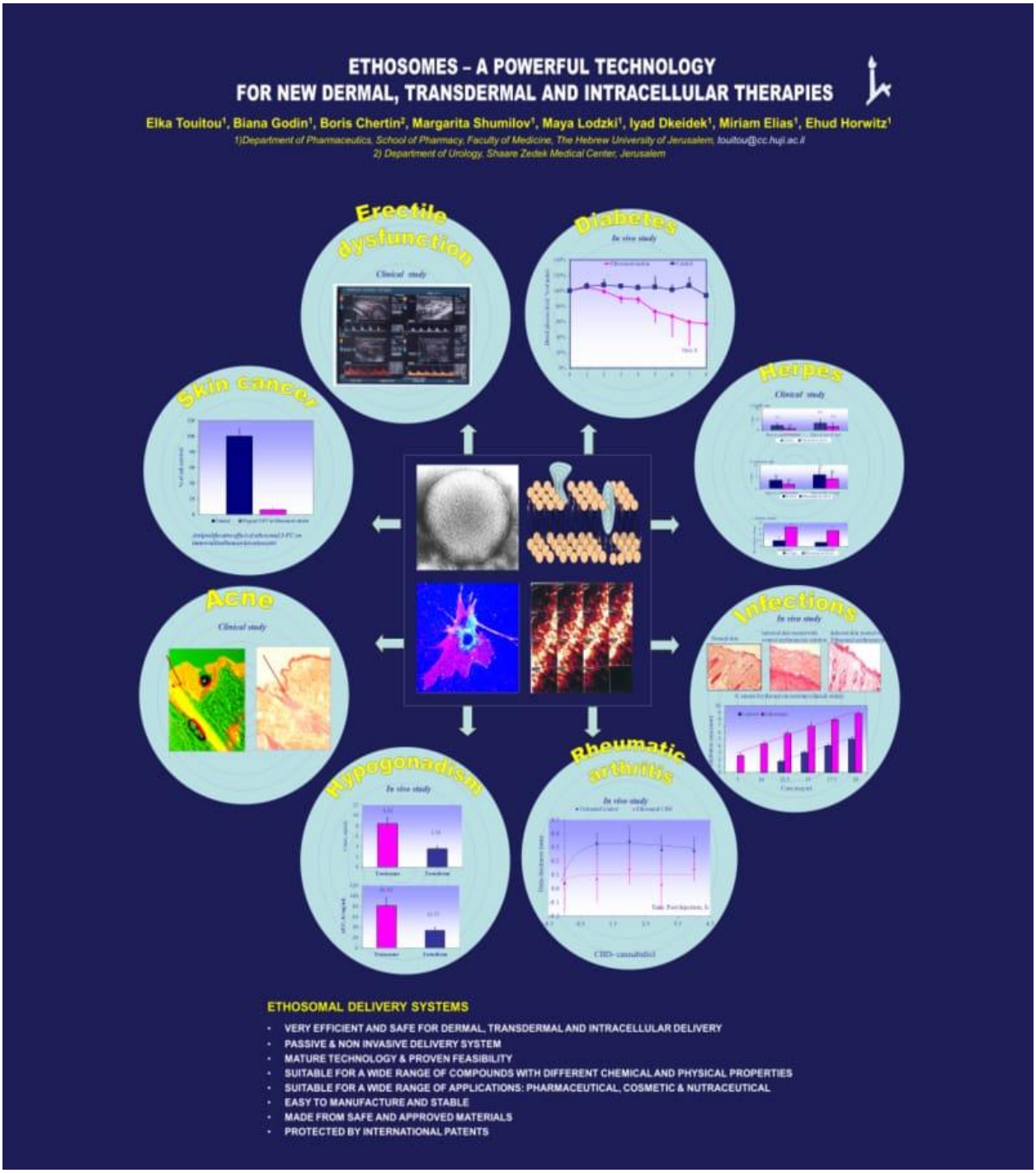
Ethosomes



Newer advancements in the patch technology have led to the development of ethosomal patch, which consists of drug in ethosomes. Ethosomal systems are made up of soy phosphatidylcholine, ethanol and water. They may form multilamellar vesicles and have a high entrapment capacity for particles of various lipophilicities. The elastic vesicles and transfersomes have also been used as drug carriers for a range of small molecules, peptides, proteins and vaccines.[38] Ethosome has a high deformability and entrapment efficiency and can penetrate through the skin completely and improve drug delivery through the skin. Likened to other liposomes, the physical and chemical properties of ethosomes make the legal transfer of the drug through the stratum corneum into a deeper skin layer efficiently or even into the blood circulation.[39] This property is very important as the topical drug carrier and transdermal delivery system. Moreover, the ethosomes

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carrier also can provide an efficient intracellular delivery for both hydrophilic and lipophilic drugs,[40] percutaneous absorption of matrine an anti-inflammatory herbal drug is increased,[41] It also permits the antibacterial Peptide to penetrate into the fibrocyte easily.[42]

From the review of literature it has been observed that, only three clinical trials have been conducted on ethosomal systems in human volunteers. Horwitz et al. carried out a pilot, double-blind, randomized clinical study to compare the efficacy of an ethosomal acyclovir preparation and commercially available acyclovir cream (Zovirax®) in treating recurrent herpes labialis in 40 human volunteers. The results revealed that the ethosomal acyclovir preparation performed betterthan Zovirax cream and showed significant improvement in all the evaluated clinical parameters, such as the time of crust formation and disappearance and pain parameters. The efficacy of ethosomal gel of clindamycin phosphate and salicylic acid was evaluated in a pilot clinical trial of 40 acne patients treated with the gel twice daily for 8 weeks. Volunteers treated with ethosomal gel showed considerable improvement in acne condition, with a decreased number of comedones, pustules, and total number of lesions compared to placebo. Ethosomal preparation of prostaglandin E1 was evaluated in a pilot clinical study in patients with erectile dysfunction. It was observed that 12 of 15 tested patients had improved peak systolic velocity and penile rigidity. Erection duration was 10–60 min. There was no reported adverse skin reactions associated with the treatment in any of the aforementioned clinical trials. [43]

Transfereosomes

Transfersomesarespecially optimized particles or vesicles that can respond to an external stress by rapid and energetically inexpensive, shape transformations.[44] The development ofnovel approaches such as transfersomes have immensely contributed in overcoming problem faced by transdermal drug delivery such as unable to transport larger molecules, penetration through the stratum corneum is the rate limiting step, physicochemical properties of drugs hinder their own transport through skin. These elastic vesicles can squeeze themselves through skin pores many times smaller than their own size and can transport larger molecules.[45] Transfersomes are applied in a nonoccluded method to the skin, which permeate through the stratum corneum lipid lamellar regions as a result of the hydration or osmotic force in the skin. It can be applicable as drug carriers for a orbit of small molecules, peptides, proteins and herbal
elements. Transfersomes can penetrate the stratum corneum and supply the nutrients, locally to maintain its functions resulting maintenance of skin[46] Transfersomes are a form of elastic or deformable vesicle, which were first introduced in the early 1990s and their elasticity is generated by incorporation of an edge activator in the lipidbilayer structure.[47] In this connection the transfersomesof Capsaicin has been made by Xiao-Yinget al.[48] which shows the better topical absorption in comparison to pure capsaicin. Examples of herbal Transfersomesand Ethosomes as drug delivery systems.

Other novel approaches

In a study by Ma et al., the effect and mechanism of Shuanghua aerosol (SHA) was investigated on upper respiratory tract infections in children aged from 3 to 14 years. SHA consists of Flos Chrysanthemum Indicum, Flos Lonicera, Herba Houttuynia, Radix Bupleurum and menthene. The control treatment was Shuanghuanglian aerosol, which consists of Flos Lonicera, Fructus Forsythiaand Radix Scutellaria. The authors conclude that SHA has obvious anti-inflammatory and antiviral effects and has a good curative effect in treating infantile upper respiratory tract infections.[49]

Gugulipid is a standardized extract prepared from the oleo gum resin of Commiphora wightii been clinically proven to reduce the levels of harmful serum lipids in the blood stream. Microparticles of Gugulipid were formulated by different techniques using Chitosan, egg albumin, sodium alginate, ethyl cellulose, cellulose acetate, gelatin and beeswax. The microparticles were evaluated for their physicochemical characteristics. The high-performance liquid chromatography (HPLC) profile showed distinct separation of Guggulsterone-E and -Z, confirming entrapment of Gugulipid in the prepared microparticles.[50]

Microcapsules with entrapped herbal water-soluble extracts of plantain, Plantago major and Calendula officinalis L. (PCE) were prepared by layer-by-layer adsorption of carrageenan and oligochitosan onto calcium carbonate microparticles with their subsequent dissolving after the treatment of ethylene diamine tetra acetic acid. Entrapment of PCE was performed using adsorption and coprecipitation techniques. The coprecipitation provided better entrapment of PCE into the carbonate matrix compared to adsorption. In vitro release kinetics was studied using artificial gastric juice. Applying the model of acetate ulcer in rats, it has been demonstrated that PCE released from the microcapsules accelerates gastric tissue repair.[51] Nanoparticles of traditional Chinese herbs(TCHs) are helpful to improve their absorption and distribution in body, and therefore enhance their efficacies. TCHs, including peach seed, safflower ,Angelica root, Szechwan lovage rhizome, rehmanniaroot, red peony root, leech, gadfly, earthworm, and ground beetle, were mixed and prepared through drying,[86] mincing, extracting, crushing into liquid particles with ultrasonic wave, filtering, and nanometerizing into nanoparticles with nanometer Collider. Nanoparticles of TCHs showed significant thrombolytic effects, resulting in quick recovery from arterial embolism and diminution of thrombi. The thrombolytic effects of nanoparticles of TCHs are much intensified than their non-nanoparticle form. There are also some research works on integrative evaluation, pharmacokinetics, and pharmacological activity of the oral prolonged-release formulations of traditional Chinese medical specialty.[52]

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Novel sustained-release implant of herb extract using chitosan has proved to be very useful. The extract of danshen (Radix Salvia miltiorrhiza), a medicinal herbal, was developed with CS–gelatin as an implant for the promotion of anastomosing and healing on muscles and tissues at the organic incision site in abdominal cavities. Measurements were made of the sustained release of tanshinone IIa, a marker component, from the material in vitro. The dissolution medium was assayed with a HPLC method. Biodegradation studies of the material were also carried both in vitro and in vivo. The film made of this material exhibited a sustained-release effect. The release profile conforms to the Higuchi equation.At most about 20% of the incorporated drug was released over 15 days in a CS–gelatin (1:2) matrix. Drug release was found to be effectively controlled by the drug-amount loaded in the matrix. The improved film (CS/gelatin ratio 1:16) can be hydrolyzed by lysozymes in vitro in 4 days.This film of 0.5 cm2 was implanted and degraded completely in rats over 28 days and the animals' wounds of abdominal incision healed well.[53]

Arthri Blend-SR is a marketed formulation containing herbal extracts and nutrients to support healthy joints and connective tissues in the body. It is a proprietary clinically validated blend of natural actives for joint care applications. The composition has the added advantage ofsustained-release technology, which benefits the continuous management of symptoms of arthritis. The blend contains Glucosamine sulfate, Boswellin (B. serrata extract) and Curcumin C3 Complex (Curcuminoids from C. longa), ingredients that work synergistically to support the management of inflammatory conditions such as arthritis. It will provide a slow-release profile of 80%–90% active ingredient release, in an 8-h period. The benefits of a sustained-release formulation are especially relevant to the bioavailability of Glucosamine.[54]

Marketed Herbal Novel Drug Delivery Formulations

Two companies dominate the market for these systems, namely, Cosmetochem and Indena. For herbal drug delivery, Cosmetochem launches Herbasec® technology in markets which are actually liposomal preparations of various herbal ingredients such as extracts of White tea, Green tea, white hibiscus, Gurana, and Aloe Vera. These extracts are used in cosmetics because of their anti-oxidant effects for prevention of aging. Indena patented the technology of phytosomes® and launches many products in market under this having diverse therapeutic benefits. Indena commercializes the plant constituents/extracts of liquorice (18ß-glycyrrhetinic acid), Ammivisnaga (visnadin), Centella asiatica (triterpenes), G. biloba (ginkgoflavonglucosides, ginkgolides, bilobalide), Hawthorn flower (vitexin-2″-O-rhamnoside), milk thistle (silymarin and Silybin), horse chestnut (escin ß-sitosterol), Terminalia sericea (sericoside), Panax ginseng (ginsenosides), grapeseed (polyphenols), Green tea (polyphenols), etc.[55]

Advantages of herbal drugs

Herbal drugs possess following advantages [56-58].

1. Low risk of side effects

Mostly herbal drugs are well tolerated by the patient, having fewer unintended consequences and fewer side effects than traditional medicine, and may be safer to use.

2. Effectiveness

Herbal drugs are more effective for long-standing health complaints that don't respond well to traditional medicine. One example is the herbs and alternative remedies used to treat arthritis. Vioxx, a well-known prescription drug used to treat arthritis, was recalled due to increased risk of cardiovascular complications. Herbal treatments for arthritis, on the other handle, have lesser side effects. Such treatments include dietary changes like adding simple herbs, eliminating vegetables from the nightshade family and reducing white sugar consumption.

3. Lower cost

Cost of herbal drugs is much less than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.

4. Widespread availability

Herbs are available without a prescription. Simple herbs, such as peppermint and chamomile, can be cultivated at home.

Disadvantages of herbal drugs

Herbal drugs possess following limitations [59-64].

1. Not suitable for many diseases

Modern medicine treats sudden and serious illnesses and accidents much more effectively than herbal or alternative treatments. An herbalist would not be able to treat serious trauma, such as a broken leg, nor would he be able to heal appendicitis or a heart attack as effectively as a conventional doctor using modern diagnostic tests, surgery, and drugs.

2. Lack of dosage instructions

Self-treatment with herbal drugs may consist of many risk factors. Moreover, with no proper direction of doses may lead to overdose.

3. Poison risk associated with wild herb Consumption of herbal drugs without correct identification of plant i.e., use of wrong part of plant may lead to poisoning.

4. Lack of regulation

Herbal products are not strictly regulated, consumers may buy inferior quality herbs. The quality of herbal products may vary among batches, brands or manufacturers. This can make it much more difficult to prescribe the proper dose of an herb. All herbal drugs are not safe, some maybe poisonous or may cause allergenic reactions.

5. Longer duration of treatment

Curing period is usually longer in comparison to conventional medication. Immense patience while undergoing herbal treatment is needed

CONCLUSION

Herbal medications have been widely employed all over the globe since ancient times and have been acknowledged by doctors and patients for their better therapeutic value as they cause fewer

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adverse effects as compared with modern medications. The drugs of Ayurvedic origin can be utilized in a more upright course with enhanced efficacy by incorporating in modern dosage forms. However, phytotherapeutics need a scientific approach to render the components in a new way to increase patient compliance and avoid repeated administration. This can be accomplished by designing NDDS for herbal ingredients. NDDS not only reduce the repeated administration to overcome noncompliance, but also help to increase the therapeutic value by reducing toxicity and increasing the bioavailability and so on. Recently, pharmaceutical scientists have shifted their focus to designing a drug delivery system for herbal medicines using a scientific approach. The novel research can also aid in capturing as well as to remain in the market. But there are many challenges with herbal drugs which need to be overcome like difficulty of conducting clinical research in herbal drugs, development of simple bioassays for biological standardization, pharmacological and toxicological evaluation methods' development, investigation of their sites of absorption, toxic herbal drugs in use, discovering various animal models for toxicity and safety evaluation, legal and regulatory aspects of herbal drugs and so on.

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