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A REVIEW ON NOVEL HERBAL DRUG DELIVERY SYSTEM

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Synopsis

Proactive and plant selections have been used to create innovative herbal formulations, including polymeric nanoparticles, nanocapsules, liposomes, phytosomes, animations, microspheres, transfersomes, and ethosomes. The novel formulations of plant actives and extracts are reported to have notable benefits over traditional formulations. These benefits include increased solubility, bioavailability, and toxicity protection; improved pharmacological activity; enhanced stability; improved tissue macrophage distribution; sustained delivery; and protection against physical and chemical degradation. A well-known manufacturer of pharmaceuticals and nutraceuticals invented the patented process known as "Phytosome," which combines phospholipids with standardized plant extracts or water-soluble phytoconstituents to create lipid-compatible molecular complexes. When the natural medicines are incorporated into contemporary dosage forms, they can be utilized more uprightly and with more effectiveness.

2. METHODS IN THE HERBAL MEDICATION DELIVERY SYSTEM

Two companies, Cosmetochem and Indena, control these systems. Herbasec® technology, a line of liposomal formulations of various herbal constituents including extracts of Guarana, Aloe Vera, White tea, Green tea, and White hibiscus, is brought to market by Cosmetochem.

distribution of herbal medications.(8) These extracts have anti-oxidant properties that help prevent aging, which is why they are used in cosmetics. Invented by Indena, the

technology of phytosomes and introduced numerous goods with a range of medicinal uses under this umbrella. The plant is commercialized by Indena.

OVERVIEW

Over the last few decades, a lot of focus has been placed on the development of innovative drug delivery systems (NDDS) for herbal medications. Traditional dosage forms, such as those with a prolonged release, are not able to meet the needs of the body for both retaining the drug component at a specific rate during the course of treatment and delivering the phytoconstituents to the intended target site for the best possible therapeutic effect. The development of nano-sized dosage forms (polymeric nanoparticles and nanocapsules, liposomes, solid lipid nanoparticles, phytosomes, and nanoemulsion) has several benefits for herbal drugs in phytoformulation research, including improved tissue macrophage distribution, sustained delivery, protection from toxicity, increased pharmacological activity, enhanced stability, and enhanced solubility and bioavailability.

Different kinds of new herbal drug delivery systems

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 as approaches for new herbal drug delivery systems.

oral dissolving pills

Asoka Lifescience Limited introduced Res-Q, the first mouth-dissolving tablet made of polyherbs and a fast-acting medication. It creates a novel drug delivery mechanism with enhanced efficacy. This is the first attempt in the field of Ayurvedic medicine to improve the efficacy of medications in treating chronic illnesses. Res-Q is a polyherbal medication that works wonders for respiratory conditions like asthma and lung issues. Bypassing the first-pass metabolism, this novel mouth-dissolving drug delivery system guarantees that the drug reaches the bloodstream immediately. It gets absorbed and dissolves in the mouth after combining with saliva. Within fifteen minutes, this Res-Q relieves respiratory distress. As a result, the product closely resembles the effectiveness of Sorbitrate, a ground-breaking mouth-dissolving medication used in cardiac.

Formulations with controlled release

An oral administrable formulation, consisting of a granulated herb and a carrier, is described in a patent as having a controlled release or stable storage of granulated herb. The formulation releases 75% of the active ingredients between 4 and 18 hours after administration. The group that includes echinacosides, hypericin, and hyperforin is chosen to contain the active ingredients. By offering an oral dosage form that is easy to take and provides optimal plasma concentrations of the biologically active compounds in a form that promotes user compliance, the invention aims to improve herbal preparations. Granulated herb is available in two dosage forms: matrix formulations, like matrix tablets, or multiparticulate formulations, like microcapsules placed inside two-piece capsules, which are used to hold.

Liposomes

These are colloidal or microparticulate carriers, typically ranging in diameter from 0.05 to 5.0 µm, that spontaneously form when specific lipids are hydrated in aqueous media.[10] The liposomes are spherical particles that freely move throughout or float into their interior, encasing a portion of the solvent. One, several, or more concentric membranes may be carried by them. Polar lipids, which are made up of the same molecules in both hydrophilic and lipophilic groups, are the building blocks of liposomes. Polar lipids self-assemble and create self-organized colloidal particles when they come into contact with water.[3] Using enhanced permeability and retention effect phenomena, liposome-based drug delivery systems have the potential to increase the therapeutic index of anticancer agents by either increasing the drug concentration in tumor cells or reducing the exposure in normal tissues.

. Drawbacks of liposome preparation: ● Poor solubility Drug/molecule encapsulation leakage and fusion

-The cost of production is high.

-Reduced stable numbers

-Phospholipids can occasionally experience an oxidation and hydrolysis-like reaction (14)

-Brief Half-life

Phytosomes

Phytosomes The majority of the bioactive components found in phytomedicines are flavonoids, which have a low oral bioavailability. Phytosomes are lipid-compatible molecular complexes that are formed from water-soluble phytoconstituent molecules, primarily polyphenols. Because phytosomes have a better ability than simple herbal extracts to navigate through lipid-rich biomembranes and ultimately reach their source, they are more bioavailable. To make phytoconstituents lipid compatible, phospholipids derived from soy—primarily phosphatidylcholine—are used as lipid-phase substances.
Originally studied for cosmetic purposes, phytosomal complexes have shown promise in recent years for drug delivery, with positive results in the areas of cardiovascular, anti-inflammatory, hepatoprotective, and anticancer applications.[31] Compared to their noncomplexed herbal extract counterpart, phytosome complexes exhibit superior pharmacokinetics and therapeutic profiles. Some phytochemicals' bioavailability has been significantly increased by the phytosome technology.

Benefits of phytosome synthesis (17)

More bioavailability because of the phospholipid complex; better absorption in the gastrointestinal tract.

A higher bioavailability results in a better therapeutic outcome.

Low dosage needed because of high bioavailability.

Increased stability.

High lipophilicity results in high penetrability; hence, it is preferred over liposomes in cosmetics.

Increased therapeutic advantages.

Phosphatidylcholine functions not only as a carrier but also as a liver protector.

2.2.4. The formulation of phytosomes has drawbacks

Phytoconstituents leave phytosomes very quickly.(18)

Lecithin, a phospholipid, can stimulate the MCF-7 breast cancer cell line's proliferation.

The phytoconstituents could be quickly eliminated by phytosomes (19)

Nanoparticles

Hydrophilic and hydrophobic drugs can be efficiently delivered through the use of nanoparticles. Submicron-sized particles, with a range of 10–1000 mm, are called nanoparticles.[4] Controlling particle size, surface characteristics, and release of pharmacologically active agents is the main objective of designing nanoparticles as a delivery system. This allows the drug to act on specific sites at the therapeutically ideal rate and dosage.[33] Biodegradable polymeric nanoparticles have garnered significant interest as possible drug delivery vehicles in recent times.[3] While the active ingredient is distributed throughout the nanospheres' matrix-like structure (the molecules), the active ingredient is contained within the nanocapsules' polymeric membrane. Numerous benefits of nanonization include higher compound solubility, lower dosages of medications, and enhanced herbal absorbency.

Niosomes

Niosomes are multilamellar vesicles that are made of cholesterol and nonionic surfactants belonging to the alkyl or dialkylpolyglycerol ether class. Previous research conducted in collaboration with L'Oreal has demonstrated that niosomes share many characteristics with liposomes that make them suitable drug carriers.[45] Niosomes are distinct from liposomes in that they have a few benefits over the latter. Liposomes have a number of drawbacks, including high cost, chemical instability of their constituents (phospholipids, for example) due to oxidative degradation, need for special handling and storage, and inconsistent purity of natural phospholipids. Niosomes are not affected by any of these issues.

Niosomal formulations' benefits

They enhance the stability of the entrapped drug and are stable and osmotically active.

There are no special requirements for handling or storing surfactants.

Can boost a drug's oral bioavailability

Enhanced skin penetration of medications is possible.

They can be applied topically, parenterally, and orally.

The surfactants are non-immunogenic, biodegradable, and biocompatible.

Enhance the medication's ability to perform therapeutically by shielding it from the biological environment and limiting its effects to target cells.

decreasing the drug's clearance.

Niosomal formulations' drawbacks

Structural instability

Combination

Fusion

Drug entrapment leakage

Drugs encapsulated undergo hydrolysis, reducing the dispersion's shelf life.

Proniosomes

Proniosome gel system is an advancement over niosome, which can be applied in a number of ways to deliver actives to the intended location.[47] Proniosomal gels are those formulations that become niosomes when they are hydrated in situ using the skin's natural water content.[48] Before being used on brief agitation in hot aqueous media, prosniosomes—water-soluble carrier particles coated with surfactant—can be hydrated to form niosomal dispersion.

Drug delivery system applied topically

There has been a growing interest in transdermal drug delivery systems (TDDS) for both systemic and topical drug delivery, with the latter being more convenient for local therapeutic effects on skin diseases.[51] With other medications, they did not, however, experience the same level of success. However, transdermal drugs have a great deal of promise as smart drug delivery systems of the future.[2] The benefits of a transdermal delivery system include easy application, reduced side effects, improved bioavailability, and regulated drug delivery. The creation of transdermal films that include herbal drug components like curcumin (Curcuma longa) and boswellic acid (Boswellia serrata) is one of the first attempts to use Ayurvedic medicines through transdermal drug delivery system (TDDS), which uses the skin as a site for continuous drug administration into the systemic circulation. Consequently.

Microspheres

Discrete spherical particles with an average size between 1 and 50 µ are known as microspheres.[52] The study and adoption of microparticulate drug delivery systems is based on their ability to deliver drugs specifically to the intended target site and to maintain the desired concentration in the relevant situation without causing side effects. Microencapsulation is a helpful technique that increases patient compliance and considerably prolongs the duration of the drug's effect. Finally, since a constant plasma concentration is maintained, the whole dose and a small number of adverse reactions may be thinned out.[53] Thus far, several plant active ingredients have been synthesized into microspheres, including rutin, camptothecin, zedoary oil, tetrandrine, quercetine, and extract from Cynara scolymus.

Emulsions

An emulsion is a nonhomogeneous dispersion system made up of two types of liquids that are incompatible with one another and that disperse as droplets in the other.[60] The water phase, surfactant, subsurfactant, and oil phase make up the emulsion, in general. It has a transparent to translucent liquid appearance. There are different types of emulsion: sub-micro-emulsion (100–600 NM), microemulsion (10–100 NM), and ordinary emulsion (0.1–100 µm). The sub-micro-emulsion is also known as a lipid emulsion, and the microemulsion is also known as a nanoemulsion. Because of its affinity for lymphatic fluids, emulsion is distributed in vivo in the targeted areas as a drug delivery system.

Ethosomes

The creation of the ethosomal patch, which contains medication within ethosomes, is the result of more recent developments in patch technology. Water, ethanol, and soy phosphatidylcholine comprise ethosomal systems. They have a high entrapment capacity for particles with different lipophilicities and can form multilamellar vesicles. A variety of small molecules, peptides, proteins, and vaccines have been administered via the use of elastic vesicles and transfersomes as drug carriers.[68] The encapsulation efficiency and deformability of emmetropes allow them to fully penetrate the skin and enhance the delivery of drugs through it. The physical and

chemical characteristics of ethosomes, when compared to other liposomes, enable the drug to be lawfully transferred through the stratum corneum into a deeper skin layer or even into the blood.

Transferasomes

Transfersomes are specifically engineered particles or vesicles with the ability to quickly and cheaply change their shape in response to external stress.[75] The creation of innovative techniques like transfersomes has greatly aided in the resolution of issues with transdermal drug delivery, including its inability to carry larger molecules, the rate-limiting step being penetration through the stratum corneum, and the physicochemical characteristics of the drugs impeding skin transport. Larger molecules can be transported by these elastic vesicles, which can fit through skin pores that are many times smaller than themselves.[76] Applying transfersomes to the skin in a nonoccluded manner allows them to penetrate the stratum corneum lipid lamellar regions due to the osmotic force or skin hydration.

Other innovative methods

The effect and mechanism of Shuanghua aerosol (SHA) on upper respiratory tract infections in children aged 3 to 14 years were examined in a study by Ma et al. Radix Bupleurum, Herba Houttuynia, Flos Chrysanthemum Indicum, Flos Lonicera, and menthene make up SHA. Shuanghuanglian aerosol, which includes Flos Lonicera, Fructus Forsythia, and Radix Scutellaria, served as the control treatment. The authors come to the conclusion that SHA is a good treatment for infantile upper respiratory tract infections and has noticeable anti-inflammatory and antiviral properties.[83]

It has been clinically demonstrated that gugulipid, a standardized extract made from the oleo gum resin of Commiphora wightii, lowers blood levels of dangerous serum lipids.

NEW HERBAL DELIVERY FORMULATIONS THAT ARE MARKETED

Cosmetochem and Indena are the two companies that control the majority of the market for these systems. Cosmetochem introduces Herbasec ® technology, which are liposomal preparations of different herbal ingredients like extracts of white tea, green tea, white hibiscus, gurana, and aloe vera, to the market for the delivery of herbal drugs. Because of these extracts' anti-oxidant properties, which help to prevent aging, they are used in cosmetics. Having patented the phytosomes ® technology, Indena releases numerous products with a range of medical uses. Licorice (18ß-glycyrrhetinic acid), Ammi visnaga (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), grape seed (polyphenols), and horse chestnut (escin ß-sitosterol) are among the plant constituents/extracts that Indena commercializes.

HERBALIZED COMPOUNDS

Excipients: An Overview

An excipient is a substance that is used as a vehicle to administer medication. Particularly, natural polysaccharide polymers are employed inpharmaceutical formulations to assist in product identification, support or safeguard bioavailability, stability, or patient acceptability during manufacturing,

or enhance any other element of the medication's general efficacy, safety, or delivery while being used or stored.

The pharmaceutical sector makes use of a rangeof plant-based excipients as colloids, including cellulose, acacia, tragacanth, starch, agar, alginates, carrageenan, guar gum, and xanthan gum.

thickening agents, gelling agents, stabilizing agents, bases for suppositories, coating materials, and dissolving, sustaining, and protecting agents. Raw materials can always be found in plant sources because they are

Herbal excipient classification

Excipients are frequently categorized based on how they are used and what role they play in pharmaceutical products:

binders.

Fillers and Diluents.

Disintegrants, glideants, and lubricants.

Coloring agents, plasticizers.

Antioxidants, preservers, and suspending agents.

Sweeteners, flavorings, and agents that enhance flavor.

Dispersing agents, gums, and printing inks.

BINDER

The purpose of binder excipients is to act as an adhesive, securing powders, granules, and other dry ingredients together to provide added mechanical strength to the finished product. Binders are used to create granule formulations that are more dependable and effective. Additionally, they can offer low activedose tablets, more volume, which are frequently used in wet granulation. Solution is dissolved using solvents, such as derivatives of gelatin cellulose.Binders are categorized based on the use for which they are designed. To polyvinyl pyrrolidone starch, sucrose and polyethylene glycol are added. OrganicAlginic acid, corn starch, acacia, and other materials are used as binders.

Fig. Binder

2. FILLERS AND DILUENTS

A diluent, sometimes referred to as a filler, diluent, or thinner, is a diluting agent. Some liquids are too thick to pump, or they simply cannot be pumped.

from one place to another or excessively thick. This could be problematic since it might not be beneficial to transfer these fluids in this form. The diluting agents are

employed to help with the decreased mobility. This lowers the viscosity of the fluids and the cost of pumping and shipping. A few instances

cellulose, lactose, mannitol, starch, and other natural diluents.

Lubricants

Lubrication accomplishes this goal of promoting a smooth process by adding specific compounds. During the formulation phase, lubricants are used to prevent materials from clumping together. They lessen friction between the particles and the formulation while maintaining its stickiness.

processing equipment. They are incorporated into formulations in very small amounts, much like solid dosage forms. Because they reduce the friction between particles,Product flow is improved by lubricants.

Examples include paraffin oil, castor oils, sodium chloride, stearic acid, and sodium stearyl fumarate.

Glidants

Glides are added to the formulation to improve the tablet-core mix material's flow. Glides are added in the early stages of compression.

to the tablet powder mix's particle configuration in order to enhance uniformity and flowability inside the die cavity of tablet presses. Talc possesses a concentration.

restriction, even though it's thought to be a better glidant than starch, due to its retardant effect on the dissolution-disintegration profile.

Glidants lessen particle friction, which facilitates the flow of tablet granulation.

Disintegrant

Disintegrants are added to oral solid dosage forms to help in deaggregation. Disintegrants are substances that are intended to swiftly dissolve solid dosageforms when they come into contact with moisture.

Aspects of the analysis of the novel herbal formulation

Visualization: Transmission electron microscopy and scanning electron microscopy can be used to visualize phytosomes.

Particle size and zeta potential: Dynamic light scattering with a computerized inspection can be used to determine the particle size and zeta potential and correlation spectroscopy of photons.

Equipment efficiency - The ultracentrifugation method can be used to determine how well a medicine is entrapped by phytosomes.

Transition temperature: Differential scanning calorimetry can be used to find the vesicular lipid systems' transition temperature.

Surface tension activity measurement: The ring method in a Du can be used to determine the drug's surface tension activity in an aqueous solution.Nouy tensiometer for rings.

Vehicle stability: Vehicle stability is ascertained by the vesicles' size and composition over time.One measures the mean size.transmission electron monitoring of structural alterations is done by dynamic light scattering.

Drug content - A suitable spectroscopic method or a modified high performance liquid chromatographic method can be used to quantify the amount of drug.

a) H1 NMR: In nonpolar liquids, the atoms that contribute to the complex's formation alter the 1H-NMR signal dramatically without any signal accumulation that is unique to each molecule. The signals coming from the protons of the flavonoids must be widened in order to stop the proton from being released. The signals in phospholipids all grow, however the singlet associated with the choline N-(CH3)3 experiences an increase in position. There are some new broad bands that appear when the sample is heated to 60°C. These

The bands primarily relate to the resonance of the flavonoid moiety, which needs to be enlarged to stop the proton from being reduced approach.

In vitro drug release study using dissolution apparatus: USP-type II dissolution apparatus was used to study the sample's in vitro drug release.

The dissolution flask was filled with 900 ml of 0.1N HCl as the dissolution medium, and the temperature and rpm were kept at 37±0.50c andthe phytosome equivalent of 100 mg was added to each dissolving apparatus bowl. The device was left to operate for ten hours. An example 5 ml measurements werewithdrawn using a 10-milliliter pipette every hour for a maximum of ten hours. Every time, a new dissolution medium (370C) was used.with the same amount of the specimen. Take 0.5 ml from this, dilute it to 10 ml, and use spectroscopy to measure the absorbance at 420.0 nm.

Excipients compatibility study - The research involved determining the physicochemical compatibility between the polymer and extract mixture.conducted by KBr dispersion method infrared spectral studies using Fourier Transform Infrared Spectrophotometer. The spectrum that emerged as a result wasexamined for variations in the spectrum.
Chromatographic and spectroscopic analysis: The spectroscopic methods listed below are used to confirm the emergence of a complex or Examine how the phospholipid and phytoconstituents interact reciprocally.

FINAL VERDICT

Since ancient times, herbal remedies have been used extensively throughout the world. Both physicians and patients have recognized the superior therapeutic value of herbal remedies due to their lower side effect rate when compared to contemporary pharmaceuticals. Modern dosage forms can help the drugs with Ayurvedic origins be used more uprightly and with greater efficacy. However, in order to increase patient compliance and reduce the need for repeated administration, phytotherapeutics require a scientific approach to render the components in a novel way. NDDS for herbal ingredients can be designed to achieve this. In addition to lowering the need for repeated administration to overcome noncompliance, NDDS also contribute to an increase in therapeutic value through lowering toxicity, raising bioavailability, and other factors. Scientists studying pharmaceuticals have recently changed.

REFERANCES

1. Medina OP, Zhu Y, Kairemo K. Targeted liposomal drug delivery in cancer Curr Pharm Des. 2004;10:2981–9
2. Mandal SC, Mandal M. Current status and future prospects of new drug delivery system Pharm Times. 2010;42:13–6
3. V. Kusum Devi, Nimisha Jain, Kusum S. Valli, Importance of novel drug delivery systems in herbal medicines, Pharmacognosy Reviews, 4(7), JanuaryJune 2010, Page no.28-29
4. Kharat A, Pawar P, Novel drug delivery system in herbal's, International journal of pharmaceutical, chemical and biological sciences,4(4),2014, page no.911.
5.Sanjida Afrin, Ishrat Jahan, et al, Novel approaches of herbal drug delivery, Journal of pharmaceutical research international, 21(5), 2018, page no 3- 7.
6. Bahuguna S. Joshi D., Singh B. and Semwal N.: A review on novel pharmaceutical approaches of herbal drugs in derma care, Dermatol and Cosmet JOJ,4(2),2021,Page no.1.
7. Thillaivanan.S, Samraj.K,Challenges, Constraints and Opportunities in Herbal Medicines – A Review,International Journal of Herbal Medicine , 2 (1),2014,Page no.21-24
8. Shyam Baboo Prasad et.al,International Journal of Current Pharmaceutical Review and Research,4(3),Page no.96
9. Manoj kumar sarangi, Sasmita padhi, Novel herbal drug delivery system: An overview ,Arch med health science,6(1),2018,page no.171-179.
10. Sharma D, Bhujbale AA; Phytosomes is a Novel Drug Delivery System based herbal formulation: An Review; Pharma Tutor , 6(3) ,2018, page no.23-26.
11. Kulkarni Giriraj T, Herbal Drug Delivery System:An Emerging Area In Herbal Drug Research ,Journal of Chronotherapy and Drug Delivery, 2(3),2011,Page no.115
12. Kulkarni et al. Liposomes: A Novel Drug Delivery System,Int J Curr Pharm Res, 3(2), 2018,Page no.10
13. Prajakta N. Dongare, Anuja S. Motule,et al, Recent development in novel drug delivery system for delivery of herbal drugs ..and updates, GSC Advanced Research and Reviews,08(02),2021, Page no.11.
14. Sharma D,Ali AAE,et al,An Updated Review on :Liposomes as drug delivery system,PharmaTutor,6(2),2018,Page no .50-62
15. Kant Shashi et al.A Complete Review on: LIPOSOMES , IRJP 2012, 3 (7), Page no.10
16. Jain et al.,Phytosome: A Novel Drug Delivery System For Herbal Medicine ,IJPSDR , 2010, 2(4), Page no.225
17. Suvarna G. Bhokare, Surekha V. Lahane, et al, Herbal Novel Drug Delivery A Review, World Journal of Pharmacy and Pharmaceutical Sciences,5(8), 2016,Page no.596-597.
18. V, A., Reddy, P.D. and S, R. 2019. Phytosomes : A Promising Technology in Novel Herbal Drug Delivery System. PharmaTutor. 7, 6 (Jun. 2019), 18-25
19. Sharma S et al., Review On Phytosomes: As A Emerging Strategy To Improve The Bioavailability Of Phytoconstituents. American Journal of PharmTech Research 2020.10(5),Page no.124
20. V. Pola chandu, A. Arunachalam, et al, Niosomes : A novel drug delivery system, International journal of novel trends in pharmaceutical sciences, 2(1),2012, Page no.25-28. 21. Sharma D, Ali AAE, Aate JR; Niosomes as Novel Drug Delivery System ,PharmaTutor, 6(3),2018 ,Page no.58
22. Hiraman P. Nandure, Dr. Prashant Puranik, et al, ethosome: A Novel Drug Carrier ,International Journal of Pharmaceutical Research and Allied Sciences,2(3),2013, Page no.20-23.

23. Siddiqua et al.,A Review on Novel Approach of Drug Delivery Ethosomes, World Journal of Pharmaceutical Research,9(5), 2020,Page no.2194.
24. Mahesh Mangnale et al. A Review on Microspheres: Method of Preparation and Evaluation.Ijppr, 20 (3),2021 Page no.486.
25. Sahil Kataria et al. Microsphere: A Review ,IJRPC , 1(4),2011 ,Page no.1186.