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An Overview: Novel Herbal Drug Delivery System

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Abstract
The term "Novel Drug Delivery System" refers to a new approach to drug delivery that addresses the limitations of traditional drug delivery systems. Our country has vast knowledge of Ayurveda, the potential of which has only recently been realised. However, the drug delivery systems used to administer the herbal medicine to the patient are traditional and out of date, resulting in decreased drug efficacy. If novel drug delivery technology is used in herbal medicine, it may improve the efficacy and reduce the side effects of various herbal medicines. As a result, it is critical to incorporate novel drug delivery systems in order to combat more serious diseases. Due to a lack of scientific rationalisation and processing difficulties, such as standardisation, extraction, and identification of individual drug components in complex polyherbal systems, herbal medicines were not considered for development as novel formulations for a long time. Many novel carriers have been reported for successful modified delivery of various herbal drugs, including nanoparticles, phytosomes, liposomes, microemulsions, and so on. This article provides an overview of various drug delivery technologies that can be used for herbal active constituents.

Keywords: Herbal drug, Nanoparticles, Liposome, Phytosome, Novel Drug delivery.

1. Introduction

According to recently reported data, more than 70% of newly formulated drugs have poor water solubility, which becomes a limiting factor in drug absorption after oral administration.[1] Among the factors that contribute to the failure of clinical trials are poor solubility of the ingredient, poor stability due to gastric and colonic acidity, poor metabolism by the effect of gut microflora, poor absorption across the intestinal wall, poor active efflux mechanism, and first-pass metabolic effects.[2,3] In this regard, developed novel drug delivery systems and carriers for herbal drugs should ideally achieve some prerequisites such as proper drug delivery at a rate oriented by the needs of the body, over the course of treatment, and passing the active entity of herbal drug to the site of action.[4] There have been numerous approaches taken to improve drug solubility, sustainability, bioavailability, and gastrointestinal permeability.[5] In the development of new pharmaceutical carriers and delivery systems, nanocarriers have received a lot of

attention. One approach to addressing this issue is to encapsulate natural plant metabolites in a biodegradable and biocompatible nanoparticle.[6]

Over the last few decades, much emphasis has been placed on the development of a novel drug delivery system (NDDS) for herbal drugs. Conventional dosage forms, including prolonged-release dosage forms, are unable to meet the requirements for both holding the drug component at a distinct rate as directed by the body's requirements throughout the treatment period, as well as directing the phytoconstituents to their desired target site to achieve the best therapeutic response. Developing nanosized dosage forms such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, phytosomes, and nanoemulsion has a number of advantages for herbal drugs, including increased solubility and bioavailability, protection from toxicity, increased pharmacological activity, increased stability, sustained delivery, and protection from physical and chemical degradation. As a result, nanosized NDDSs of herbal drugs have a promising future for improving activity and overcoming problems associated with plant medicines.[7]

Incorporating novel drug delivery technology to herbal or plant actives reduces drug degradation or presystemic metabolism, as well as serious side effects caused by drug accumulation in nontargeted areas, and improves ease of administration in paediatric and geriatric patients.[8]

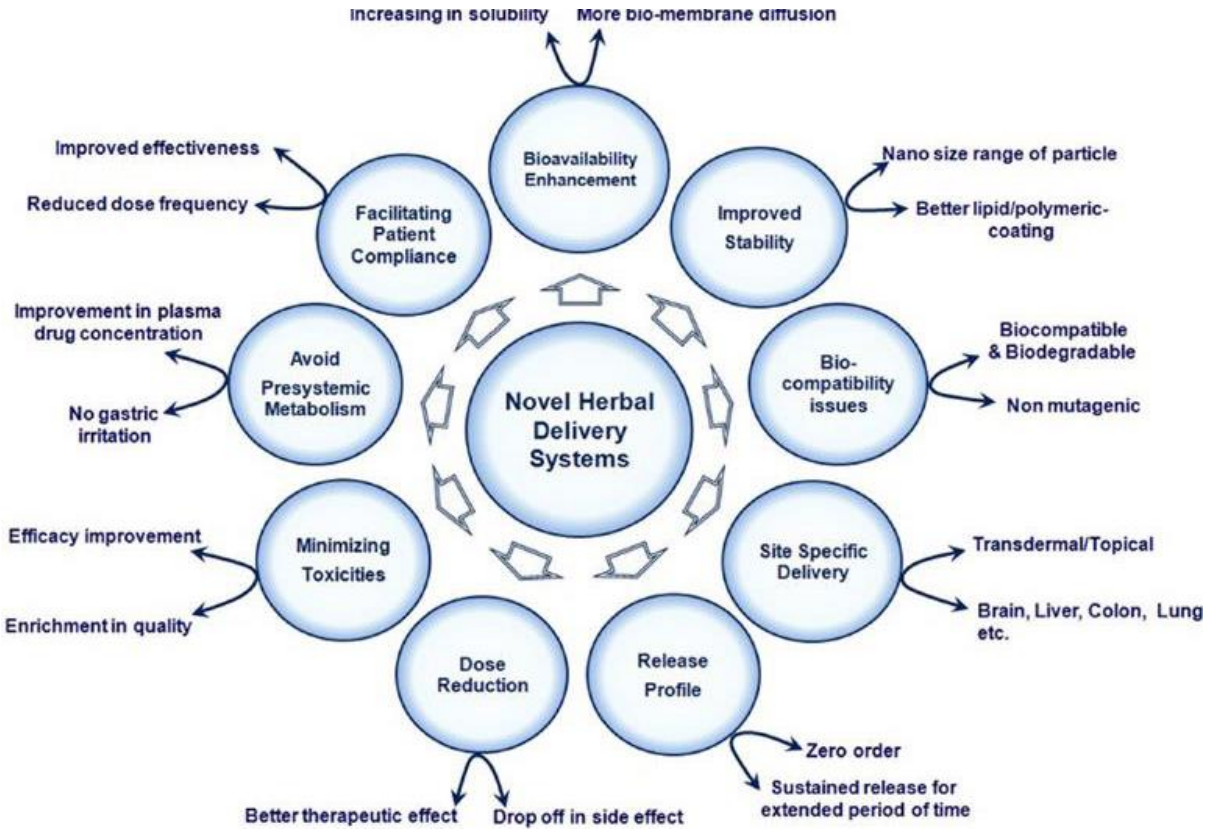

Fig. 1: Advantages of Novel Herbal Drug Delivery system

Disadvantage of current drug delivery system used in herbal formulations.[9]

1. Bulk dosing
2. Decrease bioavailability and decrease absorption
3. Show poor effect or require high amount of dose to produce desire effect.
4. High amount of raw material require processing the medicine.

5. Loss 'N' number of extinct or rare species.
6. Harmful effect on ecology which ultimately become cause of global warning.
7. No target specificity in present formulation.

Advantage of novel drug delivery system used in herbal formulations.[10]

1. Help to increase the efficacy and reduce the side effect of various herbal compounds.
2. Quantity of component becomes less with improving quality of drug effect.
3. Fewer raw material are required to achieve the desire effect and control drug delivery to provide exact specification regarding drug dose form.
4. Ready to use devices are acceptable in today's fast life style where time is important.
5. Carry maximum amount of drug to the site of action by passing all barriers. Such as acidic pH of stomach increase prolong circulation of drug into blood due to their small particle size.
6. Reduce repeat dose administration. The main aim for adaptation of novel drug delivery devices in herbal formulations are to develop better system for proper drug delivery in terms of

a) Target oriented

b) Sustain and Controlled release of drug at the site which help to increase the efficacy and reduces side effects at the site of formulation.

7. This administration not only reduces repeat administration but also helps to increase the therapeutic value by reducing toxicity and increase the bioavailability.

2. Material and Methods

Types of Novel Herbal Drug Delivery System

Various approaches to novel herbal drug delivery systems, such as liposomes, phytosomes, pharmacosomes, niosomes, nanoparticles, microspheres, transferosomes, ethosomes, transdermal drug delivery system, and proniosomes, are discussed below.

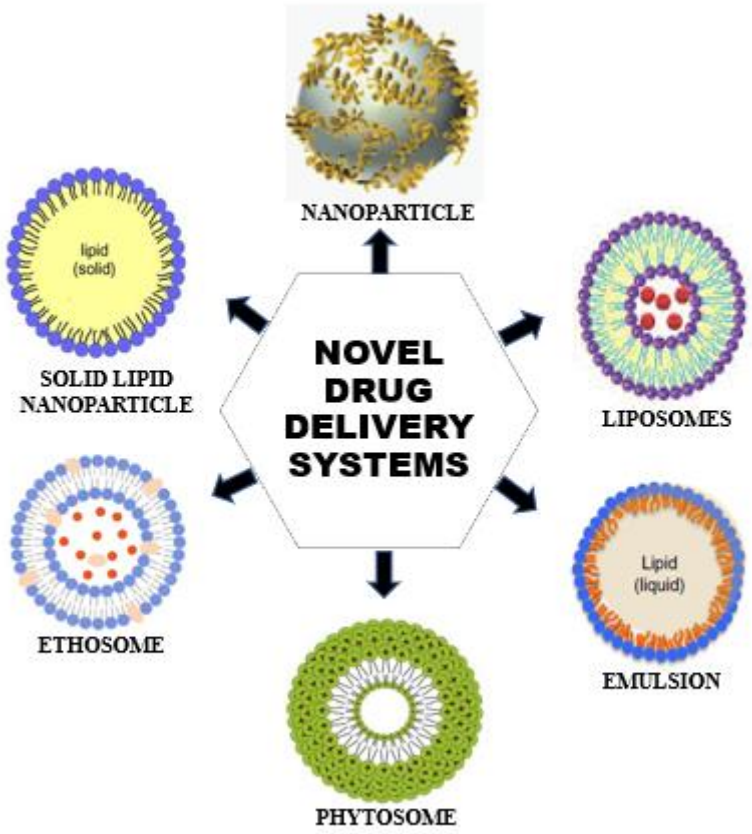

Fig. 2 Novel Herbal Drug delivery system

2.1. LIPOSOMES[11,12]

Liposomes are biodegradable, colloidal, spherical vesicles with a bilayer membrane enclosing an aqueous core (0.05-5.0 m in diameter). Liposome membranes can be made of naturally derived phospholipids with mixed lipid chains and a variety of head groups, or they can be made of pure synthetic lipids with defined acyl chains and head groups. Liposomes can encapsulate drugs with widely varying lipophilicities, either in the phospholipid bilayer, the entrapped aqueous volume, or at the bilayer interface. Liposomes, which are typically made of phospholipids, have been used to alter the pharmacokinetic profile of not only drugs, but also herbs, enzymes, and other substances. Liposomal drug delivery is advantageous because it improves the therapeutic index of anti-cancer agents by increasing drug concentration in tumour cells while decreasing exposure to normal cells. Liposomal drug delivery systems can be used to implement a variety of targeting strategies. Many herbal liposomal formulations for herbal drugs have been reported, where liposomes can improve product performance by increasing solubility, improving bioavailability, targeting at site of action, and extending drug release.

The primary advantages of using liposomes include

I. high biocompatibility
II. easiness of preparation
III. chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds

IV. simple modulation of their pharmacokinetic properties by varying the chemical composition of the player components

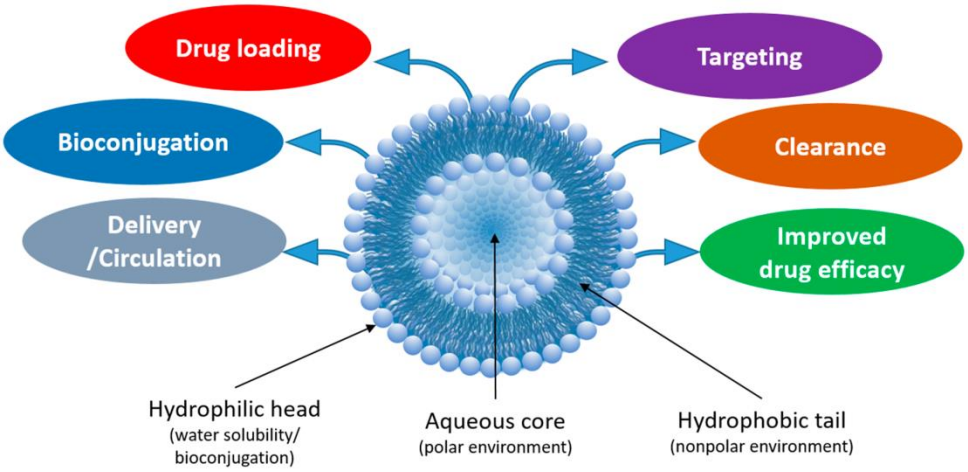

Fig. 3: Structure and mechanism of liposomes

Methods of preparation

All the methods of preparing the liposomes involve four basic stages:

1. Drying down lipids from organic solvent.
2. Dispersing the lipid in aqueous media.
3. Purifying the resultant liposome.
4. Analyzing the final product.

Advantages of liposome formulation

1. Hydrophobic and hydrophilic drug can be delivered.
2. Liposome herbal therapy acts as a carrier for small cytotoxic molecules and as vehicle for macromolecules as gene.
3. Sustained and controlled release of formulation can be possible.

2.2. PHYTOSOMES[13-16]

Phyto denotes a plant, and some implies something that resembles a cell. Phytosomes are tiny structures that resemble cells. A lipid surrounds and binds the bioactive phytoconsituents of the herb extract in this sophisticated form of herbal preparation. The majority of the bioactive components in phytomedicines are water-soluble substances such flavonoids. Terpenoids glycosides, which are a prominent class of these flavonoids, have a wide range of therapeutic effects. Because phytosomes have a lipophilic outer layer and a water-soluble herbal extract, they demonstrate better absorption than traditional herbal extracts in dose form. This leads to better bioavailability and effects.

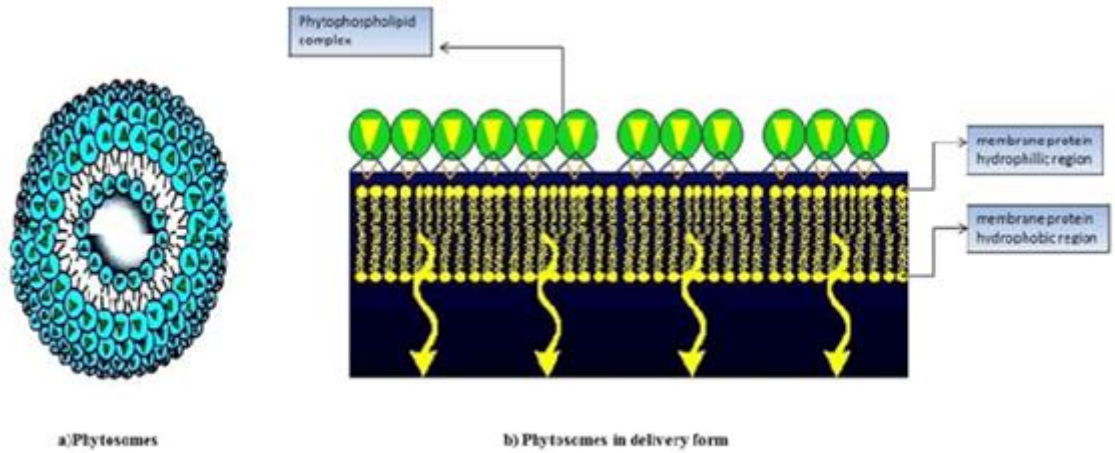

Fig. 4 Structure of phytosomes

Method of preparation[17]

In a round bottom flask (RBF), phosphatidylcholine and cholesterol were accurately weighed and then dissolved in 10 ml of chloroform and sonicated for 10 min using a bath sonicator. Rotary evaporators (45–50°C) are used to remove organic solvents. The mixture of phospholipids was created as a thin film after the solvent had been completely removed. This film was moistened in a rotating evaporator at 37 to 40 degrees Celsius for one hour. Following hydration, a lipid and plant extract mixture was sonicated for 20 minutes with an ice bath nearby to help with heat dissipation. Phytosomes were then made, placed in amber-colored bottles, and kept in the freezer (2 to 8 degrees Celsius) until needed.

Advantages of Phytosomes Phytosomes have the following advantages[18]

- Improve the absorption of lipid insoluble polar phytoconstituents, enhance the bioavailability.
- Appreciable drug entrapment which becomes very beneficial. Reduce the dose due to increased absorption.
- Phosphatidylcholine shows synergistic effect because it is a hepatoprotective also.
- Phytosomes are more stable because of the chemical bonding between the phytoconstituents and carrier i.e. phophatidylcholine.
- Effective in cosmetics.

2.3. NANOPARTICLES[19]

The average size of the drug particles in this system is up to 100nm. Size reduction results in an increase in compound solubility, a decrease in medication dosage, and an improvement in the pace at which herbal drugs are absorbed. For instance, nanonized curcuminoides. After performing several in vitro drug tests, it was discovered that Zedory turmeric oil, a traditional Chinese medicine, was loaded with nanostructured lipid carriers. This indicates that the drug release rate from the prepared nanoparticles is increased, showing promise for an IV dosage form of the oily, water-insoluble drug. Both hydrophilic and lipophilic drugs can be put into these nano carriers because they are comprised of secure synthetic biodegradable polymer material. Berberine nanoparticles encapsulated in fucose, chitosan, and heparin were created, and the delivery effectiveness was evaluated using confocal laser scanning microscopy. The proposed drug carrier efficiently controls the release of berberine, which interacts specifically at the site of H. pylori

infection, and greatly boosts berberine's suppressive effect on H. pylori growth, according to analysis of stimulated gastrointestinal media. The berberine-loaded fucose-conjugated nanoparticles demonstrated an H. pylori clearance effect in an in-vivo research, and they significantly decreased stomach inflammation in an H. pylori-infected animal study.[19]

Method of preparation

- Solvent evaporation
- Nanoprecipitation,
- Emulsification/solvent diffusion
- Salting out
- Dialysis
- Supercritical fluid technology

Advantages of herbal nanoparticle delivery system

- Nanoparticulate system delivers the herbal formulation directly to the site of action.
- Encapsulating drugs within nanoparticles can improve the solubility and pharmacokinetics of drugs.
- Nanoparticles can also reach the choice of formulations, promote the drugs through the biological barriers and increase the bioavailability of drugs.
- It can take the drug directly to the site of action without destroying surrounding environment

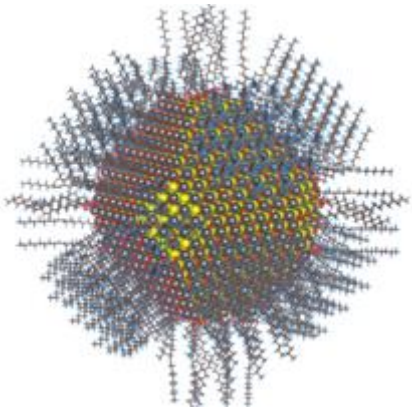

Fig. 5 Structure of nanoparticles

2.4. EMULSION[20]

Emulsions are biphasic systems in which one phase is constantly water-based while the other phase is a liquid or oil. They are non-toxic and non-irritating by nature, have a greater surface area, and may therefore permeate through skin. increased bioavailability due to high skin solubility. The non-emulsion compound's palatability and compatibility with other excipients are two important limitations of this drug delivery system. A sub-micron emulsion of a micro-emulsion is referred to as a lipid emulsion. The Neem oil (Azadirecta indica), Tween 20, and deionized water nanoemulsion formulation was successfully optimised using the high-energy technique. The smallest droplet size measured 31.03 nm. When compared to neem oil nanoemulsions with bigger droplet sizes, smaller droplet sizes were found to be more effective at controlling mosquito larvae. In place of other insecticides, neem oil nanoemulsion may be an effective

remedy for the management of vector-borne illnesses. A reported 31.03 nm droplet size exists. [20] The effectiveness was boosted by the smaller size and even distribution of these tiny particles. The nano emulsion can be utilised as an alternative to synthetic pesticides for the management of vector-borne diseases because it is conveniently accessible, economically viable, and less hazardous.

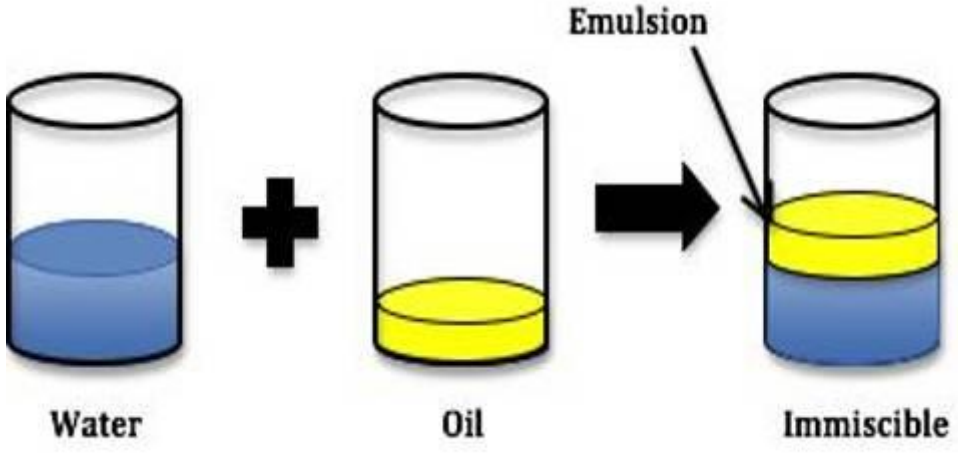

Fig. 6 Preparation of emulsion

2.5. ETHOSOMES [21]

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

Method of preparation

- Cold Method
- Hot Method
- Classic mechanical dispersion method

Advantages of ethosomal drug delivery

- Transdermal permeation of drug through skin can be enhanced.
- Large amounts of diverse groups of drugs can be delivered.
- The ethosomal drug is administered in semisolid form, resulting in improved patient compliance

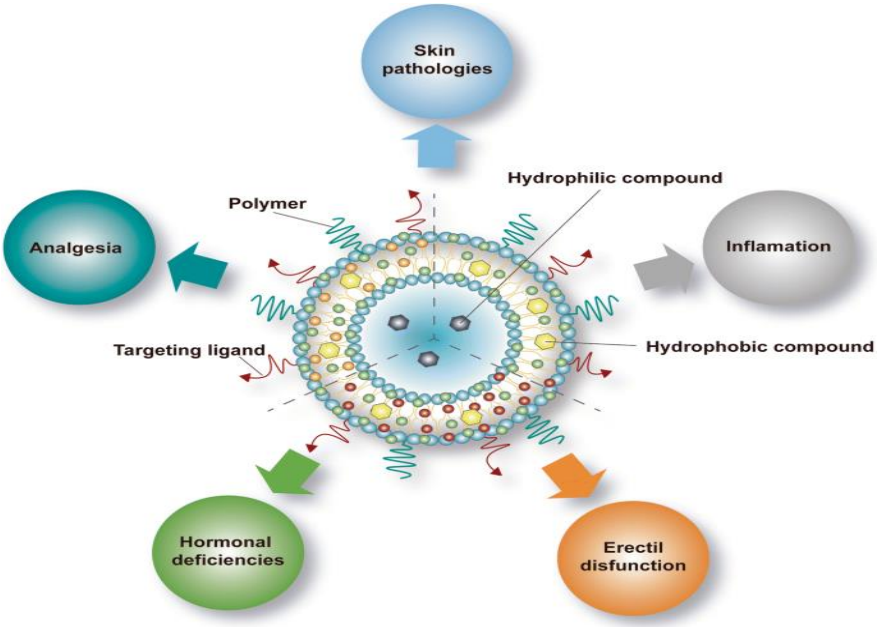

Fig. 7 Structure and uses of ethosomes

2.6. NIOSOMES[22,23]

Multilamellar vesicles called niosomes are made of cholesterol and nonionic surfactants of the alkyl or dialkylpolyglycerol ether family. The general features of niosomes as possible drug carriers are comparable to those of liposomes, according to earlier experiments conducted in collaboration with L'Oreal. In that they provide some advantages over liposomes, niosomes are distinct from liposomes. Phospholipids, one of the constituents in liposomes, are chemically fragile because to their propensity for oxidative destruction, they require specific care and memory, and the purity of natural phospholipids varies. Niosomes are not affected by any of these issues.

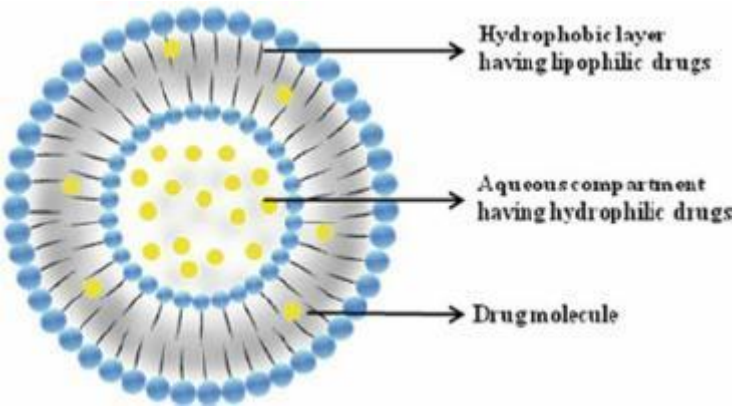

Fig. 8 structure of niosomes

2.7. TRANSFEROSOMES[24]

Transferosomes are phospholipid-based sac-like vesicles that have the ability to transport drugs when applied topically. It gets around the stratum corneum's barrier to entry. It can easily pass through the skin's intracellular pores because of its elasticity. Transferosome delivery of colchicine allows for prolonged,

site-specific, local distribution while avoiding the gastrointestinal adverse effects associated with oral dosing.

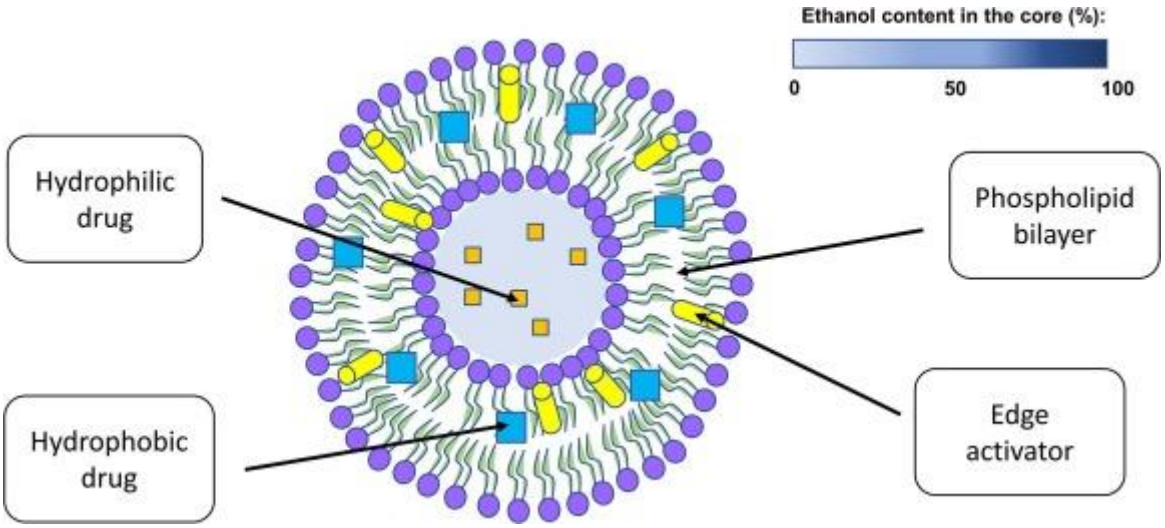

Fig. 9 Structure of transferosomes

3. Conclusion

In comparison to typical plant extracts, a variety of plant elements, including flavanoids, tannins, and terpenoids, shown improved therapeutic benefit at equivalent or lower doses. Because it offers effective and affordable drug delivery and the trends of incorporating new technologies, there is considerable potential in developing revolutionary drug delivery systems for important herbal treatments. Applying modern drug delivery techniques to botanicals creates new opportunities to investigate the full therapeutic potential of polar plant compounds. There is a lot of medicinal promise in herbal medications. Applications of new drug delivery systems to phytoconstituents can therefore result in improved bioavailability, greater solubility, and increased permeability, thereby lowering the dose and reducing side effects.

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