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# **Approaches in Novel Herbal Drug Delivery System**

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Abstract: Due to its potential and minimal side effects, herbal medicines have been used to treat diseases since ancient times. However, obstacles in the identification, processing, standardisation, and extraction of herbal pharmaceuticals rarely prompt researchers to create new methods of delivering herbal medicines. The old and antiquated method of administering herbal medications to patients is the cause of their decreased effectiveness. Nowadays, a variety of innovative drug delivery systems (NDDS) are employed, including phytosomes, ethosomes, transferosomes, herbal transdermal patches, nanoparticles, and biphasic emulsions. The effectiveness and safety of herbal medications will enhance, along with the product's stability, thanks to a novel delivery method. With the use of these procedures, plant actives and extracts can be released gradually with better patient compliance and be used more specifically. This review provides a summary of the information on numerous cutting-edge methods for enhancing the efficacy and safety of phytomedicines, the types of active components utilised, biological activity, and the use of novel formulations of herbal pharmaceuticals to improve therapeutic response.

**Keywords:** Herbal, Novel drug delivery system, herbal Pharmaceuticals, Liposomes, Phytosomes, Transferosomes, Ethosomes, Nanoparticles

#### I. INTRODUCTION

The foundation of conventional medical systems that have been practised from ancient times is made up of natural substances that have been separated from plants and are known as "herbal medications."90–95 percent of the ingredients in ancient drugs came from natural sources. According to information on the origin of pharmaceuticals, 50% of the drugs used today are derived from natural materials.

Herbal medicines are becoming more popular in today's society as a means of treating illnesses with less side effects and greater therapeutic results. Today's herbal dosage forms have progressed from straightforward mixtures and pills to extremely complex technology-based drug delivery systems, thanks to advancements in science and technology in the area of drug product formulation technology. The creation of novel drug delivery systems (NDDS) is a fresh method for using plant extracts and active ingredients [1]. The goal of a novel drug delivery system is to route the active ingredient to the site of action while delivering the medicine at a rate determined by the body's needs during the treatment period. To achieve regulated and targeted drug delivery, a variety of innovative drug delivery systems have surfaced, including different routes of administration. The inclusion of herbal medications in the delivery system also contributes to greater solubility, increased stability, protection against toxicity, increased pharmacological activity, improved tissue macrophage distribution, prolonged delivery, and defence against chemical and physical deterioration.

This present review article is to provide overview of different types of Novel drug delivery system such as liposomes, ethosomes, phytosomes, transferosomes, nanoparticles, Niosomes, Microspheres, microemulsionswith their respective advantages and disadvantages and their various methods of preparation. An effort has been made in this article to touch on a variety of topics and uses for innovative herbal medicine formulations. This presented review article also review the future aspects and approaches regarding the herbal incorporations into novel drug delivery system.

# II. LIPOSOMES

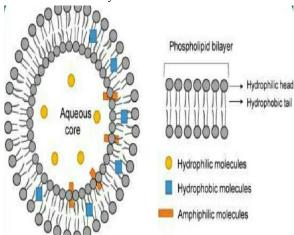
Liposomes are microscopic, spherical artificial vesicles that can be made from cholesterol and harmless, natural phospholipids. In 1965, Bangham made the first description of liposomes while researching cell membranes. He discovered that the liposomes are hydrated bilayers-based vesicles that spontaneously form as water disperses phospholipids. More research has been done on liposomes and their applications in a variety of disciplines, including science and medicine. The words "liposome" and "soma," which signify body and fat respectively in Greek, are the origins of the phrase. The lengthy hydrocarbon chain in the tail is hydrophobic, while the head is hydrophilic. Bilayers



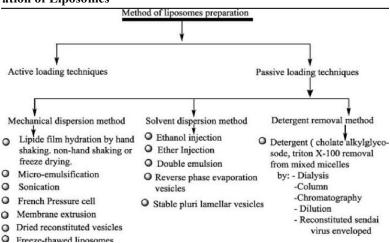
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of phospholipids are the most common kind. The ability of liposomes to mimic biological cells is the primary factor driving research into them. This guarantees that liposomes are highly biocompatible and makes them a prime contender for a drug delivery system. Applications include the delivery of enzymes, antibacterial, antiviral, antiparasitic, and fungicides as well as transdermal carriers, diagnostic instruments for vaccines, and adjuvants. Today, liposome-based anticancer and antifungal medicines are commercially available.



# 2.1 Methods of Preparation of Liposomes



# 2.2 Advantages of Liposomes

- 1. Targets tumour tissues with precision using passive targeting (Liposomal doxorubicin).
- 2. Enhanced therapeutic index and efficacy.
- 3. More stability thanks to encapsulation.
- 4. Lessening of the encapsulated compounds' toxicity.
- 5. The effect of site avoidance.
- 6. Increased effects of pharmacokinetics (reduced elimination, increased circulation life times).
- 7. Flexibility to pair with ligands that are particular to a given location to accomplish active targeting

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- 8. Flexible and biodegradable
- 9. Complies with both macro- and micro-molecules
- 10. Can transport both lipid- and water-soluble medications.

#### 2.3 Disadvantages of Liposomes

- 1. Production is expensive.
- 2. Drug leakage and fusion after being encapsulated.

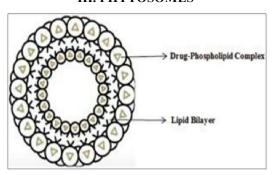


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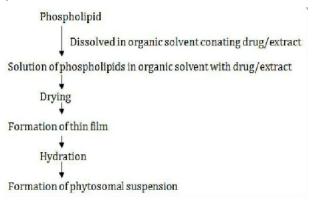
- 3. Phospholipids can occasionally go through an oxidation and hydrolysis reaction.
- 4. A quick half-life
- 5. Limited solubility

#### III. PHYTOSOMES



Phytosomes are a type of lipid-based vesicular delivery system that can be used to encapsulate pharmaceuticals and plant-derived nutraceuticals such polyphenolic chemicals. Flavonoids, which have a low oral bioavailability, make up the majority of phytomedicines' bioactive components. To create lipid-compatible molecular complexes known as phytosomes, water-soluble phytoconstituent molecules (mostly polyphenols) must be transformed. Because of their improved ability to pass through lipid-rich cell membranes and eventually enter the blood, phytosomes are more accessible than basic plant extracts.

## 3.1 Method of Preparation of Phytosomes



# 3.2 Advantages of Phytosomes

- 1. Increase the bioavailability and improve lipid-insoluble polar phytoconstituent absorption.
- 2. Considerable drug entrapment that is advantageous.
- 3. Due to improved absorption, lower the dose.
- 4. Because phosphatidylcholine also has hepatoprotective properties, it exhibits synergistic effects.
- 5. Because of the chemical connection between the phytoconstituents and the carrier, phosphatidylcholine, phytosomes are more stable.
- 6. Functions well in cosmetics.

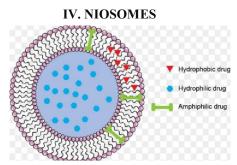
# 3.3 Disadvantages of Phytosomes

- 1. They limit its absorption whether given topically or orally.
- 2. The removal of phytoconstituents from phytosomes is simple.
- 3. Stability issue



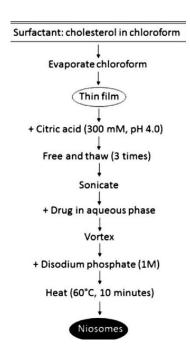
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Niosomes are multilamellar vesicles made of cholesterol and non-ionic surfactants from the class of alkyl or dialkylpolyglycerol ethers. Previous research conducted in collaboration with L'Oreal has demonstrated that niosomes often possess features that make them potential medication carriers, much as liposomes. In that they provide some advantages over liposomes, niosomes are distinct from liposomes. Because they are pricey, phospholipids, one of the constituents in liposomes, are chemically unstable due to their propensity for oxidative destruction, they need special handling and storage conditions, and the purity of naturally occurring phospholipids varies. Niosomes are not affected by any of these issues.

# 4.1 Method of Preparation



# 4.2 Advantages of Niosomes

- 1. Dose reduction.
- 2. A reduction in the negative consequences.
- 3. Make medications more permeable to the skin.
- 4. Non-immunogenic, biodegradable, and biocompatible
- 5. Optically stable and active.

# 4.3 Disadvantages of Niosomes

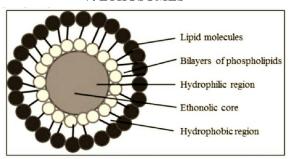
- 1. Show signs of drug fusion, aggregation, leaching, or hydrolysis, reducing shelf life.
- 2. It takes time.
- 3. Demands specific tools.
- 4. Improper drug loading.



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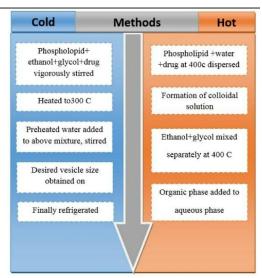
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#### V. ETHOSOMES



Ethosomes are a minimally modified version of the well-known drug carrier liposome. Alcohol (ethanol and isopropyl alcohol) and water are both present in quite high concentrations in phospholipid- and ethanol-containing lipid vesicles called ethosomes. Ethosomes are soft vesicles comprised primarily of water and phosphorane ethanol. Ethosomes can range in size from tens of nanometres (nm) to microns (). Ethosomes have a substantially higher transdermal flow and penetrate the epidermal layers more quickly.

#### 5.1 Method of Preparation of Ethosomes



# 5.2 Advantages of Ethosomes

- 1. Large molecules (peptides, protein molecules) can be delivered.
- 2. Its formulation uses non-toxic raw materials.
- 3. Improved transdermal drug administration by the skin penetration of the drug.
- 4. Ethosomal drug delivery systems are widely used in the medical, veterinary, and cosmetic industries.
- 5. High patient compliance is achieved because the ethosomal medication is administered in semisolid form (gel or cream).

# 5.3 Disadvantages of Ethosomes

- 1. Skin discomfort
- 2. Poor yield.

## VI. TRANSFERONES

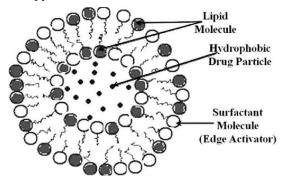
An manufactured vesicle that resembles the natural cell vesicle is called a transferosome carrier. It is hence appropriate for regulated and focused medication delivery. The complex aggregate known as a transferosome is extremely flexible and resilient to stress. It is a highly deformable vesicle with a complex lipid bilayer encasing an aqueous core. The



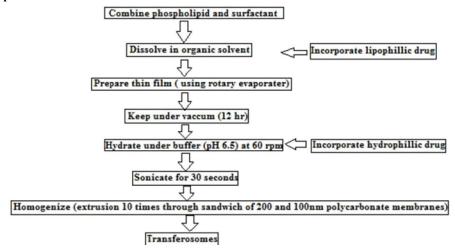
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vesicle is self-regulating and self-optimizing due to the interdependence of the local composition and shape of the bilayer. Transmission electron microscopy can be used to visualise transferosomes.



#### 6.1 Method of Preparation of Transferones



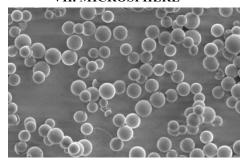
# 6.2 Advantages of Transferones

- 1. Transferosomes can bend and squeeze through passageways that are five to ten times smaller than their own diameter without suffering appreciable harm.
- 2. They have a high entrapment efficiency, which for a medication that is lipophilic is close to 90%.
- 3. This great deformability allows intact vesicles to penetrate more effectively.

# 6.3 Disadvantages of Transferones

- 1. Chemical instability
- 2. large-scale commercialization is challenging due to oxidative deterioration.
- 3. Pricey formulation

# VII. MICROSPHERE





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The average particle size of microspheres, which are discrete spherical particles, ranges between 1 and 50 microns. Microparticulate drug delivery systems are regarded as a trustworthy option for precisely delivering the drug to the target region and maintaining the desired concentration there without adverse effects. A helpful technique that increases patient compliance and considerably lengthens the duration of a drug's action is micro encapsulation.

## 7.1 Method of Preparation of Microsphere

- 1. Single emulsionmethod
- 2. Double emulsion method
- 3. Polymerisation
- 4. Air Suspension
- 5. Precipitation
- 6. Solvent Extraction
- 7. Freeze drying
- 8. Phase separation and coacervation
- 9. Spray drying
- 10. Wax coating
- 11. Hot melt method

## 7.2 Advantages of Microspheres

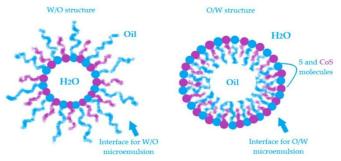
- 1. The ability to bind and release highly concentrated pharmaceuticals
- 2. An extended duration of action
- 3. Improved protein and peptide drug delivery
- 4. Reduced toxicity; a simple manufacturing process
- 5. An improved powder flow
- 6. And the solidification of oils and liquids for easier handling.

# 7.3 Disadvantages of Microspheres

- 1. Expensive
- 2. The stability of core particles may be impacted by process parameters such as temperature change, ph, solvent addition, and evaporation.
- 3. The product deteriorating as a result of heat, hydrolysis, oxidation, sun radiation, or biological factors.

# VIII. MICROEMULSION

Oil, surfactant, and water are mixed together to generate microemulsions either naturally or by mixing the three substances. The extremely low interfacial tension of these systems, which causes the creation of incredibly small droplets of the dispersed phase, facilitates the formation of microemulsion, which are thermodynamically stable. Due to their superior solubilization and extraction capabilities for organic pollutants when compared to surfactant micellar solutions, microemulsions, such as oil-in-water microemulsions, offer a potential method for the remediation of soils and ground water. They can also be used to extract organic pollutants prior to their identification.

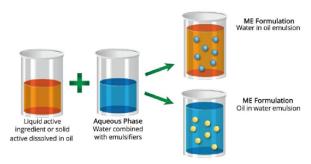




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#### 8.1 Method of Preparation of Microemulsion



#### 8.2 Advantages of Microemulsion

- 1. Increase the rate of adsorption
- 2. Penetrate the drug moiety quickly and effectively
- 3. Aid in drug masking, provide water-soluble drug dosage forms
- 4. Aid in the solubilization of lipophilic pharmaceuticals.

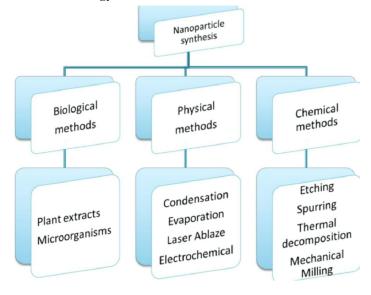
#### 8.3 Disadvantages of Microemulsion

- 1. Potential toxicity of surfactant
- 2. Causes creaming and cracking
- 3. Results in phase inversion

#### IX. NANOTECHNOLOGY

Materials in the nanoscale range are used as diagnostic instruments or to deliver therapeutic compounds to specific targeted regions in a controlled manner in nanomedicine and nano delivery systems, which is a relatively young but fast emerging discipline. r. Site-specific, target-oriented, and precise pharmaceutical administration are only a few of the benefits that nanotechnology offers in the treatment of chronic human diseases. There have been several notable recent applications of nanomedicine (chemotherapeutic agents, biological agents, immunotherapeutic agents, etc.) in the treatment of different diseases. Nanostructures can carry medications passively or actively. In the former, the hydrophobic effect is primarily used to incorporate pharmaceuticals into the structure's inner cavity.

#### 9.1 Method of preparation of Nanotechnology





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#### 9.2 Advantages of Nanotechnology

- 1. Oral drug administration
- 2. Drug discovery
- 3. Brain targeting
- 4. Long physical stability
- 5. Controlled and sustained drug release
- 6. Minimal side effects
- 7. Good potential as vaccine adjuvants
- 8. Increased permeability and retention of drugs
- 9. Longer drug circulation time

#### 9.3 Disadvantages of Nanotechnology

- 1. Due to a drug's erosive action and a lack of extensive clinical research
- 2. Lipid build-up in the liver and spleen may result in pathological change.
- 3. Hydrophilic medicines have a low drug payload
- 4. Reticoendothelial system clearance for intravenous administration of cytotoxic drugs

# 9.4 Comparison Chart

| Characters                    | Liposomes                                                                                                                                   | Transfersomes                                                                            | Ethosomes                                                                | Transethosomes                                                                                                   |
|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Vesicles                      | Bilayer<br>lipid vesicle                                                                                                                    | 2nd generation elastic<br>lipid vesicle carriers                                         | 3rd generation elastic<br>lipid vesicle carriers                         | 3rd generation                                                                                                   |
| Lamellarity                   | Uni/bilayer<br>lipid vesicle                                                                                                                | Double bilayer<br>lipid vesicle                                                          | Multiple bilayer<br>lipid vesicle                                        | Multiple bilayer<br>lipid vesicle                                                                                |
| Composition                   | Phospholipids and<br>cholesterol                                                                                                            | Phospholipids and edge<br>activator surfactant                                           | Phospholipids and ethanol                                                | Phospholipids, edge<br>activator surfactant, and<br>ethanol                                                      |
| Surfactant role               | Phospholipid (lecithin)                                                                                                                     | Sodium deoxycholate                                                                      | Phospholipid (lecithin)<br>and ethanol                                   | Sodium deoxycholate,<br>oleic acid                                                                               |
| Characteristics               | Microscopic spheres<br>(vesicles)                                                                                                           | Ultraflexible liposome                                                                   | Elastic liposome                                                         | Ultraflexible elastic<br>liposome                                                                                |
| Flexibility                   | Rigid in nature                                                                                                                             | High deformability due to the surfactant                                                 | High deformability and<br>elasticity due to the<br>ethanol               | Ultra-deformability due<br>to the surfactant and<br>ethanol                                                      |
| Permeation mechanism          | Diffusion/fusion/lipolysis                                                                                                                  | Deformation of vesicle                                                                   | Lipid perturbation                                                       | Lipid perturbation due<br>to the ethanol and<br>deformation of vesicles<br>by surfactant                         |
| ζ potential                   | Neutral                                                                                                                                     | Positive or negative                                                                     | Negative                                                                 | Positive or negative                                                                                             |
| Extent of skin<br>penetration | The penetration rate is<br>significantly lower, as<br>the stiff shape and size<br>do not allow it to pass<br>through the stratum<br>corneum | Can easily penetrate<br>through paracellular<br>space due to the flexible<br>structure   | Can easily penetrate<br>through paracellular<br>space via ethanol effect | Can easily penetrate<br>through paracellular<br>space via flexible<br>structure and ethanol<br>effect            |
| Route of administration       | Oral, parenteral, topical,<br>and transdermal                                                                                               | Topical and transdermal                                                                  | Topical and transdermal                                                  | Topical and transdermal                                                                                          |
| Limitations                   | It cannot penetrate into<br>deeper skin                                                                                                     | Due to the surfactant, it<br>may cause skin<br>irritation and stable in<br>gel form only | All drugs are non-soluble in ethanol                                     | Due to the surfactant, it<br>may cause skin<br>irritation, and drug loss<br>during the process of<br>formulation |
| Marketed products             | AmBisome,<br>DaunoXome<br>Doxil,<br>Abelcet                                                                                                 | Transfersomes®<br>(Idea AG)<br>Flexiseq                                                  | Nanominox,<br>Cellutight EF,<br>Noicellex,<br>Decorin Cream              | Nil                                                                                                              |

# X. CONCLUSION

The herbal medications can be included in NDDS, allowing us to deliver the right dosage to the target site. Thus, it can be concluded that NDDS for herbal medications will be a ground-breaking application in the traditional herbal formulations that will save preparation time and boost patient compliance. The majority of the nation's pharmaceutical firms have been submitting new patent applications and been granted them in the area of novel drug delivery methods. This finally leads to a substantial increase in demand for the goods and services provided by pharmaceutical and related firms in the near future. Modern applications of nanotechnology in innovative drug delivery systems have the potential to enhance diagnosis, therapy, and aid in the monitoring of post-administration drug composition changes in the body system. Computer aided Drug Design is a significant milestone that deserves to be addressed in this context as it provides a lot of room for the creation of these kinds of cutting-edge, new systems.



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