



Review Article

Application Of Novel Drug Delivery System For Herbal Formulation

Rutuja Patil*, Poonam Madane, Namrata Satkar, Uday Kore, Pranjal Chaugule,
Nilesh Chougule

Ashokrao Mane Institute of Pharmacy, Ambap-416112, India

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ABSTRACT

The creation of innovative drug delivery systems (NDDS) for plant actives and extracts has made significant strides in recent years. Bioactive and plant extracts have been used to create a range of innovative herbal formulations, such as polymeric nanoparticles, nanocapsules, liposomes, phytosomes, nanoemulsions, microspheres, transferosomes, and ethosomes. Compared to the traditional formulations, these innovative formulations have advantages. NDDS include improvements to solubility, bioavailability, toxicity protection, pharmacological activity and stability, better tissue macrophage distribution, and chemical degradation protection. In order to improve medicine efficiency and safety throughout the delivery process and give patients greater convenience, it is crucial to develop alternative drug delivery methods. More information on innovative herbal formulations is provided in the current study.

INTRODUCTION


Numerous studies have been conducted in recent years to create novel drug delivery systems for herbal formulations. The use of herbal medicines to treat a variety of ailments with less hazardous side effects and to deliver greater therapeutic benefits is increasing in value these days. Pharmaceutical delivery systems for innovative herbal drugs can treat specific ailments by identifying the targeted area that is afflicted and delivering the treatment there. New drug delivery systems (NDDS) can assist improve solubility, stability, and offer toxicity protection.

Additionally, it enhances pharmacological and pharmacokinetic characteristics, enhances tissue macrophage, and offers defense against mechanical and chemical deterioration. The objective of the current review article is to offer an overview of various medication delivery methods that contain active components as well as information on the benefits of such methods. [1]

The goal of this article is to touch on a variety of topics connected to the creation of unique herbal formulations, such as preparation technique, active component type, entrapment effectiveness, and applications, among others.

*Corresponding Author: Rutuja Patil

Address: Ashokrao Mane Institute of Pharmacy, Ambap-416112, India

Email : rutuspatil2001@gmail.com

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DIFFERENT TYPE OF HERBAL FORMULATION

Below are some of the numerous methods for developing unique herbal drug delivery systems, including liposomes, phytosomes, pharmacosomes, niosomes, nanoparticles, microspheres, transfersomes, ethosomes, transdermal drug delivery systems, and proniosomes, among others.

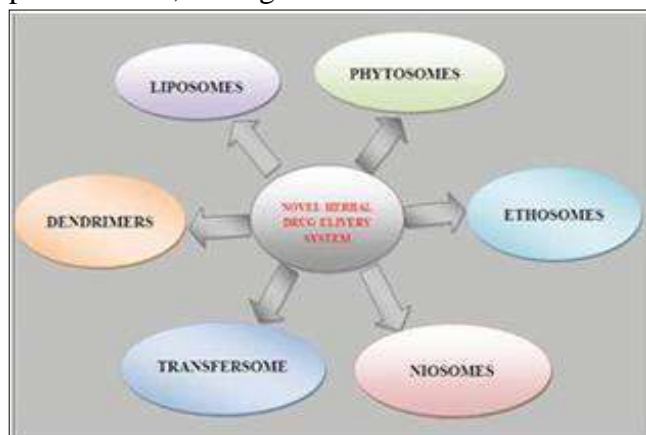


Figure 1 Novel drug delivery systems of herbal drugs [2]

1. LIPOSOMES

In their interior, liposomes are readily dilutable spherical particles that enclose a portion of the aqueous solvent. Natural or synthesized phospholipids, which are amphipathic molecules with both a hydrophobic tail and a hydrophilic polar head, are divided into two layers and make up liposomes. Liposomes, which are mostly made of phospholipids, have been utilized to alter the pharmacokinetic properties of medications, as well as of herbs, vitamins, and enzymes. Because liposomes have unique features, they improve the solubility, bioavailability, and intracellular

absorption of ingredients, which improves product performance. By delivering a medicine to the site of action and maintaining the minimal effective levels, a liposomal drug delivery system can improve a product's therapeutic effectiveness. [3]

• ADVANTAGES

1. Because of their unique features, liposomes are exploited as medication delivery systems.
2. Liposomes lower the dosage necessary.
3. It delivers medication to an exact place of action.
4. It can combine with both small and large molecules.
5. It can transfer between drugs that are hydrophilic and hydrophobic.
6. Drugs that are hydrophilic and hydrophobic can be administered.
7. Liposome herbal treatment serves as a medium for both macromolecules such as genes and tiny cytotoxic chemicals.
8. Formulation release that is regulated and sustained is conceivable.

• DAIGRAM

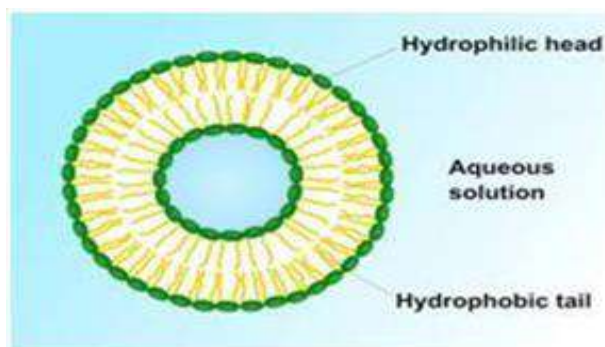


Figure 2 Structure of liposomes[4]

TABLE

Sr. no	Formulation	Biological activity	Application of liposome formulation	Method of preparation	References
1.	Quercetin	Antioxidant and anti-inflammatory and anti-cancer	Reduced dose, and side effect enhance penetration in BBB and bioavailability	By using mixture of egg phosphatidylcholine quercetin and	[5]

				dispersion in polyethylene glycol	
2.	Cur cumin liposome	Antioxidant and anticancer	Long circulating with high entrapment	Ethanol injection method	[6]
3.	Myrtle liposome	Antibacterial and antioxidant	Increase its activity	Thin film method	[7]
4.	Rutin	Antiaging antioxidant	Good entrapment efficiency, prolong drug release, enhance skin hydration	Thin film hydration technique	[8]
5.	Eugenol	Moisturizer, skin care	High entrapment efficiency value	Ethanol injection method	[9]
6.	Black pepper	Anti-inflammatory antibacterial	Enhancement of anti-inflammatory effect.	Rotary flush evaporator method	[10]
7.	Capsaicin liposome	Treat Muscles/joint pain,	Increase in skin permeation as well as prolongation of duration of action	Reverse evaporation technique	[11]
8.	Garlicin	Antioxidant	Increase efficiency	Reverse phase evaporation method	[12]

2. PHYTOSOMES

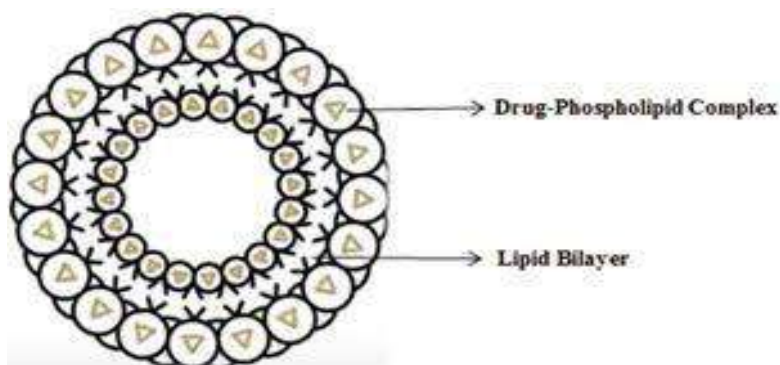
"Phyto" stands for plant, and "some" denotes "cell-like," which together make up the word "phytosome." To create phytosomes, the normalized extract and molecularly-bound active components of a plant are combined with phospholipids. The phospholipids around the active substance in the phytosome's structure are present. Phytosomal herbal products are more effective than traditional herbal extracts because they can be absorbed and used by the body effectively. Better bioavailability and enhanced pharmacological and pharmacokinetic features are produced by phytosome drug delivery systems. [13]

• ADVANTAGES

1. Since the active component is better absorbed via the phytosome drug delivery system, a smaller dosage is needed.
2. The development of phospholipid complexes in phytosomes can increase bioavailability.
3. The stability of this kind of distribution method is better.
4. The phytosome drug delivery technology can increase therapeutic effectiveness by increasing bioavailability.
5. It improved gastrointestinal tract medication absorption [14]
6. Increase the bioavailability and improve lipid-insoluble polar phytoconstituent absorption.
7. Considerable drug entrapment that is advantageous.
8. Due to enhanced absorption, lower the dosage.
9. Because phosphatidylcholine also has hepatoprotective properties, it exhibits synergistic effects.
10. The chemical connection between the phytoconstituents and the carrier, phosphatidylcholine, makes phytosomes more stable.
11. Effective for cosmetics.[15]



- **DIAGRAM**



- **TABLE [17,18]**

Sr. No.	Formulation	Active ingredient	Application of phytosomal formulation	Biological activity
1.	Ginseng phytosome	Ginsenosides	Increase absorption	Immunomodulator
2.	Green tea phytosome	Epigallocatechin	Increase absorption	Anticancer and antioxidant
3.	Curcumin phytosome	Curcumin	Increase bioavailability	Antioxidant and anticancer

Formulation	Active Ingredients	Application of Phytosomal formulation	Biological activity	Method of preparation	Dose	Route of administration	References
Ginkgo biloba Phytosomes	Flavonoids	Flavonoids of GVP stabilize the ROS	Cardio-protective, antioxidant activity	Phospholipids complexation	100 mg and 200 mg/kg	Subcutaneous	[19]
Ginkgoselect phytosome	Flavonoids	Inhibits lipid peroxidation (LPO), stabilize the ROS	Hepatoprotective, antioxidant	Phospholipids complexation	25 and 50 mg/kg	Oral	[19]
Silybin Phytosome	Flavonoids	Absorption of silybin phytosome from silybin is approximately seven times greater	Hepatoprotective, antioxidant for liver and skin	Silybin-Phospholipid complexation	120 mg	Oral	[20]
Grape seed phytosome	Procyanidins	The blood TRAP nTotal Radical-trapping	Systemic antioxidant	Phospholipids complexation	50–100 mg	Oral	[21]

		(Antioxidant Parameter were significantly)					
Quercein Phytosome	Quercetin	Moisturizer, skin care	Antioxidant, Anticancer	Quercetin-phospholipid	100 mg	Oral	[22]

3. EMULSION

The term "emulsion" describes a non-homogeneous dispersion system made up of two kinds of liquid that cannot dissolve one another but which one disperses in the other as droplets [23].

Emulsions typically contain an oil phase, a water phase, a surfactant, and a sub-surfactant. It has a clear to translucent liquid look. Ordinary emulsion (0.1-100 m), micro-emulsion (10-100 nm), sub-micro-emulsion (100-600 nm), etc. are several types of emulsion. The sub-micro-emulsion of them is also known as a lipid emulsion, and the micro-emulsion is also known as a nanoemulsion. Due to its affinity for the lymph, emulsion distributes in vivo as a medication delivery method in a targeted manner. Because the medicine is packed in the inner phase and kept away from direct contact with the body and tissue fluid, it can also be released over an extended period of time [24]. Oil droplets are phagocytosed by macrophages when the oily or lipophilic medications are produced into O/W or O/W/O emulsions. These oil droplets are then concentrated in the liver, spleen, and kidney, where the amount of the dissolved drug is quite significant. Water-soluble drugs may be easily concentrated in the lymphatic system by intramuscular or subcutaneous injection, even though they are often manufactured as W/O or W/O/W emulsion. The target dispersion of the emulsion particle depends on its size.

Elementum emulsion is a novel anti-cancer medication with excellent application potential. Additionally, it does not hinder the marrow and does not affect the heart or liver.

ADVANTAGES

1. Nano-emulsions are thought to be the best option for oral delivery. The creation of a stable nano emulsion for oral medication administration using high-gravity technologies provided a foundation for continuous manufacture.[25]
2. The efficiency of medications when applied topically and transdermally may be increased by nano-emulsions.[26]
3. Nano-emulsion are frequently thought of as effective drug delivery methods for the targeted administration of lipophilic cytotoxic anticancer drugs.[27]
4. Rats treated with a nano-emulsion mixture of gentamycin and eucalyptus essential oil showed improved wound healing activity.in contrast to the norm [28]
5. Drug bioavailability is increased by nano-emulsions of antitubercular medications, which may easily penetrate biological barriers to reach systemic Mycobacterium TB infection.[29]
6. Vitamin D, whose deficiency is widely known globally, has a wide variety of skeletal and non-skeletal activities that may be produced by exposure to sunlight and absorbed from fortified foods. A possible method for increasing vitamin D bioavailability is the nano-emulsion delivery technology.[30]

- **DIAGRAM**



Cross section of nanoemulsion

TABLE [31-36]

Formulations	Active ingredient	Applications of emulsion formulation	Biological activity	Method of preparation	Route of administration	Reference
Self-nanoemulsifying	Zedoary	Improved aqueous	Hepatoprotection	Drawing ternary phase	Oral	[31]
Zedoary essential oil	Turmeric Oil	Dispersion stability and oral bioavailability	Anticancer and Antibacterial	Diagram		
Triptolide micro-emulsion	Triptolide	Enhance the penetration of drugs through the stratum corneum by increased hydration	Anti-inflammatory	High Pressure Homogenization method	Topical	[32]
Docetaxel submicron emulsion	Docetaxel	Improve residence Time	Anticancer	High Pressure Homogenization method	Intravenous	[33]
Berberine nanoemulsion	Berberine	Improve residence time and absorption	Anticancer	Drawing ternary phase diagram	Oral	[34]
Silybin nanoemulsion	Silybin	Sustained Release	Hepatoprotective	Emulsification method	Intramuscular	[35]
Quercetin micro-emulsion	Quercetin	Formulation on enhance penetration into stratum corneum	Antioxidant	High Pressure Homogenization method	Topical	[36]

4. ETHOSOMES

Ethosomes are a relatively minor variation of the drug delivery Liposome. Ethosomes are phospholipid carriers with a high ethanol

concentration (20–45%), which increases drug permeability through the skin by fluidizing the lipids there[37]. Ethosomes are essentially a mixture of ethanol, phospholipids, and water that

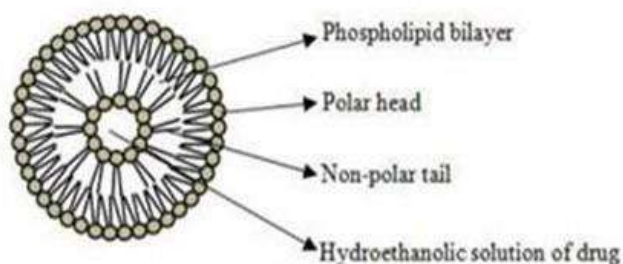
let medications penetrate the skin more effectively. It increases blood circulation and increases medication delivery to the deeper layers of skin. The size range of ethosomes can range from nanometers to microns. According to the demands of the patient, ethosomes can administer medication in the form of gel or cream.

• **ADVANTAGES**

1. It improves medication distribution through the skin by fluidizing the lipids of the skin.
2. The pharmaceutical, veterinary, and cosmetic industries mostly employ ethosomal drug delivery systems.

3. It improves the drug's molecule's therapeutic effectiveness.
4. The semisolid form of ethosomal medication administration resulted in improved patient compliance
5. It lessens the encapsulated agent's toxicity.[38]
6. It is possible to improve medication transdermal absorption via skin.
7. A variety of drug classes in large quantities can be given.
8. The semisolid form in which the ethosomal medication is delivered increases patient compliance [39]

• **DIAGRAM**



• **TABLE**

Sr. No.	Botanical	Active ingredient	Biological activity	Application of ethosomal formulations
1.	Sophora Alopecyroides	Sophora Alopecuroidsetosomes	Anticancer and Anti-inflammatory	Enhanced delivery of drug deeply penetrated into the skin
2.	Glycyrrhiza glabra	Amonium Glycyrrhizinate Ethosomes	Anti-inflammatory	Enhanced Anti-inflammatory activity

5. MICROSPHRE

A microsphere is made up of microscopic, spherical particles with dimensions between one and one thousand micrometers. Microparticles are another name for microspheres. Microspheres can be made from synthetic or natural materials. Microspheres come in a variety of forms, including (a) microcapsules and (b) micrometrics. Microcapsules are those in which the unique capsule wall completely encloses the material that has been collected. When a material is collected and spreads across the microsphere matrix, this is

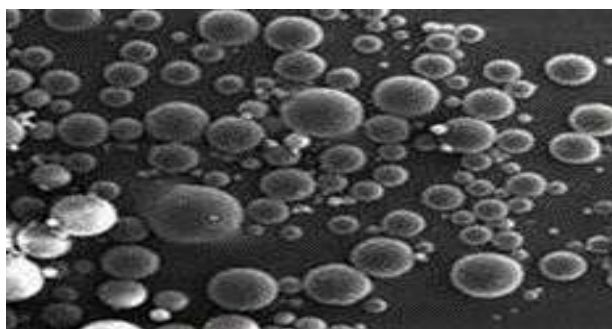
referred to as a micrometric[41]. These Microspheres can be administered either orally or intravenously. The therapeutic efficacy of a medicine can be increased by using a microsphere drug delivery method, which can also help with some of the challenges of traditional therapy[42] Because microspheres may be injected or eaten, they can be customized for desired release profiles, employed for site-specific drug delivery, and in certain situations, can even give organ-targeted release, medicine administration using micro particle systems is useful. [43] Reports on

magnetic microspheres and immunological microspheres are also often published in recent years. As a result of the antibody and antigen being coated or adsorbed on the polymer microspheres, immunological microspheres have immune competence.

ADVANTAGES

1. Drugs may be released from the formulation with ease when using a microsphere drug delivery technology.
2. It increases the formulation's therapeutic effectiveness[44].
3. By reducing drug dose frequency, the microsphere increases patient compliance[45].
4. It can be employed for medication delivery to particular sites and organs[46,47].

• DIAGRAM



Structure of Microsphere

• TABLE [48]

Sr. No.	Formulation	Active ingredient	Application of formulation	Biological activity	Route of administration
1.	Zedoary oil microsphere	Zedoary oil	Higher bioavailability	Hepatoprotective	Oral
2	Rutin-alginatechitosan	Rutin	Targeting into cardiovascular region	Cardiovascular and cerebrovascular diseases	In vitro

6. NANOPARTICLES

Nanoparticles are small, either nano- or sub-nanoscale structures made of organic or synthetic polymers. Sizes of nanoparticles range from 1 to 100 nm. The medicine is contained within this nanoparticle structure and can quickly go to the site of action. Nanoparticles may be classified into two groups, namely nanospheres and nanocapsules, based on the formulation method[49]. While nanospheres are based on matrix systems in which the drug is physically and evenly spread, nanocapsules are those in which the

drug is contained to the cavity surrounding by unique polymer membrane. Recently, nanocarriers have been employed for drug delivery, and due to their special characteristics, they may also be used in chemotherapy[50]. Both hydrophilic and hydrophobic medicines may be delivered effectively using nanoparticles. The size range of nanoparticles, which are submicron-sized particles, is 10 to 1000 nm. Controlling particle size, surface characteristics, and the release of pharmacologically active substances are the main objectives when developing nanoparticles as a

delivery system in order to accomplish the drug's site-specific activity at the therapeutically ideal pace and dosing regimen. Biodegradable polymeric nanoparticles have received a lot of interest recently as possible medication delivery systems[51].

• **ADVANTAGES**

1. It facilitates medication distribution to a targeted place of action

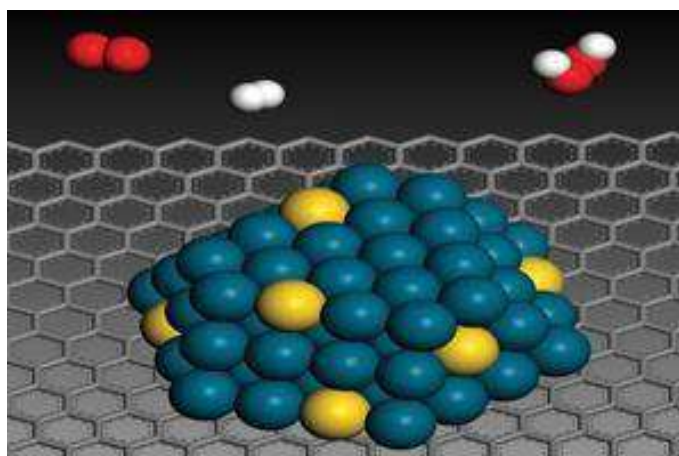
2. It can enhance the drug's pharmacokinetic action and solubility.

3. It can facilitate dosage size reduction.

4. It can increase the medications' bioavailability and help them get past biological barriers.

5. It can increase the drug's stability[52]

• **DIAGRAM**



Structure of Nanoparticles

• **TABLE**

Sr. No.	Herbal medicine	Chemical classification	Biological activity	Application of formulation
1.	Ginkgo biloba	Flavonol and flavone glycosides	Brain activation	Improving the cerebral blood flow and metabolism
2.	Quercetin	Flavonoids obtained from Quercetum	Antioxidant	Increase antioxidant activity
3.	Triptolide	Organic heteroheptacyclic compound	Anti-inflammatory activity	Decreasing the toxicity
4.	Berberine	Organic heteroheptacyclic compound	Anticancer	Sustained drug release
5.	Zedoary	Obtained from curcuma zedoary	Hepatoprotection on anticancer and anti-bacterial	Increase the drug loading and stability

CONCLUSION

When compared to traditional plant extracts, a novel medication delivery method that included multiple plant elements demonstrated improved therapeutic impact. As beneficial herbal medicines offer effective and affordable drug delivery, there

is therefore significant potential for the development of innovative drug delivery systems. In contrast to the traditional plant extract or phytomolecule, a greater amount of the active element is therefore present at the site of action (liver, brain, heart, kidney, etc.) at a similar or

lower dose. As a result, the therapeutic effect is improved, easier to notice, and lasts longer. The delivery of a number of top-notch phytoconstituents has been accomplished with NDDS. The creation of innovative medicine delivery methods for plant actives and extracts thus has a lot of potential.

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