

Global Need for Novel Herbal Drug Formulations

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ABSTRACT

In India over the ancient times people used plants to extract plant actives to make drug formulations. Herbal drugs have enormous therapeutic potential which can be explored through various beneficial drug delivery systems. In recent time the less use of herbal formulations due to lack of their standardization. Great advancement has been made in the uses of plant therapeutics, on development of novel herbal formulations like polymeric nanoparticles, nanocapsules, liposomes, phytosomes, nanoemulsions, microspheres, transferosomes and ethosomes etc. These formulations have reported to have various advantages over the traditional formulations such as improved solubility & bioavailability, reduced toxicity, controlled drug delivery, protection of plant actives from degradation. Also these having the drug targeting properties with improved selectivity, drug delivery and effectiveness with dose reduction which not only increase the safety but also patient compliance. This review article illuminates the current status of novel herbal formulations and explains the different method of preparation of such formulations. In nutshell the combinations used of novel drug delivery technology and herbal medicines provides a boon for a safer and effective therapy for humans.

Keywords: Novel herbal formulations, Standardization, Traditional formulations, nanoparticles, phytosomes, toxicity.

INTRODUCTION

India has a very long, safe, and continuous usage of many herbal drugs in the official recognized alternate system of health¹. Herbal therapy is an ancient science of Indian system of medicine. Traditional formulation contains plant material as its core ingredient². Herbal medicines are the oldest form of health care known to mankind and as we know the future of medicine is rooted in the past, before chemists undertook to synthesize synthetic silver bullets for all that ailments, and before pharmaceutical companies hitched our collective health to what has become for them a multibillion dollar wagon³. In the past, almost all the medicines were from the plants; the plant being man's only chemist for ages. Herbs are staging a comeback, herbal 'renaissance' is happening all over the globe and more and more people are taking note of herbal therapies to treat various kinds of ailments in place of mainstream medicine. There are three main reasons for the popularity of herbal medicines:

- There is a growing concern over the reliance and safety of drugs and surgery.
- Modern medicine is failing to effectively treat many of the most common health conditions.
- Many natural measures are being shown to produce better results than drugs or surgery without the side effects⁴.

Knowledge and use of plants as herbal medicines has occurred in various populations throughout human evolution⁵. World Health Organization [WHO] has defined herbal medicines as finished, labeled medicinal products that contain active ingredients, aerial or

underground parts of the plant or other plant material or combinations. WHO estimates that 80% of the world populations presently use herbal medicine for primary health care³. However, during the second half of the twentieth century, especially in the Western world, herbal medicines were gradually replaced by allopathic medicines. Allopathic treatments are currently more widely used than traditional medicines, especially in developed countries. However, most developing countries continue to use these natural medicines, most likely because obtaining a synthetic drug is expensive⁵. The therapeutic and phytochemical importance of herbal medicine has been built for the improvement of human health, but its broader application is restricted due to the low bioavailability, the problems come with poor lipid-soluble compounds due to limited membrane permeability. Many herbal products demonstrated low therapeutic action due to their solubility problems which finally resulted in low bioavailability despite their extraordinary potential. But there is large number of population that depends on traditional medicinal practices in order to fulfill their basic health needs. The nature of the molecule plays an essential role in enhancing the rate and extent of absorption of molecules when administered through any path. Generally, to overcome these limitations of absorption, developing novel herbal drug delivery system with better absorption profile is of premier importance⁶. In the past few decades, considerable attention has been focused on the development of novel drug delivery system [NDDS] for herbal drugs. The novel carriers should ideally fulfill two prerequisites. Firstly, it should deliver the drug at a rate

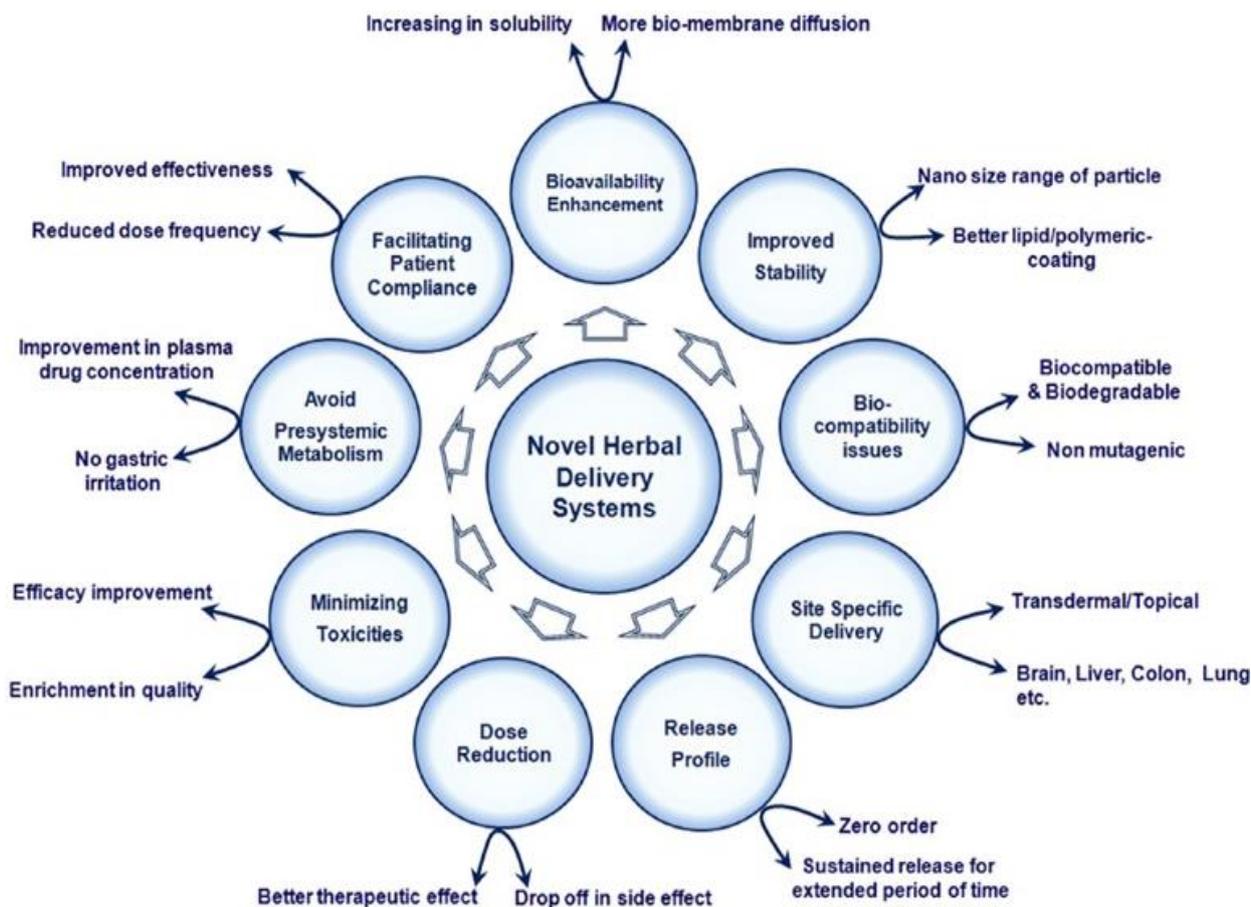


Figure 1: Salient features of Novel Drug Delivery System⁶.

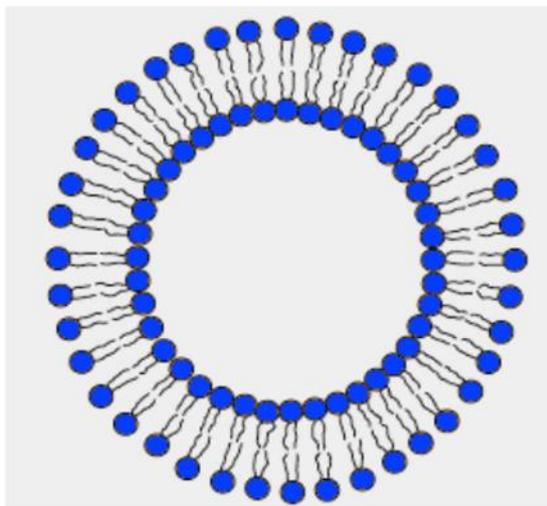


Figure 2: A cross section of liposome¹².

directed by the needs of the body, over the period of treatment. Secondly, it should channel the active entity of herbal drug to the site of action. Whereas conventional dosage forms are unable to achieve these points. In phyto-formulation research, developing nano-dosage forms [polymeric nanoparticles and nanocapsules, liposomes, solid lipid nanoparticles, phytosomes and nanoemulsions etc.] have a number of advantages for herbal drugs, including enhancement of solubility and bioavailability,

protection from toxicity, enhancement of pharmacological activity, enhancement of stability, improving tissue macrophages distribution, sustained delivery, protection from physical and chemical degradation etc. Thus the nano sized novel drug delivery systems of herbal drugs have a potential future for enhancing the activity and overcoming problems associated with plant medicines⁷.

Novel drug delivery system

In novel drug delivery technology, the incorporation of the drug in carrier system is done or changing the structure of the drug at molecular level to achieve the distribution rate. The new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, often called Novel drug delivery systems [NDDS], which are based on interdisciplinary approach that combine polymer science, pharmaceuticals, bioconjugate chemistry and molecular biology⁹. Novel drug delivery systems are designed to achieve a continuous delivery of drugs at predictable and reproducible kinetics over an extended period of time in the circulation. The potential advantages of this concept include minimization of drug related side effects due to controlled therapeutic blood levels instead of oscillating blood levels, improved patient compliance due to reduced frequency of dosing and the reduction of the total dose of drug administered⁹. Novel technology

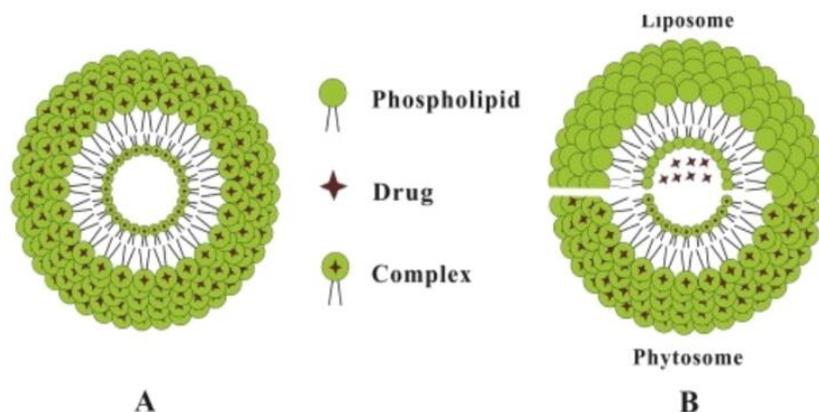


Figure 3: Schematic representation of the structure of phytosome (A) and major difference between liposome and phytosome (B)¹³.

has shown great potential for improving the effectiveness and efficiency of delivery of nutraceuticals and bioactive compounds¹⁰. Various drug delivery and drug targeting systems are currently under development to minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone³. Novel drug delivery system can include those based on physical mechanisms and those based on biochemical mechanism¹¹. Novel drug delivery system is the booming technology in the field of medicine.

Prospective approach of novel herbal formulations

Liposomes

Liposome is a bilayer vesicular carrier system of phospholipids/cholesterol that varies in size from 25 to 2.5 μ m. The distinct advantages are their ability to encapsulate various materials and their structural versatility. Liposome can encapsulate drugs with widely varying solubility or lipophilicity⁶. They encapsulate a fraction of the solvent, in which they freely diffuse [float] into their interior. They can have one, several or multiple concentric membranes. Liposomes are constructed of polar lipids which are characterized by having a lipophilic and hydrophilic group on the same molecules. Upon interaction with water, polar lipids self-assemble and form self-organized colloidal particles. A cross-section of a liposome [Fig. 1] depicts the hydrophilic heads of the amphiphile orienting towards the water compartment while the lipophilic tails orient away from the water towards the center of the vesicle, thus forming a bilayer. Consequently, water soluble compounds are entrapped in the water compartment and lipid soluble compounds aggregate in the lipid section. Uniquely, liposomes can encapsulate both hydrophilic and lipophilic materials⁷. Liposome composed of natural lipids is biodegradable, biologically inactive, non-immunogenic, and possesses limited intrinsic toxicity⁶. Liposomes usually formed from phospholipids, have been used to change the pharmacokinetics profile of, not only drugs, but herbs, vitamins and enzymes. Because of their unique properties liposomes are able to enhance the performance of products by increasing ingredient solubility, improving ingredient bioavailability, enhanced intracellular uptake and altered pharmacokinetics and bio-distribution⁷.

Methods of liposome preparation

General methods of preparation

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

- Drying down lipids from organic solvent.
- Dispersing the lipid in aqueous media.
- Purifying the resultant liposome.
- Analyzing the final product.

Method of liposome preparation and drug loading

The following methods are used for the preparation of liposome:

- Passive loading techniques
- Active loading technique.

Passive loading techniques include three different methods:

- Mechanical dispersion method.
- Solvent dispersion method.
- Detergent removal method (removal of non-encapsulated material).

Mechanical dispersion method

The following are types of mechanical dispersion methods:

- Sonication.
- French pressure cell: extrusion.
- Freeze-thawed liposomes.
- Lipid film hydration by hand shaking, non-hand. shaking or freeze drying.
- Micro-emulsification.
- Membrane extrusion.
- Dried reconstituted vesicles

Advantages of Liposome formulation:

- Liposome is used for drug delivery systems due to its unique structural properties.
- Liposome can carry both the hydrophobic and hydrophilic drug. Therefore, liposome as a drug carrier can indiscriminately deliver drugs through the cell membrane.
- Liposome herbal therapy acts as a carrier for small cytotoxic molecules and as vehicle for macromolecules as gene.
- Liposome formulation can produce sustained and controlled release of formulation and enhances the drug

Table 1: Liposomal herbal formulation⁷.

| Formulations | Active ingredients | Applications of liposomes formulations | Biological activity | Method of preparation | % Entrapment efficiency | Route of administration |
|---------------------------------|--------------------------------------|---|---------------------------------|--|-------------------------|-------------------------|
| Quercetin liposomes | Quercetin | Reduced dose and enhanced penetration in BBB | Antioxidant and anticancer | Reverse evaporation technique | 60% | Intranasal |
| Liposome encapsulated silymarin | silymarin | Improve bioavailability | Hepatoprotective | Reverse evaporation technique | 69% | Buccal |
| Liposoma arborescence | Artemisia arborescence essential oil | Enhance penetration in cytoplasmic barrier | Antiviral | Film method and sonication | 60-74% | <i>In-vitro</i> |
| Ampelopsin liposome | Ampelopsin | Increase efficiency | Anticancer | Film-ultrasound method | 62-3% | <i>In-vitro</i> |
| Paclitaxel liposome | Paclitaxel | High entrapment efficiency and pH sensitive | Anticancer | Thin film hydration method | 94% | <i>In-vitro</i> |
| Curcumin liposome | Curcumin | Long circulating and high entrapment efficiency | Anticancer | Ethanol injection method | 88% | <i>In-vitro</i> |
| Garlicin liposomes | Garlicin | Increase efficiency | Antioxidant for lungs | Reverse phase evaporation method | 90% | - |
| Flavonoids liposomes | Quercetin and rutin | Enhanced binding of flavonoids with Hb | Antioxidant for Hb | Solvent evaporation method | - | <i>In-vitro</i> |
| Usnea acid liposomes | Usnea acid | Increased solubility and localization | Antimicrobial | Hydration of a thin lipid film with sonication | 99.5% | <i>In-vitro</i> |
| Wogonin liposomes | Wogonin | Sustained release effect | Anticancer | Film dispersion | 81% | <i>In-vivo</i> |
| Colchicine liposomes | Colchicine | Enhance skin accumulation and prolong release | Antigout | Rotary evaporation sonication method | 66% | Topical |
| Catechins liposomes | Catechins | Increase permeation through skin | Antioxidant and chemoprotective | Rotary evaporation sonication method | 93% | Transdermal |
| Breviscapine liposomes | Breviscapine | Sustain delivery | CVS diseases | Double emulsification method | 87.9% | Intramuscular |

- Solubility.

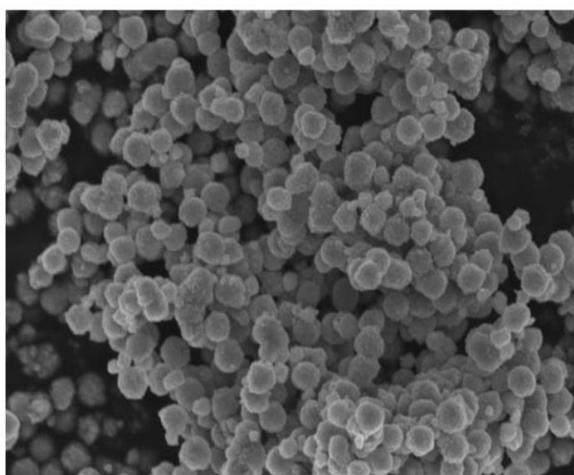
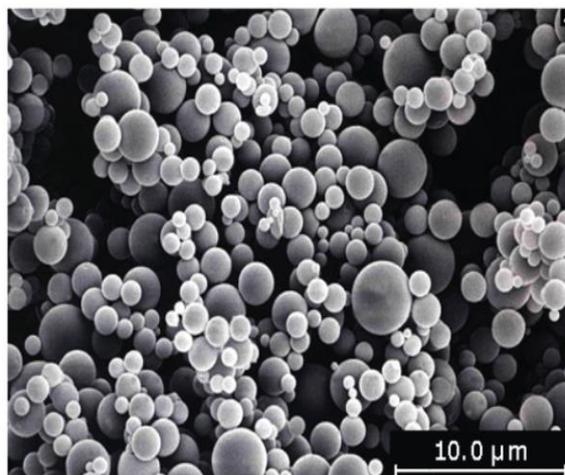
Phytosomes

Phytosome is a novel technology that emerged in 1989. The term “phyto” means plant/herb while “some” means cell-like structure. Phytosome is a technology used as controlled- and sustained-release delivery systems consisting of phospholipid complex system of herbal extract or phytoconstituents in the Nano size range [<100

nm] of particles. Phytosomes result from the reaction of a stoichiometric amount [1:1 or 1:3] of the phospholipid [phosphatidylcholine] with the standardized extract or phytoconstituents in a nonpolar solvent. It is a patented technology to encapsulate standardized extracts or phytoconstituents into phospholipids to fabricate molecular complexes for enhancing their permeation and bioavailability, especially for those which have poor

Table 2: Phytosomal herbal formulation⁴.

| Biological source | Chemical Classification | Advantages | Uses | Active ingredients |
|-------------------|--------------------------|-------------------------------|---|---|
| Silibium marianm | Flavonoids | Increase absorption | in Hepatoprotective, antioxidant | Silybin |
| Vitis vinifera | Proanthocyanidinis | Increase antioxidant property | in Antioxidant anticancer | and Catechin, epicatechin |
| Curcuma longa | Polyphenols | Increase bioavailability | in Antioxidant, inflammatory anticancer | anti- and Curcumin, demethoxycurcumin and bisdemethoxycurcumin |
| Thea sinensis | Polyphenols, Flavon-3-ol | Increase bioavailability | in Antioxidant, protective anticancer | neuro- and Epigallocatechin-3-gallate, epigallocatechin, Epicatechin-3-gallate, Epicatechin |
| Panax ginseng | Saponin glycosides | Inhibit lipid peroxidation | lipid Immunomodulator | Ginseng |
| Ginko biloba | Terpenoids | Improve bioavailability | In cerebral insufficiency | Ginkoflavoneglucoside, ginkgolides, ginkgoic acids and Bilobalide |

Figure 4: Metal oxide nanoparticles¹⁶.Figure 5: Microspheres¹⁹.

aqueous solubility and strong tendency of self-aggregate⁶.

Method of preparation

Accurately weighed quantity of phosphatidylcholine and cholesterol were dissolved in 10 ml of chloroform in a round bottom flask (RBF) and sonicated for 10 min using bath sonicator. Organic solvent removal is done by Rotary evaporator (45-50°C). After complete removal of solvent thin layer of phospholipids mixture was formed. This film was hydrated with methanolic extract of plant in rotary evaporator (37- 40°C for 1 hour). After hydration, mixture of lipid and plant extract was sonicated for 20 minutes in presence of ice bath for heat dissipation. Then prepared phytosomes were filled in amber colored bottle and stored in freezer (2-8 °C) until used¹⁴.

Advantages of Phytosome formulation¹⁵

- It is able to permeate the hydrophilic botanical extract to be better absorbed in intestinal lumen.
- Phytosome increases the absorption of active constituents, so its dose size required is small.

- There is appreciable drug entrapment and improvement in the solubility of bile to herbal constituents, and it can target the liver.
- In Phytosome, chemical bonds are formed between phosphatidylcholine molecules, so it shows good stability.
- Phytosome improves the percutaneous absorption of herbal phytoconstituents.

Nanoparticles

Nanoparticles are nano- or sub-nano-sized structures composed of synthetic or semi-synthetic polymers. In recent times, nanoparticles of herbal medicines have attracted much attention. Nanoparticles are colloidal systems with particles varying in size from 10 nm to 1000 nm. It is an effective system as the formulation is encapsulated in it easily and can easily reach the effective site. The nano-spheres are the solid-core spherical particulates which are nano metric in size¹⁵. The nano-spheres have a matrix type structure in which the active ingredient is dispersed throughout [the particles], whereas the nanocapsules have a polymeric membrane and an active ingredient core. Nanonization possesses many

Table 3: Nanoparticle herbal formulations⁴.

| Biological source | Chemical Classification | Advantages | Uses | Active ingredients |
|------------------------|-------------------------|---|---|--------------------------|
| Cuscuta Chinesis | Flavonolignans | Improve water solubility | Anticancer, immunostimulatory and antihepatotoxic | Ethanollic extract |
| Glycyrrhiza globra | Saponin glycosides | Improve bioavailability | Anti-inflammatory, antiviral and antihepatotoxic | Glycyrrhizic acid |
| Tripterygium wilfordii | Diterpene oxide | Increase solubility and decrease toxicity | Anticancer and anti-inflammatory | Triptolide |
| Ginkgo biloba | Flavonoids | Increase cerebral blood flow | Brain function activation | Extract of ginkgo biloba |
| Naringenin | Flavonoids | Increase solubility | Hepatoprotective | - |
| Artemisia annua | Alkaloids | Increase therapeutic index | Anticancer | Paclitaxel |
| Berberis vulgaris | Isoquinoline | Sustained drug release | Anticancer | Berberine |
| Comptothea acuminata | Quinoline | Increase solubility | Anticancer | Hydroxycamtothecin |
| Stephaniata trandria | Bisbenzylisoquinoline | Sustained drug release | Anti-inflammatory, antiplatelet action, immunosuppressive and calcium channel blocker | Tetrandrine |

Table 4: Emulsion herbal formulation⁴.

| Biological source | Category | Application | Uses | Active ingredients |
|-----------------------|-----------------------|---|---|--------------------|
| Silibum marianum | Flavanolignans | Increase in solubility and therapeutic activity | Hepato-protective | Silymarin |
| Berberis vulgaris | Isoquinoline alkaloid | Improve residence time and absorption | Anticancer | Berberine |
| Sophora alopencerides | Alkaloids | Increase in percutaneous permeability | Anti-bacterial, Anti-inflammatory, Anti-virus | Matrine |
| Curcuma zedooria | Resins | Improved aqueous dispersibility, stability and oral bioavailability | Hepato-protection, Anticancer, and anti-bacterial | β-elemene |
| Ubiquinone | Benzoquinone | Enhancement in solubility, bioavailability | Antioxidant | - |
| Colchicum autumnale | Indole alkaloid | Improved oral bioavailability | Treatment of gout | Colchicine |
| Genista tinctoria | Isoflavones | Improved skin Permeation | Anticancer | genistein |

advantages, such as increasing compound solubility, reducing medicinal doses, and improving the absorbency of herbal medicines compared with the respective crude drugs preparations⁷.

Methods of preparation¹⁷

Methods for preparation of nanoparticles from dispersion of preformed polymer

- Solvent evaporation

- Nanoprecipitation
- Emulsification/solvent diffusion
- Salting out
- Dialysis
- Supercritical fluid technology (SCF)

Methods for preparation of nanoparticles from polymerization of monomers

- Emulsion : mini emulsion , micro emulsion

Table 5: Microsphere herbal formulations⁷.

| Formulations | Active ingredients | Advantages | Uses | Method of preparation | Size in μm | Route of Administration |
|---------------------------------------|-------------------------|--|---|---|-----------------------|-----------------------------------|
| Rutin-alginate-chitosan microcapsules | Rutin | Targeting into cardiovascular and cerebrovascular region | Cardiovascular and cerebrovascular diseases | Complex-coacervation method | 165-195 | In vitro |
| Zedoary oil microsphere | Zedoary oil | Sustained release and Higher bioavailability | Hepato-protective | Quasi-emulsion-solvent diffusion method | 100-600 | Oral |
| CPT loaded microspheres | Camptothecin | Prolonged-release of camptothecin | Anticancer | Oil-in-water evaporation method | 10 | Intraperitoneal and intravenously |
| Quercetin microspheres | Quercetin | Significant decrease in the dose size | Anticancer | Solvent evaporation | 6 | In vitro |
| Cynara scolymus microspheres | Cynara scolymus extract | Controlled release of nutraceuticals | Nutritional supplement | Spray-drying technique | 6-7 | Oral |

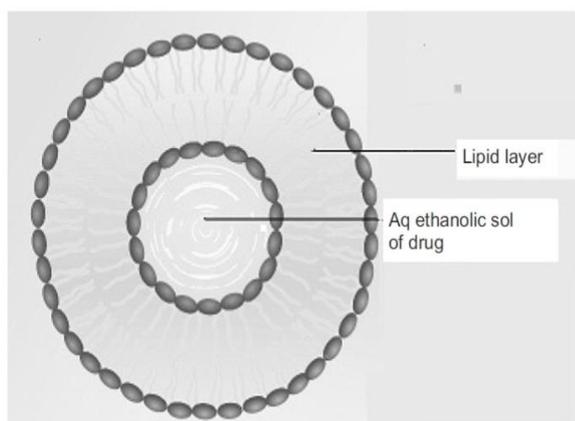


Figure 6: Structure of ethosome²².

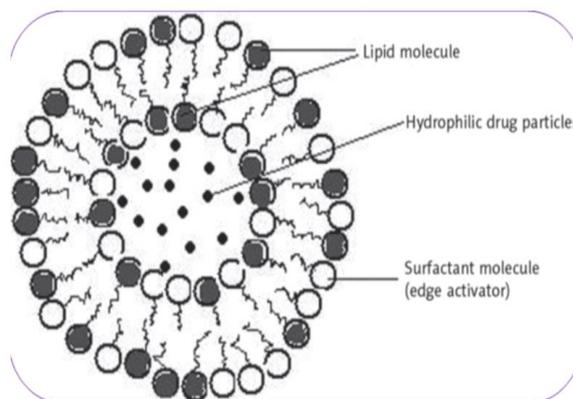


Figure 7: Structural representation of one transferosomes unit²⁴.

- Interfacial polymerization
 - Controlled/Living radical polymerization(C/LRP)
- Advantages of herbal nanoparticles drug delivery system¹⁵
- 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.

Emulsions

Emulsion is a biphasic system in which one phase is intimately dispersed in the other phase in the form of minute droplets ranging in diameter from 0.1 μm to 100 μm . In emulsion, one phase is always water or aqueous phase, and the other phase is oily liquid, i.e., non-

aqueous. Its appearance is translucent to transparent liquid. Emulsion can be classified into ordinary emulsion [0.1–100 μm], micro-emulsion [10– 100 nm], sub-micro-emulsion [100–600 nm], etc. Among them, the micro-emulsion is also called nanoemulsion, and the sub-micro-emulsion is also called lipid emulsion¹⁵. As a drug delivery system, emulsion distributes in vivo in the targeted manner due to its affinity to the lymph. In addition, the drug can be sustained release in a long time because the drug is packaged in the inner phase and kept off direct touch with the body and tissue fluid. After the oily drugs or lipophilic drugs being made into o/w or o/w/o emulsion, the oil droplets are phagocytosed by the macrophage and get a high concentration in the liver, spleen, and kidney in which the amount of the dissolved drug is very large. While water soluble drug is produced into W/O or W/O/W emulsion, it can be easily concentrated in the lymphatic system by intramuscular or subcutaneous injection. The size of the emulsion particle has an impact on its target distribution. Apart from its

Table 6: Ethosomal herbal formulations⁴.

| Biological Source | Category | Application | Use | Active ingredient | |
|------------------------|---------------------------------|--|-----------------------|---|--|
| Glycyrrhiza glabra | Triterpenoid saponins glycoside | Improved inflammatory and sustained action | Anti-activity release | Treatment of dermatitis, eczema and psoriasis | Ammonium glycyrrhizinate |
| Cannabis sativa | Renin | Improved compliance and increased permeation | patient and skin | Treatment of Rheumatoid arthritis | Tetrahydrocannabinol(THC) |
| Tripterygium wilfordii | Diterpene oxide | Increased percutaneous permeability | | Anti-inflammatory, Anti-tumour | Triptolide |
| Sophora alopecuroides | Quinazoline alkaloid | Increased permeability | | Anticancer, Antiendotoxic | Matrine, oxymatrine, sophoridine, sophocarpine(Alkaloid extract) |
| Curcuma longa | Resins | Improved bioavailability | | Anti-inflammatory | Curcumin |

Table 7: Transferosomes herbal formulations⁴.

| Biological Source | Category | Application | Use | Active Ingredients |
|---------------------|-----------------|----------------------------|-------------------------|--------------------|
| Capsicum annum | Resins | Increased skin penetration | Treatment of Rheumatism | Capsaicin |
| Curcuma longa | Resins | Increase skin permeability | Anti-inflammatory | Curcumin |
| Catharanthus roseus | Indole alkaloid | Increase in permeability | Anticancer | Vincristine |
| Colchicum autumnale | Amino alkaloid | Reduction in GIT effects | Treatment of gout | Colchicine |

targeted sustained release, producing the herbal drug into emulsion will also strengthen the stability of the hydrolyzed materials, improve the penetrability of drugs to the skin and mucous, and reduce the drugs' stimulus to tissues⁷.

Method of preparation of emulsion¹⁸.

- Phase inversion method
 - Sonication method
 - High pressure homogenizer
 - Micro fluidization
 - Production with high amplitude ultrasound
- Advantages of emulsion-based formulations¹⁵
- It can release the drug for a long time because it is packed in the inner phase and makes direct contact with the body and other tissues.
 - As a result of the lipophilic drugs being made into o/w/o emulsion, the droplets of oil are phagocytosed by macrophages and increase its concentration in liver, spleen and kidney.
 - As the emulsion contains herbal formulation, it will increase the stability of hydrolyzed formulated material and improve the penetrability of drug into skin and mucous. The new type, viz., Elementum emulsion, is used as an anti-cancer drug and causes no harm to the heart and liver

Microspheres

Microsphere refers to spherical micro particles with a diameter of 1-1000 nm. Biodegradable polymers are frequently used for the development of microsphere matrixes such as polylactic acid and copolymer of lactic acid and glycolic acid. Apart from them, there is an extensive range of microspheres prepared from albumin,

albumin dextran sulfate, and fibrinogen. Administration of medication via micro particulate systems is advantageous because microspheres can be ingested or injected and; they can be tailored for desired release profiles and used site-specific delivery of drugs and in some cases can even provide organ-targeted release. Immune microsphere possesses the immune competence as a result of the antibody and antigen was coated or adsorbed on the polymer microspheres⁶.

Methods of preparation of microsphere²⁰

- Spray Drying
- Solvent Evaporation
- Single emulsion technique
- Double emulsion technique
- Phase separation coacervation technique
- Spray drying and spray congealing
- Solvent extraction
- Quasi emulsion solvent diffusion

Advantages of Microsphere formulation¹⁵

- Administration of medication via micro-particulate system is advantageous because microspheres can be ingested or injected, and they can be tailored for desired release profiles and used for site-specific delivery of drugs and in some cases can even provide organ targeted release.
- Drug can be easily released from the formulation.
- It can protect the specific function of drugs, and can release the drugs into an outer phase for a long period.

Ethosomes

Ethosomes are phospholipids-based elastic nano-vesicles having high content of ethanol [20%-45%]. Ethanol is known as an efficient permeation enhancer and has been

reported to be added in the vesicular system to prepare the elastic nano-vesicles¹⁵. It is assumed that the alcohol interacts with ethosomal lipids and SC bilayer lipids, thus allowing the soft, malleable ethosomes to penetrate. Recently, ethosomes have been shown to be promising and novel vesicular systems that have appeared in the fields of herbal product and drug delivery⁶. In recent years, ethosomes have become new liposome carriers with high deformability; high entrapment efficiency and a good transdermal permeation rate in the drug-delivery system, and are suitable for transdermal administration. Compared with other liposomes, the physical and chemical properties of ethosomes make these more effective for drug delivery through the stratum corneum into the blood circulation, which is very important in the design of a transdermal drug-delivery system²¹.

Method of preparation of ethosomes²³

- Cold Method
- Hot Method
- Classic mechanical dispersion method

*Advantages of ethosomal drug delivery*¹⁵

- Ethosomes enhance transdermal permeation of drug through skin.
- Ethosomes are a platform for the delivery of large amounts of diverse groups of drugs.
- The ethosomal drug is administered in semisolid form, resulting in improved patient compliance.

Transferosomes

The name means “carrying body”, and is derived from the Latin word ‘transferre’, meaning ‘to carry across’, and the Greek word ‘soma’, for a ‘body’. A Transferosome carrier is an artificial vesicle which resembles the natural cell vesicle. Thus it is suitable for targeted and controlled drug delivery⁴. Transferosomes are vesicular system consisting of phospholipids as the main ingredient with 10-25% surfactant [such as sodium cholate] and 3-10% ethanol. The surfactants work as “edge activators,” conferring ultra-deformability on the structure of transferosome, which helps them to squeeze through pores in the stratum corneum. The hypothesized mechanism of action of transferosome is described as followings:

1. vesicles act as drug carriers and intact vesicles enter the SC carrying vesicle-bound drug molecules into the skin and
2. vesicles act as penetration enhancers and enter the SC and then modify the intercellular lipid lamellae and consequently facilitate the penetration of unbound drug molecules into and across the SC. the transferosome of capsaicin has been prepared, which exhibited better topical absorption in comparison to pure capsaicin⁶.

Method of preparation of transferosomes^{25,26}

- Thin film hydration method
- Modified hand shaking, lipid film hydration technique

CONCLUSION

Herbal medicines have been widely used all over the globe since ancient times and it has been believed by large population for its better therapeutic value as they

have fewer adverse effects when compared with allopathic medicines. Research at great extent is going on in the area of development of novel drug delivery and targeting system for herbal drugs. However, research is still at the exploring stage novel drug delivery systems will provide a great platform for chemist to conquer various challenges coupled with herbal formulations. There is a great potential in the development of novel herbal drug delivery system as these are safe, effective and people are regaining faith in herbal medicines as compared to modern medicine. Collaboration of modern technology with herbal drugs will led to enhanced bioavailability & improved solubility, reduced toxicity, controlled release delivery, effectiveness with dose reduction. The novel herbal drug delivery system will not only increase the market of herbal drugs but will also play a major role in providing better and effective therapy to humans.

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