



CURRENT REVIEW ON NOVEL HERBAL DRUG DELIVERY SYSTEMS

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ABSTRACT

Novel herbal drug delivery systems represent an innovative approach to enhancing the efficacy and bioavailability of plant-based medicines. This review explores the latest advancements in the development of these systems, including nanotechnology-based carriers, liposomes, and polymeric nanoparticles. It discusses how these novel delivery methods improve the stability, solubility, and targeted delivery of herbal compounds. The review also highlights the challenges faced in integrating herbal drugs with modern delivery technologies, such as regulatory hurdles and formulation complexities. By examining recent research and technological progress, this review aims to provide insights into the future directions of herbal drug delivery systems and their potential to revolutionize herbal medicine.

Keywords: Herbal drug delivery systems, Nanotechnology, Liposomes, Polymeric nanoparticles, Bioavailability, Plant-based medicines, Drug formulation

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INTRODUCTION

Herbal drugs referred as plants materials or herbalism, involves the use of whole plants or parts of plants, to treat injuries or illnesses. Herbal drugs are use of therapeutic herbs to prevent and treat diseases and ailments or to support health and healing. These are drugs or preparations made from a plant or plants and used for any of such purposes. Herbal drugs are the oldest form of health care known to mankind. There are many herbal products offered that assert to treat the symptoms of a broad range of problems, from depression to cold and flu. World Health Organization (WHO) has distinct herbal drugs as complete, labeled medicinal products that have vigorous ingredients, aerial or secretive parts of the plant or other plant material or combinations (Bodhisattwa *et al.*, 2011).

According to the world health organization (WHO) guideline, herbal remedies are

calculated as plant derived components with therapeutic effect and various human health benefits that contain main raw materials from one or more plants. For preparation of herbal medicine we have been using whole plants or parts of the plant like leaves, roots, seeds, bark, flowers, stems and extracts of all of these, therefore herbal medicine also known as botanical medicine or plant medicine or herbalism. WHO issued a guideline for measurement of the safety, efficacy and quality control of herbal drugs (Firenzuoli *et al.*, 2004; Chiappelli *et al.*, 2006).

Herbal drugs are of two types

The types are as (Kulkarni *et al.*, 2019) follows -

- Single/ crude drugs
- Multiple herbal formulations

Single /crude drugs: All mainly whole, fragment or cut plant, plant parts usually dried forms, but sometimes fresh. It also includes algae, fungi and lichen.

Multiple herbal formulations: Formulations are obtained by subjecting herbal ingredients to various manufacturing process such as extraction, distillation, expression, fractions, partition, chromatography and formulations.

Traditional use of herbal drugs

By definition, ‘traditional’ use of herbal medicines implies substantial historical use, and this is certainly true for many products that are available as ‘traditional herbal medicines’. In many developing countries, a large proportion of the population relies on traditional practitioners and their armamentarium of medicinal plants in order to meet health care needs. Although modern medicine may exist side-by-side with such traditional practice, herbal medicines have often maintained their popularity for historical and cultural reasons. Such products have become more widely available commercially, especially in developed countries. In this modern setting, ingredients are sometimes marketed for uses that were never contemplated in the traditional healing systems from which they emerged. An example is the use of ephedra (= Ma huang) for weight loss or athletic performance enhancement (Shaw, 1998).

Limitations of Conventional Dosage Forms

This overcomes limitations of old methods of drug administration. Drawbacks of conventional dosage forms. Conventional dosage forms possess following limitations -

- Poor patient compliance, increased chances of missing the dose of a drug with short half-life for which frequent
- Administration is necessary.
- The unavoidable fluctuations of drug concentration may lead to under medication or over medication.
- A typical peak-valley plasma concentration time profile is obtained which make attainment of steady-state condition difficult.
- The fluctuations in drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index whenever over medication occur (Dongare *et al.*, 2021).

Benefits of novel herbal drug delivery systems

- The novel herbal drug delivery system can be used to achieve site specificity.
- Novel drug delivery system enhances the surface area of the drugs, therefore allows quicker absorption and rapid onset of action.
- The enhanced penetration of nanoparticles through the Blood Brain Barrier (BBB).
- Providing high efficacy.
- Enhanced stability.
- Reduce undesirable effects and toxicity.
- Long-term stability by protecting plant activities from degradation.
- Decrease allergic potential of herbal substances.
- Improved solubility & bioavailability.
- Controlled drug delivery (Sanjida *et al.*, 2018).

Types of novel herbal drug delivery systems

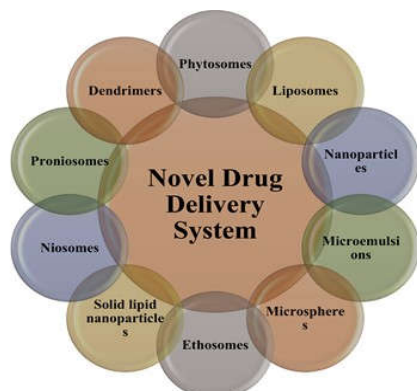


Figure 1: Types of Novel Herbal Drug Delivery Systems

Phytosomes

With a close resemblance to liposomes, phytosomes are a cutting-edge lipid-based delivery system that can be exploited to entrap numerous phytoconstituents with polyphenolic bases to promote their absorption when delivered. The drug itself is conjugated with lipids to generate vesicles, which promote phytosomal entrapment efficiency even further. As a result, the dose requirement has been minimised while the drug's bioavailability has been significantly increased. Phytosomes possess numerous benefits, such as the lipid layer surrounding the phytoconstituent. Phytosomes have the capacity to penetrate skin and hence significantly enhance effectiveness. Phospholipid, aka phosphatidylcholine, is among the essential components of phytosomes, serves as a vesicle, and has health advantages such as hepatoprotective action (Hardeep and Gauri, 2023).

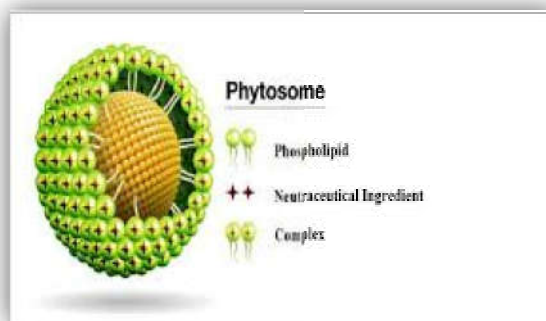


Figure 2: Structure of Phytosome

Nanoparticles

Nanoparticles are nano- or sub-nano-sized structures composed of synthetic or semisynthetic polymers. 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. Microencapsulation of herbal extract in nanoparticulate is an effective way used to protect drug or food ingredients against deterioration, volatile losses, or premature interaction with other ingredients (Amol *et al.*, 2014).

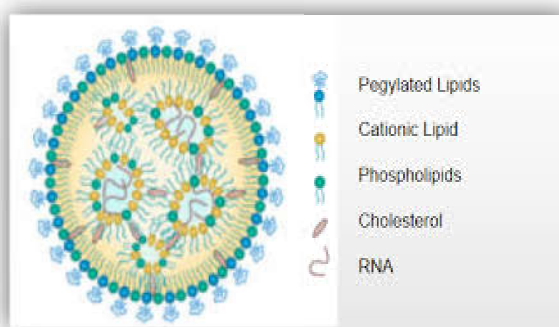


Figure 3: Structure of Nanoparticles

Niosomes

Niosomes are multilamellar vesicles that are made of cholesterol and nonionic surfactants belonging to the alkyl or dialkylpolyglycerol

ether class. Previous research conducted in collaboration with L'Oreal has demonstrated that niosomes share many characteristics with liposomes that make them suitable drug carriers. Niosomes are distinct from liposomes in that they have a few benefits over the latter. Liposomes have a number of drawbacks, including high cost, chemical instability of their constituents (phospholipids, for example) due to oxidative degradation, need for special handling and storage, and inconsistent purity of natural phospholipids. Niosomes are not affected by any of these issues (Biradar *et al.*, 2023).

Microspheres

Microspheres are discrete spherical particles ranging in average particle size from 1 to 50 μ . Microparticulate drug delivery systems are studied and taken on as a reliable one to rescue the drug to the target site with specificity, to assert the desired concentration at the situation of interest without untoward effects. Microencapsulation is a useful method which extends the duration of drug effect significantly and improves patient compliance. Finally, the entire dose and few adverse reactions may be thinned out since a steady plasma concentration is kept. So far, a series of active ingredients of plants, such as rutin, camptothecin, zedoary oil, tetrandrine, quercetine, and *Cynara scolymus* extract, has been made into microspheres. In addition, reports on immune microsphere and magnetic microsphere are also usual in recent years. Immune microsphere possesses the immune competence as a consequence of the antibody, and antigen was coated or adsorbed on the polymer microspheres (Sarangi *et al.*, 2018).

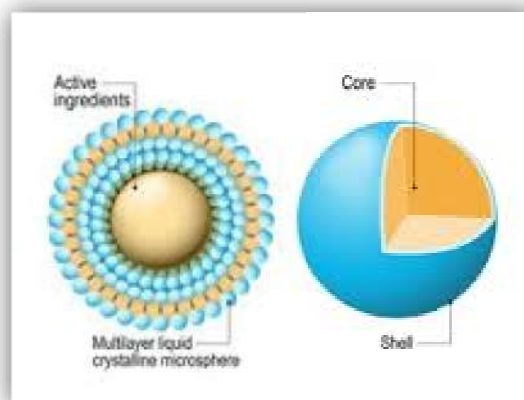


Figure 4: Structure of Microspheres

Mouth Dissolving Tablet

Asoka Life science Limited launched Res-Q, the world's first poly-herbal mouth dissolving tablet, fast mouth dissolving drug. It has a novel drug delivery system that imparts increased efficacy. In Ayurvedic medicine segment, this is the first attempt to make medicines more effective in managing chronic ailments. Res-Q is a poly-herbal medicine highly effective for lung problems and other respiratory ailments like asthma. This unique mouth dissolving drug delivery system ensures that the drug reaches the blood directly and the first pass metabolism is bypassed. It dissolves in mouth by mixing with the saliva and get absorbed. This Res-Q provides relief from respiratory distress within fifteen minutes. This way, this drug resembles the efficacy of Sorbitrate, a revolutionary mouth dissolving drug used in cardiac distress (Parakh and Gothoskar 2003).

Transdermal Films

An investigation aimed to formulate transdermal films incorporating herbal drug components such as Boswellic acid (*Boswellia serrata*) and curcumin (*Curcuma longa*) is one of the first few attempts to

utilize ayurvedic drugs through transdermal drug delivery system (TDDS), which utilizes skin as a site for continuous drug administration into the systemic circulation. Thus this delivery system avoids the first pass metabolism of the drug without the pain associated with injection; moreover, the system provides a sustained drug delivery with infrequent dosing via zero-order kinetics and the therapy can be easily terminated at any time. Use of turmeric in TDDS for the local action of the drug at the site of administration can also be considered as a new version of ayurvedic turmeric poultice or lepa (Verma *et al.*, 2007).

Dendrimer

A dendrimer is a tree-like synthesized polymer that was characterized as having a single central core that gives frequent branches of variously armed macromolecules (external capping and multifunctional groups) to achieve better targeting to specific sites. The unique feature of this polymer is that its structure and hydrophilicity are easily controllable during formation to get higher solubility, permeability, biocompatibility, biodistribution, clearance and consequently reducing side effects. Instantly, the polyamidoamine (PAMAM) dendrimers have recently been studied as carriers as they can be developed in various shapes, sizes and surfaces, in order to get functionalized nanoscale formulas. Thus, this dendrimer can offer to target ligands to promote particular binding to cellular receptors. Additionally, the small size of this dendrimer renders it to be promptly cleared from the body through the renal and escape from the reticuloendothelial system (Rahman *et al.*, 2020).

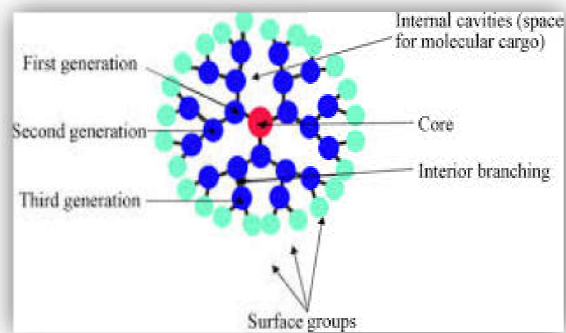


Figure 5: Structure of Dendrimer

Solid Lipid Nanoparticles

The average mean size of solid lipid nanoparticles ranges from 50 nm to 1000 nm. Solid lipid nanoparticles are composed of lipid matrix, which becomes solid at room temperature and also at the body temperature. The main features of solid lipid nanoparticles (SLNs) with regard to parenteral application are the excellent physical stability, protection of incorporated labile drugs from degradation. To cross bloodbrain barrier, it should be made for selection of lipids and surfactants. The SLNs are prepared by different methods such as homogenization and the warm micro-emulsion high-speed stirring ultrasonication and solvent-diffusion method. Lipids show compatibility with lipophilic drugs and increase the entrapment efficiency and drug-loading into the SLN (Chaturvedi *et al.*, 2011).

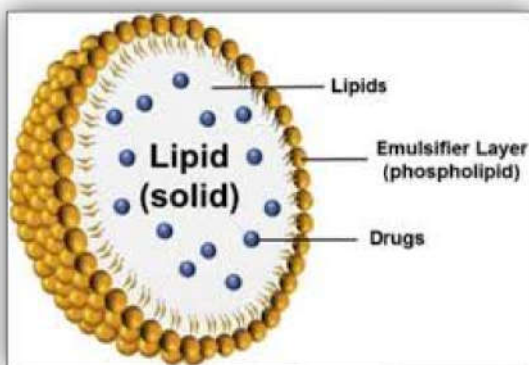


Figure 6: Structure of Solid Lipid Nanoparticles

Liposomes

These are microparticulate or colloidal carriers, usually 0.05–5.0 μm in diameter which forms spontaneously when certain lipids are hydrated in aqueous media. The liposomes are spherical particles that encapsulate a fraction of the solvent, in which they freely pass around or float into their interior. They can carry one, several, or multiple concentric membranes. Liposomes are constructed of polar lipids, which are characterized by having a lipophilic and hydrophilic group of the same molecules. On interaction with water, polar lipids self-layup and form self-organized colloidal particles. Liposome-based drug delivery systems offer the potential to raise the therapeutic index of anticancer agents, by increasing the drug concentration in tumor cells or by lessening the exposure in normal tissues exploiting enhanced permeability and retention effect phenomenon or by utilizing targeting strategies (Sarangi *et al.*, 2018).

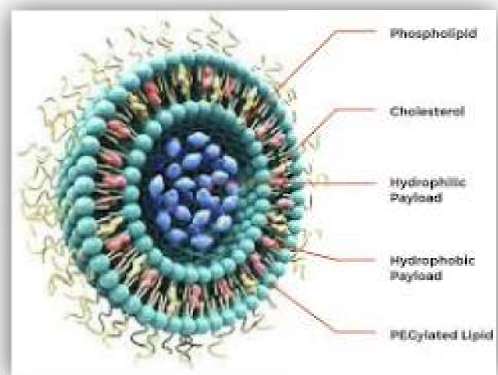


Figure 7: Structure of Liposomes

Marketed Herbal Novel Drug Delivery Formulations

Two companies dominate the market for these systems, namely, Cosmetochem and Indena. For herbal drug delivery, Cosmetochem launches Herbasec[®] technology in markets which are actually liposomal preparations of various herbal ingredients such as extracts of White tea, Green tea, white hibiscus, Gurana, and Aloe Vera. These extracts are used in cosmetics because of their anti-oxidant effects for prevention of aging. Indena patented the technology of phytosomes[®] and launches many products in market under this having diverse therapeutic benefits. Indena commercializes the plant constituents/extracts of liquorice (18 β -glycyrrhetic acid), *Ammivisnaga* (visnadin), *Centellaasiatica* (triterpenes), *G.biloba* (ginkgoflavonglucosid, ginkgolides, bilobalide), Hawthorn flower (vitexin-2"-O-rhamnoside), milk thistle (silymarin and Silybin), horse chestnut (escin β -sitosterol), *Terminalia sericea* (sericoside), *Panax ginseng* (ginsenosides), grape seed (polyphenols), Green tea (polyphenols), etc (Pinto, 2010).

CONCLUSION

Novel herbal drug delivery systems are advancing the field of herbal medicine by enhancing the efficacy, stability, and bioavailability of plant-based compounds. Techniques such as nanotechnology, liposomes, and polymeric nanoparticles are revolutionizing how herbal drugs are formulated and delivered, enabling more precise targeting and improved therapeutic outcomes. Despite these advancements, challenges remain, including regulatory issues and the complexity of integrating herbal extracts with modern delivery technologies. Continued research and innovation in this area hold the promise of overcoming these barriers and optimizing the therapeutic potential of herbal medicines, paving the way for more effective and personalized treatments.

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