

# Importance of Novel Drug Delivery Systems in Herbal Medicines

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**Abstract:** A novel drug delivery system offers an innovative approach to administering medications that address the limitations of traditional methods. Our country possesses a rich knowledge base of Ayurveda, which has recently gained recognition for its potential. However, the current drug delivery methods used to administer herbal medicine are outdated, leading to reduced efficacy of the treatments. By applying novel drug delivery technologies to herbal medicine, it may be possible to enhance their effectiveness while minimizing side effects. The integration of novel drug delivery systems with Indian Ayurvedic medicines is crucial for addressing more serious health conditions. For many years, herbal medicines were overlooked for development into novel formulations due to a lack of scientific validation and challenges related to standardization, extraction, and identification of individual components in complex polyherbal systems. However, modern phytopharmaceutical research can address these scientific needs—such as determining pharmacokinetics, understanding mechanisms of action, identifying sites of action, and establishing accurate dosages—allowing herbal medicines to be incorporated into advanced drug delivery systems. These systems can include technologies such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, and solid lipid nanoparticles. This article summarizes various drug delivery technologies that can be applied to herbal actives, along with relevant examples.

**Keywords:** Herbal, Medicines, Novel drug delivery system, Phytopharmaceuticals

## INTRODUCTION

The future of medicine is rooted in the past before chemists undertook to synthesize synthetic silver bullets for all those ailments, and before

pharmaceutical companies hitched our collective health to what has become a multibillion-dollar wagon. In the past, almost all the medicines were from 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 effects. [1]

Also, there is increasing evidence that many current drug therapies simply suppress symptoms and ignore the underlying disease processes. In contrast, many natural products appear to address the cause of many diseases and yield superior clinical results. Unfortunately, most physicians and patients are not aware that these natural alternatives exist. But research in this field is a never-ending process. [2]

The method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. On the other hand, the very

slow progress in the efficacy of the treatment of severe diseases has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, bio-recognition, and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology. [3]

A novel drug delivery system is a novel approach to drug delivery that addresses the limitations of traditional drug delivery systems. Modern medicine cures a particular disease by targeting exactly the affected zone inside a patient's body and transporting the drug to that area. A drug delivery system is the method by which an optimum amount of the concerned drug is administered to the patient in such a way that it reaches exactly the 'site of action' and starts working then and there. Novel drug delivery system attempts to eliminate all the disadvantages associated with conventional drug delivery systems. There are various approaches by which novel drug delivery can be achieved. [4,5]

#### NOVEL DRUG DELIVERY APPROACHES

Various drug delivery and drug targeting systems are currently under development to minimize drug degradation and loss, prevent harmful side effects, and increase drug bioavailability and the fraction of the drug accumulated in the required zone. Among drug carriers, one can name soluble polymers, microparticles made of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, and micelles. The carriers can be made slowly degradable, stimuli-reactive (e.g. pH- or temperature-sensitive), and even targeted (e.g. by conjugating them with specific antibodies against certain characteristic components of the area of interest). Targeting is the ability to direct the drug-loaded system to the site of interest. Two major mechanisms can be distinguished for addressing the desired sites for drug release: (i) passive and (ii) active targeting. An example of passive targeting is the preferential accumulation of chemotherapeutic agents in solid tumors as a result of the enhanced vascular permeability of tumor tissues compared with healthy tissue. A strategy that could allow active targeting involves the surface functionalization of drug carriers with ligands that are

selectively recognized by receptors on the surface of the cells of interest. Since ligand-receptor interactions can be highly selective, this could allow a more precise targeting of the site of interest. [1]

Controlled drug release and subsequent biodegradation are important for developing successful formulations. Potential release mechanisms involve: (i) desorption of surface-bound / adsorbed drugs; (ii) diffusion through the carrier matrix; (iii) diffusion (in the case of nanocapsules) through the carrier wall; (iv) carrier matrix erosion and (v) a combined erosion/diffusion process. The mode of delivery can be the difference between a drug's success and failure, as the choice of a drug is often influenced by the way the medicine is administered.[6] Sustained (or continuous) release of a drug involves polymers that release the drug at a controlled rate due to diffusion out of the polymer or by degradation of the polymer over time. Pulsatile release is often the preferred method of drug delivery, as it closely mimics the way by which the body naturally produces hormones such as insulin. It is achieved by using drug-carrying polymers that respond to specific stimuli (e.g. exposure to light, changes in pH or temperature). [7]

For over 20 years, researchers have appreciated the potential benefits of nanotechnology in providing vast improvements in drug delivery and drug targeting. Improving delivery techniques that minimize toxicity and improve efficacy offers great potential benefits to patients, and opens up new markets for pharmaceutical and drug delivery companies. Other approaches to drug delivery are focused on crossing particular physical barriers, such as the blood-brain barrier, to better target the drug and improve its effectiveness; or on finding alternative and acceptable routes for the delivery of protein drugs other than via the gastrointestinal tract, where degradation can occur. [8]

Presently novel drug delivery systems have been widely utilized only for allopathic drugs, but they have their limitations hence, turning to safe, effective, and time-tested Ayurvedic herbal drug formulation would be a preferable option.

#### POTENTIAL OF NOVEL DRUG DELIVERY FOR HERBAL DRUGS

Our country has a vast knowledge base of Ayurveda whose potential has only been realized in recent years. However, the drug delivery system used for

administering the medicine to the patient is traditional and out-of-date, resulting in reduced efficacy of the drug. In the case of herbal extracts, there is a great possibility that many compounds will be destroyed in the highly acidic pH of the stomach. Other components might be metabolized by the liver before reaching the blood. As a result, the required amount of the drug may not reach the blood. If the drug does not reach the blood at a minimum level, which is known as the 'minimum effective level' then there will be no therapeutic effect.

Phytopharmaceuticals are pharmaceuticals using traditional compounds derived from botanicals instead of chemicals. Natural ingredients are more easily and more readily metabolized by the body. Therefore they produce fewer, if any, side effects and provide increased absorption in the bloodstream resulting in more thorough and effective treatments. Pharmaceuticals made from chemical compounds are prone to adverse side effects. The human body will tend to reject certain chemical compounds which do not occur naturally. These rejections occur in the form of side effects; some as mild as minor headaches, and others as severe as to be potentially lethal. It is important to note while phytopharmaceuticals produce fewer to no side effects, chemical interactions with other prescription drugs can occur. Furthermore, as they are single and purified compounds, they can be easily standardized making it easier to incorporate them in modern drug delivery systems compared to herbs.[9]

Lipid-based drug delivery systems have been investigated in various studies and have shown their potential in controlled and targeted drug delivery. Pharmacosomes are amphiphilic phospholipid complexes of drugs bearing active hydrogen that bind to phospholipids. They impart better biopharmaceutical properties to the drug, resulting in improved bioavailability. Phytosomes are novel compounds comprising lipophilic complexes of components of plant origin like *Silybum Marianum*, *Ginkgo Biloba*, *ginseng*, and so on, with phospholipid.[10] They are also called phytolipids delivery systems. They have high lipophilicity and improved bioavailability and therapeutic properties. These are advanced forms of herbal extract that have improved pharmacokinetic and pharmacological parameters, whose result can advantageously be used in the treatment of acute liver diseases, either metabolic or infective origin. Phytosomes are produced by a patent process in which individual

components of herbal extract like flavonolignans and terpenoids are bound on a molecular level to the phospholipids like phosphatidylcholine through a polar end. Phytosomes are used as a medicament and have a wide scope in cosmetology. Many areas of phytosomes are to be revealed in the future in the prospect of pharmaceutical application. Phytosomes form a bridge between the conventional delivery system and the novel delivery system. [1,11]

If the herbs themselves or the purified phytopharmaceuticals or phytosomes are incorporated into novel drug delivery systems, we can get the benefits of both. Thus it is important to incorporate the novel drug delivery system in Indian Ayurvedic medicines to combat serious diseases. [1,8]

#### HERBAL NOVEL DRUG DELIVERY SYSTEMS

As herbal novel drug delivery systems have a lot of potential, several researchers are working towards developing novel drug delivery systems like mouth dissolving tablets, sustained and extended-release formulations, mucoadhesive systems, transdermal dosage forms, microparticles, microcapsules, nanoparticles, implants, etc. of herbs. Some of them are at the laboratory stage and some have reached the mark. Some of the research work done in this area is summarized below. [1,6]

Asoka Life Science Limited launched Res-Q, the world's first poly-herbal mouth-dissolving tablet, a fast mouth-dissolving drug. It has a novel drug delivery system that imparts increased efficacy. In the 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 the mouth by mixing with the saliva and gets 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. [12]

A patent describes an orally administrable formulation for the controlled release or stable storage of a granulated herb, comprising a granulated herb and a carrier, the formulation releases 75% of the active ingredients between 4 and 18 h after

administration. The active ingredients are selected from the group consisting of hypericin, hyperforin, and echinacosides. The invention seeks to provide improved herbal preparations, whose preparations offer a convenient oral dosage form of herbs for supplying optimum plasma concentrations of the biologically active compounds that facilitate user compliance. The oral-controlled and stable release dosage form of the granulated herb is in either matrix formulations such as matrix tablets or in multi-particulate formulations like microcapsules put into two-piece capsules that are done to obtain a drug delivery system, which will ensure a steady supply of the active components for a sustained period.[13]

Another US patent invention is a new stable herbal drug formulation in the form of sustained-release micro granules containing *Ginkgo Biloba* extract as well as the process for preparing it. Plant extracts have poor flowability and compressibility properties. Thus, formulation of such extracts in the form of sustained-release tablets is difficult, as it requires homogeneous mixtures of extracts with pharmaceutical excipients during all compression steps. Microgranules can be manufactured by several different processes, for example, extrusion-spheronization, fluid air bed process, or a coating-pan method. Extrusion-spheronization is suitable for pellets with a high content of active substance but needs more equipment. For the manufacture of the granules of the invention, the coating-pan method is preferred, as it requires only simple equipment and operation. [14]

A study on a palatal mucoadhesive tablet containing a herbal formulation showed the sustained release abilities of buccal adhesive tablets comprising mucoadhesive polymers. The ingredients of the herbal formulation i.e. sage, *Echinacea*, *Lavender*, and *Mastic gum* have previously demonstrated antimicrobial activity. In the study, the herbal formulation comprised of these four herbal medicinals was incorporated into a slow-dissolving mucoadhesive tablet, designed to fit the palate. Results indicated that the adhesive tablet containing the herbal formulation is effective in reducing oral malodor and VSC levels. [15]

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. The 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*. [16]

A patent describes the herbal-based oral composition for periodic retention within the buccal cavity of a human, comprising of a mixture of herbs like *Radix Polygoni Multiflori*, *Rhizoma Drynariae*, *Rhizoma Ligustici Chuanxiong*, *Calculus Bovis*, *Indigo Naturalis*, *Herba Ecliptae*, *Pericarpium Trichosanthis*, *Radix Sophorae Flavescens*, *Spina Gleditsiae*, *Radix Angelicae Sinensis*, *Fructus Mori* and *Halitum*. The formulations selected for oral retention were from the group consisting of gels, pastes, and chewing gums. The herbal ingredients are selected and prepared to provide a composition that is effective at causing human scalp and facial hair to darken, reduce loss of scalp hair, and promote hair growth after a period of repeated usage.[17]

In a study by Ma and colleagues, the effect and mechanism of Shuanghua aerosol (SHA) was investigated on upper respiratory tract infections in children aged from 3 to 14 years. Shuanghua aerosol consists of *Flos Chrysanthemum Indicum*, *Flos Lonicera*, *Herba Houttuynia*, *Radix Bupleurum*, and menthene. The control treatment was Shuanghuanglian aerosol (SHLA), which consists of *Flos Lonicera*, *Fructus Forsythia*, and *Radix Scutellaria*. The authors conclude that SHA has obvious anti-inflammatory and antiviral effects and has a good curative effect in treating infantile upper respiratory tract infections. [18]

Gugulipid is a standardized extract prepared from the oleo gum resin of *Commiphora wightii* been clinically proven to reduce the levels of harmful serum lipids in the bloodstream. Microparticles of guggulipid were formulated by different techniques using chitosan, egg albumin, sodium alginate, ethyl cellulose, cellulose acetate, gelatin, and beeswax. The microparticles were evaluated for their physico-chemical characteristics. The HPLC profile showed a distinct separation of Guggulsterone-E and -Z; confirming the entrapment of guggulipid in the prepared microparticles. [19]

Microcapsules with entrapped herbal water-soluble extracts of plantain *Plantago major* and calendula *Calendula officinalis* L. (PCE) were prepared by layer-by-layer adsorption of carrageenan and oligochitosan onto calcium carbonate microparticles with their subsequent dissolving after the treatment of EDTA. Entrapment of PCE was performed by using adsorption and co-precipitation techniques. The co-precipitation provided better entrapment of PCE into the carbonate matrix compared to adsorption. *In vitro*, release kinetics was studied using artificial gastric juice. Using the model of acetate ulcer in rats, it has been demonstrated that PCE released from the microcapsules accelerates gastric tissue repair.[20]

Nanoparticles of TCH (traditional Chinese herbs) help improve their absorption and distribution in the body and therefore enhance their efficacies. Traditional Chinese herbs, including *peach seed*, *safflower*, *angelica root*, *Szechwan lovage rhizome*, *Rehmannia root*, *red peony root*, *leech*, *gadfly*, *earthworm*, and *ground beetle*, were mixed and prepared through drying, mincing, extracting, crushing into liquid particles with ultrasonic wave, filtering and nanometerizing into nanoparticles liquid with nanometer collider. Nanoparticles of TCH showed significant thrombolytic effects, resulting in quick recovery from arterial embolism and diminution of thrombi. The thrombolytic effects of nanoparticles of TCHs are much intensified than their non-nanoparticle form. There are also some research works on integrative evaluation, pharmacokinetics, and pharmacological activity of the oral prolonged-release preparations of traditional Chinese medicine. [21]

Novel sustained-release implant of herb extract using chitosan has proved to be very useful. The extract of danshen (*Radix Salvia miltiorrhiza*), a medicinal herbal, was developed with CS–gelatin as an implant for the promotion of anastomosing and healing on muscles and tissues at the organic incision site in abdominal cavities. Measurements were made of the sustained release of tanshinone IIa, a marker component, from the material *in vitro*. The dissolution medium was assayed with a high-performance liquid chromatography method. Biodegradation studies of the material were also conducted both *in vitro* and *in vivo*. The film made of this material exhibited a sustained release effect. The release profile conforms to the Higuchi equation. At most about 20% of the incorporated drug was

released over 15 days in a CS–gelatin (1:2) matrix. Drug release was found to be effectively controlled by the drug amount loaded in the matrix. The improved film (CS/gelatin ratio 1: 16) can be hydrolyzed by lysozymes *in vitro* in four days. This film of 0.5 cm<sup>2</sup> was implanted and degraded completely in rats over 28 days and the animals' wounds of abdominal incision healed well. [22]

ArthriBlend-SR is a marketed formulation containing herbal extracts and nutrients to support healthy joints and connective tissues in the body. It is a proprietary clinically validated blend of natural actives for joint care applications. The composition has the added advantage of sustained release technology, which benefits the continuous management of symptoms of arthritis. The blend contains Glucosamine sulfate, Boswellin (Boswellia serrata extract), and Curcumin C3 Complex (Curcuminoids from Curcuma longa), ingredients that work synergistically to support the management of inflammatory conditions such as arthritis. It will provide a slow-release profile of 80–90% active ingredient release, in an 8-h period. The benefits of a sustained-release formulation are particularly relevant to the bioavailability of glucosamine. [23]

## CONCLUSION

Herbal medicines have been widely used all over the world since ancient times and have been recognized by physicians and patients for their better therapeutic value as they have fewer adverse effects as compared with modern medicines. The drugs of Ayurvedic origin can be utilized in a better form with enhanced efficacy by incorporating modern dosage forms. However, phytotherapeutics need a scientific approach to deliver the components in a novel manner to increase patient compliance and avoid repeated administration. This can be achieved by designing novel drug delivery systems for herbal constituents. Novel drug delivery systems not only reduce the repeated administration to overcome non-compliance but also help to increase the therapeutic value by reducing toxicity increasing the bioavailability and so on. Recently, pharmaceutical scientists have shifted their focus to designing a drug delivery system for herbal medicines using a scientific approach. The novel research can also aid in capturing as well as remaining in the market. But many challenges with herbal drugs need to be overcome like difficulty of conducting clinical research in herbal drugs, development of simple bioassays for biological standardization,

pharmacological and toxicological evaluation methods' development, investigation of their sites of absorption, toxic herbal drugs in use, discovering various animal models for toxicity and safety evaluation, legal and regulatory aspects of herbal drugs and so on.

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