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Recent development in novel drug delivery systems for delivery of herbal drugs: An updates

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Abstract

In the recent years, herbal medicines have gained worldwide attention of peoples and researchers due to their esthetic value, more patient's compliance and prominent therapeutic effects. Novel drug delivery systems for delivery of herbal drugs possesses several advantages over conventional formulations. It includes enhancement of solubility, bioavailability, and protection from toxicity, etc. The herbal drugs can be used in a more upright course with enhanced efficacy by incorporating them into suitable dosage forms. This can be achieved by designing novel drug delivery systems for such drugs. Such systems are polymeric nanoparticles, nanocapsules, phytosomes, animations, microsphere, etc. The present article highlights the current condition of the development of novel herbal formulations and summarizes their type of active components, biological activity, and applications of novel formulations.

Keywords: Novel Drug Delivery; Herbal drug; Nanoparticles; Liposome; Phytosome

1. Introduction

The use of herbal medicines has gain worldwide attention due to their esthetic value, more patient's compliance and prominent therapeutic effects. Ethno-botanical information of such plants and their usage by indigenous cultures is useful in the conservation of traditional system of medicine, biodiversity, to promote health care system [1-2]. There are thousands of such types of plants widely available throughout the world. Such plants include, *Withania somnifera*, *Aloe vera*, *Azadirachta indica*, *Murraya Koenigii*, *Carica papaya*, *Allium sativum*, etc [3-17].

Novel drug delivery systems for delivery of herbal drugs possesses several advantages over conventional formulations [18]. 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 produce therapeutic effects [19]. 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.

2. Conventional Dosage Forms

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 zone, various drug delivery and drug targeting systems are currently under development Novel drug delivery system is a new approach to drug delivery. It helps the drug to act longer and more effectively.

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This overcomes limitations of old methods of drug administration [20]. Drawbacks of conventional dosage forms. Conventional dosage forms possess following limitations [21].

- 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.

3. Novel Drug Delivery Systems

In novel drug delivery technology; control of the distribution of drug is achieved by incorporating the drug in carrier system or in changing the structure of the drug at molecular level. Novel drug delivery systems possess following advantages [22].

- Enhancement of solubility.
- Increased bioavailability.
- Protection from toxicity.
- Enhancement of pharmacological activity.
- Enhancement of stability.
- Improved tissue macrophages distribution.
- Sustained delivery.
- Protection from physical and chemical degradation.

4. Herbal drugs

Herbal formulation means a dosage form consisting of one or more herbs or processed herb(s) in specified quantities to provide specific nutritional, cosmetic benefits, and/or other benefits meant for use to diagnose treat, mitigate diseases of human beings or animals and/or to alter the structure or physiology of human beings or animals.

Herbal preparations are obtained by subjecting whole plant, fragmented or cut plants, plants parts to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates [23-24].

4.1. Advantages of herbal drugs

Herbal drugs possess following advantages [25-27].

4.1.1. Low risk of side effects

Mostly herbal drugs are well tolerated by the patient, having fewer unintended consequences and fewer side effects than traditional medicine, and may be safer to use.

4.1.2. Effectiveness

Herbal drugs are more effective for long-standing health complaints that don't respond well to traditional medicine. One example is the herbs and alternative remedies used to treat arthritis. Vioxx, a well-known prescription drug used to treat arthritis, was recalled due to increased risk of cardiovascular complications. Herbal treatments for arthritis, on the other handle, have lesser side effects. Such treatments include dietary changes like adding simple herbs, eliminating vegetables from the nightshade family and reducing white sugar consumption.

4.1.3. Lower cost

Cost of herbal drugs is much less than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.

4.1.4. Widespread availability

Herbs are available without a prescription. Simple herbs, such as peppermint and chamomile, can be cultivated at home.

4.2. Limitations of herbal drugs

Herbal drugs possess following limitations [28-33].

4.2.1. Not suitable for many diseases

Modern medicine treats sudden and serious illnesses and accidents much more effectively than herbal or alternative treatments. An herbalist would not be able to treat serious trauma, such as a broken leg, nor would he be able to heal appendicitis or a heart attack as effectively as a conventional doctor using modern diagnostic tests, surgery, and drugs.

4.2.2. Lack of dosage instructions

Self-treatment with herbal drugs may consist of many risk factors. Moreover, with no proper direction of doses may lead to overdose.

4.2.3. Poison risk associated with wild herbs

Consumption of herbal drugs without correct identification of plant i.e., use of wrong part of plant may lead to poisoning.

4.2.4. Lack of regulation

Herbal products are not strictly regulated, consumers may buy inferior quality herbs. The quality of herbal products may vary among batches, brands or manufacturers. This can make it much more difficult to prescribe the proper dose of an herb. All herbal drugs are not safe, some may be poisonous or may cause allergenic reactions.

4.2.5. Longer duration of treatment

Curing period is usually longer in comparison to conventional medication. Immense patience while undergoing herbal treatment is needed.

5. Novel Drug Delivery Systems (NDDS)

Herbal drugs are becoming more popular in the modern world for their application to cure variety of diseases with less toxic effects and better therapeutic effects. There is a great possibility for herbal drugs 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 actual amount of the drug may not reach the blood. If the drug doesn't reach the blood at a minimum level which is known as 'minimum effective level' then there will be no therapeutic effect [34].

5.1. NDDS for Delivery of Herbal Drugs

Drug delivery system used for administering the herbal medicine to the patient is traditional and out-of-date, resulting in reduced efficacy of the drug. Also, for long-time herbal medicines were not considered for development as novel formulations owing to lack of scientific justification and processing difficulties, such as standardization, extraction and identification of individual drug components in complex polyherbal systems [35]. Modern phytopharmaceutical research can solve the scientific needs such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required, etc [36].

5.2. Types of Novel Herbal Drug Delivery Systems

Various approaches in case of novel herbal drug delivery system includes different types of formulations such as liposomes, phytosomes, pharmacosomes, niosomes, nanoparticles, microspheres, transferosomes, ethosomes, transdermal drug delivery system and proniosomes, etc are discussed below (Fig. 1).

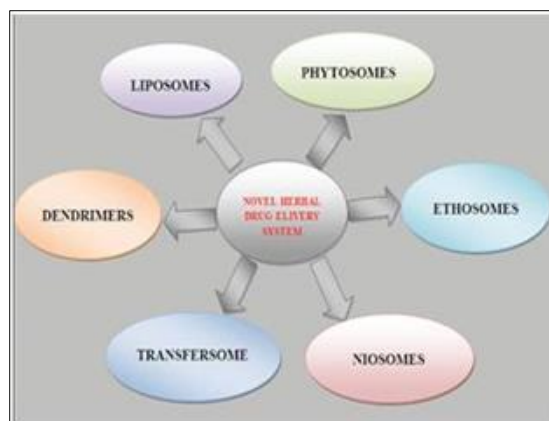


Figure 1 Novel drug delivery systems of herbal drugs [36]

5.2.1. Liposomes

Characteristics

Liposomes are spherical particles that encapsulate a fraction of the solvent, in which they freely diffuse or float into their interior. These are micro-particulate or colloidal carriers, usually 0.05-5.0 μm in diameter which forms spontaneously when certain lipids are hydrated in aqueous media. They can have one, several or multiple concentric membranes [37]. Liposomes are constructed of polar lipids which are characterized by having a lipophilic and hydrophilic group on the same molecules.

The primary advantages of using liposomes include (i) the high biocompatibility, (ii) the easiness of preparation, (iii) the chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds, and (iv) the simple modulation of their pharmacokinetic properties by varying the chemical composition of the player components (Fig. 2) [38].

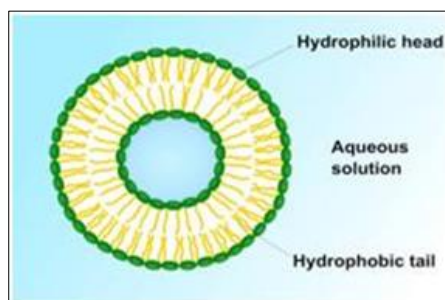


Figure 2 Structure of liposomes [38]

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.

Advantages of liposome formulation

- Hydrophobic and hydrophilic drug can be delivered.
- Liposome herbal therapy acts as a carrier for small cytotoxic molecules and as vehicle for macromolecules as gene.
- Sustained and controlled release of formulation can be possible.

5.2.2. Phytosomes

Characteristics

Most of the bioactive constituents of phytomedicines are flavonoids, which are poorly bioavailable when taken orally. Water-soluble phytoconstituents molecules (mainly polyphenoles) can be converted into lipid-compatible molecular complexes, which are called phytosomes. Phytosomes are more bioavailable as compared to simple herbal extracts owing to their enhanced capacity to cross the lipid rich biomembranes and finally reaching the blood [39].

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, 1 hr). After hydration, mixture of lipid and plant extract was sonicated for 20 min. 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 used (Fig. 3) [40].

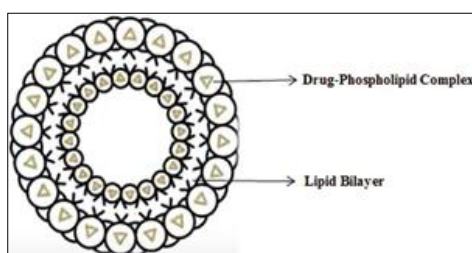


Figure 3 Structure of phytosomes [40]

Advantages of Phytosomes

Phytosomes have the following advantages [41],

- Improve the absorption of lipid insoluble polar phytoconstituents, enhance the bioavailability.
- Appreciable drug entrapment which becomes very beneficial.
- Reduce the dose due to increased absorption.
- Phosphatidylcholine shows synergistic effect because it is a hepatoprotective also.
- Phytosomes are more stable because of the chemical bonding between the phytoconstituents and carrier i.e. phosphatidylcholine.
- Effective in cosmetics.

5.2.3. Nanoparticles

Characteristics

Nanoparticles are efficient delivery systems for the delivery of both hydrophilic and hydrophobic drugs. Nanoparticles are the submicron size particles having size range 10 to 1000 nm. The major goal behind designing nanoparticle as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen. In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices (Fig. 4) [42]

Method of preparation

- Solvent evaporation,
- Nanoprecipitation,
- Emulsification/solvent diffusion,
- Salting out,
- Dialysis,
- Supercritical fluid technology (SCF) [43].

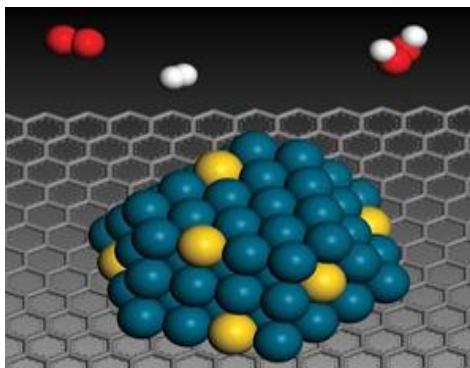


Figure 4 Nanoparticles

Advantages of herbal nanoparticle delivery system

- 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 [44].

5.2.4. Niosomes

Niosomes are multilamellar vesicles formed from non-ionic surfactants of the alkyl or dialkyl polyglycerol ether class and cholesterol. Earlier studies, in association with L'Oreal have shown that, in general, niosomes have properties as potential drug carriers similar to liposomes [45].

Niosomes are different from liposomes in that they offer certain advantages over liposomes. Liposomes face problems such as they are expensive, their ingredients like phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special storage and handling and purity of natural phospholipids is variable. Niosomes do not have any of these problems [46].

5.2.5. Proniosomes

Proniosome gel system is step forward to niosome, which can be utilized for various applications in delivery of actives at desired site. Proniosomal gels are the formulations, which on in situ hydration with water from the skin are converted into niosomes. Proniosomes are water-soluble carrier particles that are coated with surfactant and can be hydrated to form a niosomal dispersion immediately before use on brief agitation in hot aqueous media [46].

Advantages of proniosomes

- More stable during storage and sterilization.
- Easy to transfer and distribution.

5.3. Transdermal Drug Delivery Systems

Transdermal drug delivery system has been an increased interest in the drug administration via the skin for both local therapeutic effects on diseased skin (topical delivery) as well as for systemic delivery of drugs. However, they did not have had such expected success with other drugs. But immense potential lies in transdermal drug as future smart drug delivery devices [47].

Transdermal delivery system provides the advantage of controlled drug delivery, enhanced bioavailability, reduction in side effects and easy application. Transdermal formulation of boswellic acid and curcumin has been developed for continuous drug administration [48].

5.3.1. Microspheres

Characteristics

Microspheres are discrete spherical particles ranging in average particle size from 1 to 50 microns. Microparticulate drug delivery systems are considered and accepted as a reliable one to deliver the drug to the target site with specificity, to maintain the desired concentration at the site of interest without untoward effects. Micro encapsulation is a useful method which prolongs the duration of drug effect significantly and improves patient compliance (Fig. 5) [49].

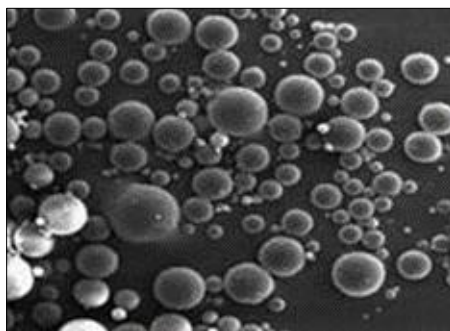


Figure 5 Structure of microsphere

Methods of preparation

- Spray Drying
- Solvent Evaporation
- Single emulsion technique
- Double emulsion technique
- Phase separation coacervation technique.
- Spray drying and spray congealing
- Solvent extraction
- Quassi emulsion solvent diffusion [50].

5.3.2. Ethosomes

Characteristics

Newer advancements in the patch technology have led to the development of ethosomal patch, which consists of drug in ethosomes. Ethosomal systems are made up of soya phosphatidylcholine, ethanol and water. They may form multilamellar vesicles and have a high entrapment capacity for molecules of various lipophilicities. The elastic vesicles and transferosomes have also been used as drug carriers for a range of small molecules, peptides, proteins and vaccines (Fig. 6) [51].

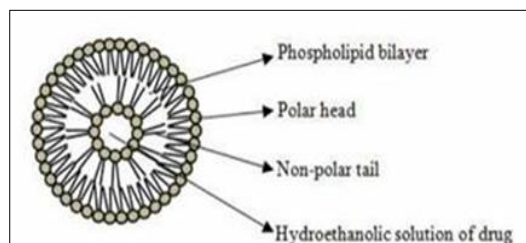


Figure 6 Structure of ethosomes

Method of preparation [52]

- Cold Method
- Hot Method
- Classic mechanical dispersion method

Advantages of ethosomal drug delivery

- Transdermal permeation of drug through skin can be enhanced.
- Large amounts of diverse groups of drugs can be delivered.
- The ethosomal drug is administered in semisolid form, resulting in improved patient compliance [53].

6. Analysis of NDSS systems of herbal drugs

NDSS systems containing either isolated phytoconstituents extracts or parts or whole drug are analyzed by routine quality control techniques. The quality control techniques includes high performance thin layer chromatography, high performance liquid chromatography, Uv-spectrophotometry, gas chromatography, etc [54-71]

7. Conclusion

By incorporating the herbal drugs in NDSS, we can deliver the proper amount of dosage to the target site. Thus it conclude that, NDSS for herbal drugs will be a revolutionary application in the conventional herbal formulations which will save the time of preparations and will increase the patient compliance too.

Compliance with ethical standards

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Disclosure of conflict of interest

Author declare that there is no conflict of interest.

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