2012 International Conference on Environment, Chemistry and Biology
IPCBEE vol.49 (2012) © (2012) IACSIT Press, Singapore
DOI: 10.7763/IPCBEE. 2012. V49. 34

Novel Herbal Drug Delivery System (NHDDS): the need of Hour

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Abstract. Novel herbal drug delivery system opens new wistars for delivery of herbal drugs at right place, at right concentration, for right period of time and also gives scientific angle to verify the standardization of herbal drug. For a long time, herbal medicines were not considered for development as novel formulations owing to lack of scientific justification and processing difficulties. Phytosome is a patented technology developed by a leading manufacturer of drugs and nutraceuticals, to incorporate standardized plant extracts or water soluble phytoconsituents into phospholipids to produce lipid compatible molecular complexes. Asoka Life science Limited launched the world's first poly-herbal mouth dissolving tablet, fast mouth dissolving drug. An investigation was aimed to formulate transdermal films incorporating herbal drug components such as boswellic acid (*Boswellia serrata*) and curcumin (*Curcuma longa*). Modern phytopharmaceutical research can solve the scientific needs (such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required etc.) of herbal medicines to be incorporated in novel drug delivery system, such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles and so on. The herbal drugs can be utilized in a better form with enhanced efficacy by incorporating them in modern dosage forms. This can be achieved by designing novel drug delivery systems for herbal constituents.

Key words: Drug delivery, herbals, nanoparticles, phytosomes, vesicles.

1. Introduction

From time immemorial it has been the endeavour of the physician and the apothecary to provide patients with the best possible forms of medicines so that recovery from disease is faster and complete. The drugs are delivered in a suitable formulation keeping in view the safety, efficacy and acceptability among other factors, and the formulation is usually known as dosage form or drug delivery system. With the progress in all spheres of science and technology, the dosage forms have evolved from simple mixtures and pills to highly sophisticated technology intensive drug delivery systems, which are known as Novel Drug Delivery Systems (NDDS). [1] In the past few decades, considerable attention has been focused on the development of novel drug delivery system for herbal drugs. [2] 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. However, some limitations of herbal extracts/ plant actives like instability in highly acidic pH, liver metabolism etc. has led to drug levels below therapeutic concentration in the blood resulting in less or no therapeutic effect. Incorporation of novel drug delivery technology to herbal or plant actives minimizes the drug degradation or pre systemic metabolism and serious side effects by accumulation of drugs to the non targeted areas and improves the ease of administration in the paediatric and geriatric patients. [3] Conventional dosage forms including prolonged-release dosage forms are unable to meet the ideal prerequisites of novel carriers like

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ability to deliver the drug at a rate directed by the need of the body and to channel the active entity of herbal drug to the site of action.

For good bioavailability, natural products must have a good balance between hydrophilicity (for dissolving into the gastrointestinal fluids) and lipophilicity (to cross lipidic biomembranes). Many phytoconstituents like polyphenolics have good water solubility, but are, nevertheless, poorly absorbed [4] either due to their multiple-ring large size molecules which can not be absorbed by simple diffusion, or due to their poor miscibility with oil and other lipids, severely limiting their ability to pass across the lipid –rich outer membranes of the enterocytes of the small intestine. [5]

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 medicines. [2]

Novel herbal drug carriers cure particular disease by targeting exactly the affected zone inside a patient's body and transporting the drug to that area. Novel drug delivery system is advantageous in delivering the herbal drug at predetermined rate and delivery of drug at the site of action which minimizes the toxic effects with increase in bioavailability of drugs. 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. Incorporation of herbal drugs in the delivery system also aids to increase in solubility, enhanced stability, protection from toxicity, enhanced pharmacological activity, improved tissue macrophage distribution, sustained delivery and protection from physical and chemical degradation. For example, liposomes act as potential vehicles to carry anti cancer agents by increasing amount of drug in tumour area and decrease the exposure or accumulation of drug in normal cells/tissues thereby preventing tissue toxicity effects. The phytosomal carriers have been studied for effective delivery of herbal extracts of ginseng (*Ginkgo biloba*) etc. Direct binding of phosphatidylcholine to herbal extract components led to better absorption characteristics as compared to conventional delivery of herbal extracts. Other vesicular assemblies like microspheres, nanoemulsions, polymeric nanoparticles etc. have been proved beneficial to carry herbal components. The present review article is aimed to provide an overview of different types of drug delivery systems incorporating active ingredients and potential advantages of such systems. [3] In the present article, an attempt has been made to touch upon various aspects and applications related to novel herbal drug formulations.

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.

2.1. Liposomes

These are micro-particulate or colloidal carriers, usually 0.05-5.0μm in diameter which forms spontaneously when certain lipids are hydrated in aqueous media. [6] The liposomes are spherical particles that encapsulate a fraction of the solvent, in which they freely diffuse or 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. [2]

2.2. Phytosomes

Most of the bioactive constituents of phytomedicines are flavonoids, which are poorly bioavailable when taken orally. Water-soluble phytoconstituent 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. The lipid-phase substances employed to make phytoconstituents lipid-compatible are phospholipids from soy, mainly phosphatidylcholine. [7] Phytosomal complexes were first investigated for cosmetic applications, but mounting evidence of potential for drug delivery has been cumulated over the past few years, with beneficial activity in the realms of cardiovascular, anti-inflammatory,

hepatoprotective and anticancer applications. [8] Phytosome complexes show better pharmacokinetic and therapeutic profile than their non-complexed herbal extract. The Phytosome technology has markedly enhanced the bioavailability of selected phytochemicals. [9]

2.3. Nanoparticles

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. [3] 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. [10] In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices [2].

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. [11] 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. [12]

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. [13] Proniosomal gels are the formulations, which on *in situ* hydration with water from the skin are converted into niosomes. [14] 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. [15]

2.6. Transdermal Drug Delivery System

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. [16] 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. [1] 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. [3]

2.7. Microspheres

Microspheres are discrete spherical particles ranging in average particle size from 1 to 50 microns. [17] 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. Eventually the total dose and few adverse reactions may be reduced since a steady plasma concentration is maintained. [18]

2.8. Ethosomes

Newer advancements in the patch technology have lead 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. [19]

2.9. Transfereosomes

Transfersomes are specially optimized particles or vesicles, that can respond to an external stress by rapid and energetically inexpensive, shape transformations. [20] The development of novel approaches like transferosomes have immensely contributed in overcoming problem faced by transdermal drug delivery such as unable to transport larger molecules, penetration through the stratum corneum is the rate limiting step, physicochemical properties of drugs hinder their own transport through skin. These elastic vesicles can squeeze themselves through skin pores many times smaller than their own size and can transport larger molecules. [21]

3. Conclusion

Herbal medicine is now globally accepted as a valid alternative system of therapy in the form of pharmaceuticals, functional foods etc., a trend recognized and advocated by World Health Organization (WHO). But the drug delivery system for herbal drugs is quite traditional and out of date. An extensive research is going on in the area of novel drug delivery and targeting for plant actives and extracts. However, research in this area is still at the exploratory stage. A number of plant constituents like flavonoids, tannins, terpenoids etc. showed enhanced therapeutic effect at similar or less dose when incorporated into novel drug delivery vesicles as compared to conventional plant extracts. Hence, there is a great potential in development of novel drug delivery system for valuable herbal drugs as it provides efficient and economical drug delivery. Also, the trend of incorporating NDDS for herbal drugs has also been adopted at industrial scale.

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