Review Article

Application of Novel Drug Delivery Sysytem For Herbal Formulations

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ABSTRACT

Novel Drug Delivery System (NDDS) is defined to the approaches, formulations, technologies, and system which provide a therapeutic amount of drug to the appropriate site in the body. If the novel drug delivery technology is applied in herbal actives and extracts. It may help in increasing the efficacy and reducing the side effect of variety of novel herbal formulation like polymeric nanoparticle, nanocapsules, liposomes, nanoemulsion, phytosomes, microsphere and ethosomes has been reported using bioactive and plant extracts. These novel formulations have advantage over the conventional formulations. NDDS include enhancement of solubility, bioavailability, protection against toxicity, enhancement of pharmacological activity and stability, improve tissue macrophage distribution and protection against chemical degradation. The most important aim to design alternative drug delivery technologies is to increase efficiency and safety of drug in the process of drug delivery and provide more convenience for the patients. The present paper includes more information regarding novel formulation of herbal formulation.

Keywords: Novel drug, herbal formulation technology, Nanoparticle.

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INTRODUCTION

In the recent decades, extensive research has been done for the development of Novel Drug Delivery System related to herbal formulations. These days, herbal drugs are becoming more valuable for their application to cure various diseases with minimum toxic effects and provide better therapeutic effects. Pharmaceutical conveyor of novel herbal drug can cure particular diseases by selecting the targeting effected area and delivered the drug to that targeting area. Novel drug delivery system (NDDS) can help to increase in solubility, stability and provide protection against toxicity. It also improves pharmacological, pharmacokinetic property, improved tissue macrophage and provide protection against physical and chemical degradation. The goal of the present review article is to provide an overview of different types of drug delivery systems that includes the active ingredients and also provide the information regarding advantages of such systems[1].

Different types of herbal formulation

Liposomes

Liposomes are spherical particles that encapsulate a portion of the aqueous solvent in which they are freely diffuse in their interior portion. Liposomes are composed of bi-layered of natural or synthetic phospholipids which are amphipathic molecules that have both hydrophobic tail and hydrophilic polar head. Mostly liposomes are formed from phospholipids and have been used to change the pharmacokinetic property not only drugs but herbs, vitamins and enzymes. Because of Liposomes have distinctive properties, it increases the performance of product by increasing ingredient solubility, improving ingredient bioavailability and enhance intracellular uptake. Liposomal drug delivery system can enhance the therapeutic efficacy of a product by delivery it to the site of action and by maintaining the minimum effective levels[2].

Advantages of Liposome formulation

1. Liposomes are used to drug delivery system due to its distinctive properties.
2. Liposomes reduces the dose requirement.
3. It delivers drugs at specific site of action.
4. It can incorporate with micro and macro molecules.
5. It can transfer with both hydrophobic and hydrophilic drug.

Table 1: Herbal liposomal formulation[3-5]

Sr. No.	Herbal medicine	Chemical classification	Pharmacological activity	Benefit of formulation
1.	Curcurmin	Natural polyphenol isolated from the root of *Curcuma longa*	Antitumor, antioxidant, anti amlodipine and anti-inflammatory	Improved intravenous delivery of curcumin to tissue macrophages
2.	Silymarin	Flavonol glycoside obtained from dried fruits of *Silybus marianum*	Hepatoprotective agent	Enhanced permeation and stability of silymarin
3.	Colchicine	Alkaloid isolated from *Colchicuma utumnale*	Antigout and anti-inflammatory	Increase permeation through skin
4.	Quercetin	Flavonoid obtained from Quercetum	Antioxidant and anticancer	Reduce inflammation, kill cancer cells and control blood sugar

Phytosomes

Phytosome comprises of two words i.e., “Phyto" means plant and “Some" means cell-like. Phytosomes are prepared by complexing the normalized extract and active ingredients of a herb bind to the phospholipid on a molecular level. In the structure of Phytosome, active ingredient is present which is enclosed by the phospholipids. Phytosomal herbal products are modern forms which absorb and utilizes in effective manner which gives better results than conventional herbal extracts. Phytosome drug delivery system produces better bioavailability, enhance pharmacological and pharmacokinetic properties[6].

Advantages of Phytosome formulation

1. Phytosome drug delivery system can improve the absorption of active ingredient, so required dose size is small in quantity.
2. In Phytosome, phospholipids complex formation can enhance the bioavailability.
3. This type of delivery system has higher stability.
4. Enhancement of bioavailability can improve therapeutic efficacy using phytosome drug delivery system.
5. It increased drug absorption in gastrointestinal tract[7].

Table 2: Herbal Phytosome Formulations [8-9]

Sr. No.	Formulation	Active ingredient	Application of phytosomal formulation	Biological activity	Route of administration
1.	Ginseng phytosome	Ginsenosides	Increase absorption	Immunomodulator	Oral
2.	Green tea phytosome	Epigallocatechin	Increase absorption	Anticancer and antioxidant	Oral
3.	Curcumin phytosome	Curcumin	Increase bioavailability	Antioxidant and anticancer	Oral

Ethosomes

Ethosomes are a bit slight alternation of drug conveyor Liposome. Ethosomes are phospholipids vehicles having large content of ethanol (20-45%) which enhance the permeability of drug through the skin by fluidising the skin lipids[10]. Basically, ethosomes consist of ethanol, phospholipids and water that enhance the penetration of various drugs into the skin. It causes the increase drug delivery reach to the deeper layer of skin and increase the blood circulation. Ethosomes size range may vary from nano meters to microns. Drug is administrated by ethosomes are available in the form of gel and cream as per the patient needs.

Advantages of Ethosome formulation

1. It enhances delivery of drug through the skin by fluidising the skin lipids.
2. Ethosomal drug delivery system is mostly used in pharmaceutical, veterinary and cosmetic field.
3. It increases efficacy and therapeutic effect of drug molecule.
4. Ethosomal drug delivery system, administrated in the semisolid form, results to improve patient compliance.
5. It reduces the toxicity of encapsulated agent[11].

Table 3: Herbal ethosomal formulations[12]

Sr. No.	Botanical	Active ingredient	Biological activity	Application of ethosomal formulations
1.	*Sophora Alopecyroides*	Sophora Alopecuroidsetosomes	Anticancer and Anti-inflammatory	Enhanced delivery of drug deeply penetrated into the skin
2.	*Glycyrrhiza glabra*	Amonium Glycyrrhizinate Ethosomes	Anti-inflammatory	Enhanced Anti-inflammatory activity

Microsphere

Microsphere consists of small spherical particles having diameters in the range from 1 to 1000 micro-meter. Microspheres are sometimes referred to as microparticles. Microsphere can be prepared from natural or synthetic materials. There are different types of microsphere available such as (a) Microcapsule and (b) Micrometrics. Microcapsules are those in which captured substance is specifically surrounded by the distinct capsule wall. Micrometrics are those in which captured substance is dispersing throughout the microsphere matrix[13]. These Microspheres can be administrated through oral route and either by injection. Microsphere drug delivery system can overcome some of the difficulties of conventional therapy and enhanced the therapeutic efficacy of the drug[14].

Advantages of Microsphere formulation

1. By the use of microsphere drug delivery system, drug can be easily release from the formulation.
2. It improves the therapeutic efficacy of the formulation[15].
3. The microsphere decreases the drug dosing frequency that's way improving patient compliance[16].
4. It can be used for site specific and organ targeted drug delivery[17,18].

Table 4: Microsphere herbal formulations[19]

Sr. No.	Formulation	Active ingredient	Application of formulation	Biological activity	Route of administration
1.	Zedoary oil microsphere	Zedoary oil	Higher bioavailability	Hepatoprotective	Oral
2	Rutin-alginate-chitosan	Rutin	Targeting into cardiovascular region	Cardiovascular and cerebrovascular diseases	In vitro

Nanoparticle

Nanoparticles are nano or sub-Nano-sized structures which are composed of natural or synthetic polymers. Nanoparticle has size range from 1-100nm. In this Nanoparticle system, the drug is entrapped in it and can easily reach to the site of action. According to the method of formulations, nanoparticles can be divided into two categories namely as nanosphere and nanocapsules[20]. Nanocapsules are those in which the drug is enclosed to the cavity surrounded by distinct polymer membrane while nanosphere are based upon the matrix systems in which the drug is physically and uniformly dispersed. Nanocarriers are recently used to drug delivery and their unique properties which results their potential used in chemotherapy[21].

Advantages of Nanoparticles

1. It helps in drug delivery at specific site of action.
2. It can improve the solubility and pharmacokinetic activity of drug.
3. It can help to reduce dose size.
4. It can promote the drugs throughout the biological barriers and enhance the bioavailability of drugs.
5. It can enhance the stability of drug[22].

Table 5: Herbal Nanoparticle formulations[23-24, 1]

Sr. No.	Herbal medicine	Chemical classification	Biological activity	Application of formulation
1.	*Ginkgo biloba*	Flavonol and flavone glycosides	Brain activation	Improving the cerebral blood flow and metabolism
2.	Quercetin	Flavonoids obtained from Quercetum	Antioxidant	Increase antioxidant activity
3.	Triptolide	Organic heteroheptacyclic compound	Anti-inflammatoy activity	Decreasing the toxicity
4.	Berberine	Organic heteroheptacyclic compound	Anticancer	Sustained drug release
5.	Zedoary	Obtained from curcuma zedoary	Hepatoprotection Anticancer and anti-bacterial	Increase the drug loading and stability

Nano-emulsion

Nano-emulsion are nano size emulsion manufactured for improving the delivery of active pharmaceutical ingredients. Droplet size of nano-emulsion falls typically into range 20-200nm. The carrier is solid sphere, and their surface is amorphous and lypophilic with a negative charge as a drug delivery system they enhance the therapeutic efficacy of the drug and minimize adverse toxic effect. Nano-emulsion are biphasic dispersion of two immiscible liquid i.e., either water in oil or oil in water droplet stabilized by amphiculous surfactant[25].

Advantaged of Nano-emulsion

1. Nano-emulsions are considered as an ideal alternative for the oral administration. Stable nano-emulsion for oral drug delivery was successfully prepared by high-gravity technology which offered a platform for continuous manufacturing[26].
2. Nano-emulsions are considered in increasing dermal and transdermal effectiveness of drugs[27].
3. Nano-emulsion are extensively envisaged as efficient drug delivery systems for the targeted delivery of lipophilic cytotoxic antineoplastic agents in the cancer therapeutics[28].
4. Enhanced wound healing activity was found in rat with Nano-emulsion formulation of eucalyptus essential oil in comparison with standard gentamycin[29].
5. Nano-emulsions of antitubercular drugs can easily cross the biological barriers to reach the systemic infection of *Mycobacterium tuberculosis* and improves drug bioavailability[30].
6. Vitamin D has a wide range of skeletal and non-skeletal functions which can be synthesized through sun exposure and taken up from fortified foods, its inadequacy is well known worldwide. Nano-emulsion delivery system is a promising approach to improved vitamin D bioavailability[31].

Table 6: Herbal Nano-emulsion formulations

Sr. No.	Formulation	Active ingredient	Application of emulsion formulation	Biological activity	Route of administration
1.	Triptolide micro-emulsion	Triptolide	Enhance the penetration of drugs through the stratum corneum by increasing hydration	Anti-inflammatory	Tropical
2.	Silybin Nano emulsion	Silybin	Sustained release formulation	Hepatoprotective	Intramuscular
3.	Berberine Nano emulsion	Berberine	Improved absorption	Anticancer	Oral

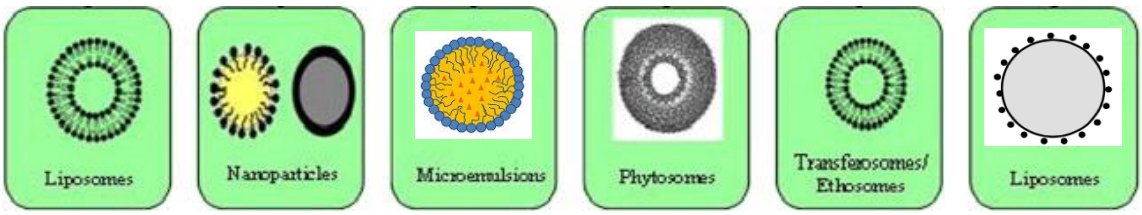

Figure 1: NDDS for plant actives and extracts[32]

CONCLUSION

Novel drug delivery system incorporated various plant constituents showed enhanced therapeutic effect as compared to conventional plant extracts. Thus, development of novel drug delivery system for valuable herbal drugs has great potential as they provide efficient and economical drug delivery. However, certain limitations of herbal medicines behavior require more studies to achieve the accurate therapeutic role of novel drug delivery system.

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