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A Review on Use of Herbal Drugs for Solid Lipid Nanoparticles

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Abstract:-Our country has a vast knowledge base of Ayurveda, importance of which is realized in the recent years. The conventional drug delivery system used for administering the herbal medicine to the patient is traditional and out-of-date as it reduces efficacy of the drug. If the novel drug delivery technology is applied in herbal medicine, it may increase the efficacy by reducing the side effects of various herbal compounds. This is the basic idea behind incorporating herbal drug in novel method of drug delivery. This article summarizes various nanoparticulate technologies that have been studied for the delivery of herbal medicines and which are gaining more attention for improved therapeutic response.

Keywords:-Herbal Medicines, Novel Formulation, Nanoparticles, Drug Delivery, Drug Targeting.

I. INTRODUCTION

Medicinal plants are important part of human health care history, culture and tradition. Herbal drugs as compared to synthetic chemicals are well accepted by modern society throughout the world as they are based on empirical observations. According to estimation of WHO, to satisfy the primary health care need, most of the population of the world prefer medicines derived from plant extracts.
As the plants acts as reservoir of therapeutic agents and they retain their historical significance as well as useful as a model compounds for the synthesis of various medicinal agents for synthetic and semi synthetic structure modification, as biochemical and pharmacological probes and to use the whole plant or part of it as a herbal remedy.

Since ancient times herbal medicines have been used in practice in various Asian countries. Now a days global market for herbal medicines has tremendously increased. **[1]** As Herbal medicines can treat diseases with remarkable fewer side effects as compared to synthetic ones. [2]

As highly complex and complicated chemical structured compounds are present in the plant sources, which can be used to synthesize abundant molecules from them. The structures of which are beyond the imagination of synthetic chemist. In various medicines, chemical moieties are used and are extracted from higher plants. Chemical composition present in herbal medicine is responsible for pharmacological action of the drug. [3]Natural products and their derivatives represent more than 50% of all drugs in clinical use in the world.

Thus, these days herbal medicines used all over the world and have been accepted by physician for patient compliance as they have less adverse effects as compared to modern drugs. Medicinal plants are now attracting more attention than ever because they are providing more benefits to the society. [4]

With the tremendous advancement in the Information Technology and market value of herbal products, safety, efficacy and quality of herbal traditional medicines have become the subject of research. The patentability of traditional medicine and associated knowledge is the major reason of increasing international attention in recent years.

Various conventional dosage forms does not fulfill the modern requirement of drug delivery system like delivering the drug as per rate according to need of the body, presence of active constituent of herbal drug to particular site of action for longer period of time, avoidance of various barriers like extremely acidic environment of stomach, first pass metabolism and many more.

Thus to acquire proper bioavailability in minimum effective concentration, to enhance the desired therapeutic effect in controlled manner novel drug delivery system has emerged along with the surprising advantages over the conventional dosage forms for herbal medicines also.[5]

II. ADVANTAGES OF NOVEL DRUG DELIVERY SYSTEM FOR HERBAL DRUGS

- Acceptance by the people as they have long history of use and better patient tolerance.
- Renewable source.
- Easier manufacturing and cultivation process.

- Easy availability.
- Bioavailability and solubility enhancement
- Protection from toxicity
- Enhancement of pharmacological action
- Enhancement of stability
- Improvement in tissue macrophage distribution
- Sustained delivery
- Protection from physical and chemical degradation

Many researchers have worked on different novel drug delivery system for the herbal drugs which includes

A. Phytosome

One of the Phospholipids based drug delivery system for Herbal drug is Phytosome in which Polyphenolic phytoconstituents with phosphotidyl choline complexed in a molar ratio resulting into promising drug delivery system. Phytosome produced comparatively better results than conventional herbal extracts as well as produced better pharmacokinetic profile. [6]

B. Liposome

Liposomes are amphipathic molecules, have hydrophobic tail and hydrophilic polar head. Liposomes are concentric bi-layered vesicles in which aqueous volume is entirely enclosed by a membranous lipid bi-layer composed of natural or synthetic phospholipids. [7]

C. Nanoparticles

Nanoparticles drug delievery system which not only improves the absorbance of herbal formulation but also the solubility of herbal drugs due to their nano-sized and unique structure of synthetic or semi-synthetic polymers. Nanoparticles are colloidal systems with particles ranging from 10 nm to 1000 nm. It contains the drug embedded in the matrix or adsorbed on to the surface. [8]

D. Emulsions

By using oil, water and surfactant along with co-surfactant a clear, isotopic and thermodynamically stable Micro- emulsion is prepared. Micro – emulsion can be prepared in minute droplets ranging in diameter from 0.1 µm to 100 µm by intimately dispersing one phase in other phase to obtain a biphasic system. These droplets are coated with a surfactant to reduce surface tension between two liquid layers. [9]

E. Microspheres

Microspheres which are prepared from various natural or synthetic materials available in size range from 1 µm to 1000 µm. [10]

F. Ethosomes

Ethosomes are one of the novel drug delivery system which helps the drug to reach the deep layers of skin. As ethanol is known as an efficient permeation enhancer reported to be added in the vesicular system to prepare the elastic nano vesicles. Ethosomes were developed as a novel lipid carries composed of ethanol, phospholipids and water to improve the delivery of various drugs. [11]

In different drug delivery systems nanotechnology is emerging at very exponential rate due to their nano sized structures.

In novel drug delivery systems specially nanocarries has gained popularity, due to their unique and nano size and increased prolonged circulation in the blood.

While designing the novel drug delivery system, targeted delivery of drug molecules is the most important and challenging research among various colloidal delivery systems. [12] Nanoparticles posses various advantages as compared to other delievery systems, due to their small size, large surface area , surface area changing ability.[13] Solid lipid Nanoparticles developed as colloidal drug delievery system such as emulsions, liposomes, polymeric micro nanoparticles. [14] SLNs are prepared from lipid, emulsifier and water solvent by using different methods and shows remarkable advantages by incorporating various herbal drugs like *Curcumin*, *Bacopa mannieri* etc. and enhance their therapeutic value at less dose, compared to conventional dosage forms.

III. SOLID LIPID NANOPARTICLES AS A DRUG DELIVERY SYSTEM FOR HERBAL DRUGS

Solid lipid nanoparticles were first discovered in 1991which are colloidal lipid carriers, solid at room temperature and body temperature.[15] It is a colloidal carrier system used specially for the delivery of lipophilic drugs.[16] Among all these novel drug delivery system.SLN possesses remarkable advantages, as

- SLN has better stability compared to liposomes. [17]
- In SLN, both hydrophilic and lipophilic drugs can be loaded.
- It is made of lipid matrix (physiological lipids), which decrease danger of chronic and acute toxicity.[12]

A. Solid Lipid Nanoparticles

To avoid the drawbacks of other colloidal systems like emulsions, liposome and polymeric nanoparticles, solid lipid nanoparticle can be used. [18] Solid lipid nanoparticles have higher physicochemical stability and protect the labile drugs from degradations the production could be done on large scale

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basis.[19] These are colloidal particles composed of highly purified triglycerides. The structures are made up of solids, lipids or mixtures of them and surfactants used for stability [20] SLN are formed by a core of solid lipid with a part of lipid matrix which is a bioactive material and stabilized by a surfactant layer.

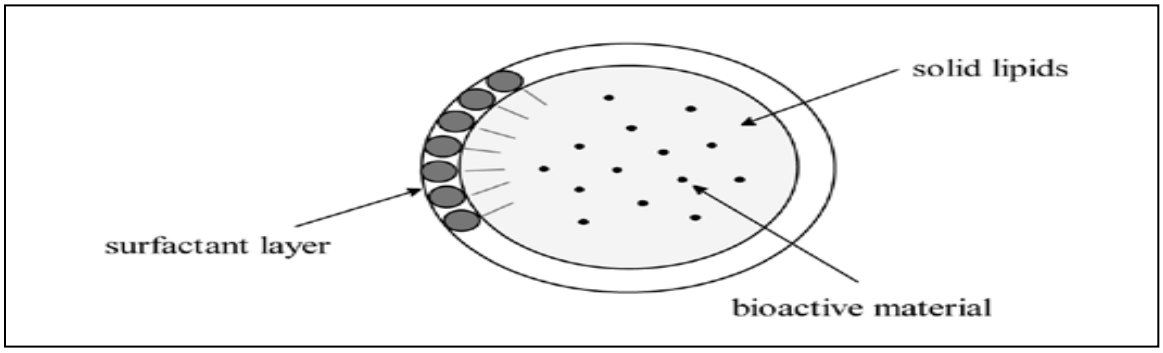

Fig.1. Structure of Solid Lipid Nanoparticles Stabilized By Surfactant Layer

The matrix of lipid particle is solid which protect the drug from chemical degradation. Crystallization of product cause efficient encapsulation and release of drugs [21] As their size is small (50-1,000 nm) and biocompatibility of SLN, used for various routes of administration like oral, parentral, percutaneous. [22]

IV. METHODS OF PREPARATION FOR SLN

A. High Pressure Homogenizations

A liquid with a high pressure (100-2000 bar) push through a narrow gap (in the range of few microns) by a homogenizers. The fluid moves at very short distance with high velocity (over 1000 km/h), very high shear stress, cavitations forces disrupt the particles down to the submicron range. Normally 5-10% lipid content is used but investigation on 40% lipid content is in process. High pressure homogenization can be done by two methods. In both methods basic step involves the drug incorporation in lipid by dissolving or dispersing the drug in the lipid.

a). Hot Homogenization

It is done at temperature more than melting point of the lipid and hence, considered as hot homogenization of emulsion. A pre-emulsion of the drug loaded lipid is melted and aqueous emulsifier phase is attained by high – shear mixing device. Pre-emulsions quality will change the final product. Droplets in the size range of few micrometers should be obtained in this process.

b). Cold Homogenization

It is High pressure milling of a suspension. Hence Proper temperature control and regulation is required. In this method as like in the hot homogenization i.e salublization or dispersing of the drug in the melt of the bulk lipid and then solid lipid nanoparticle are dispersed in a chilled emulsifier solution. [23-26]

B. Ultra Sonication

To get smaller particle size of Solid Lipid Nanoparticles Ultrasonication and High speed
homogenization is required to be used. In the probe sonicator or bath sonicator is used. [2427]

C. Solvent Evaporation Method

In water immiscible organic solvent (e.g. cyclohexane) The lipophilic material is dissolved which gets emulsified in an aqueous phase, after evaporation of solvent, nanoparticles with particle size 25nm mean size are produced by precipitation of lipid in aqueous medium. The solution was emulsified by high speed homogenization. Solvent was removed from emulsion by evaporation under reduced pressure. (40-60mbar) [24]

D. Solvent Emulsification Diffusion Method

The particulars with size 30-100 nm can be attained by this method and mean particle size depends upon lipid concentration in the organic phase and emulsifier used. Lipid dissolved in organic phase in water bath at 50^0c and acidic aqueous phase is used to balance zeta potential to form coacervation of SLN and then separated by centrifugation method. The SLN suspension is formed rapidly.[28-30]

E. Supercritical Fluid Method

SLN can be manufactured by rapidly expansion of supercritical CO2 solution. CO_2 (99.99%) is good choice as solvent for this method and has the advantage of solvent-less processing. [13]

F. Micro Emulsion Based Method

It is two phase system and made up of inner and outer phase (e.g o/w micro emulsion)The mixture of low melting fatty acid (e.g stearic acid) an emulsifier (e.g. polysorbate 20) co- emulsifers (e.g. butanol) and water is stirred at the temp 65-70ºc. The hot microemulsion is dispersed in cold water (2-3ºC) by stirring. In solid products (tablets, pellets) SLN dispersion can be used as a granulation fluid by granulation process. If particle content is less too much of water should be removed. High temperature gradients helps lipid crystallization and aggregation can be avoided. Due to dilution, attainable lipid contents are lowered compared with HPH based formulation.[24]

G. Spray Drying Method

Lyophilization can be replaced by this method. In this lipid is used with melting point more than 70º c. With SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixtures (10/90 v/v) best results were obtained. [24, 26]

H. Double Emulsion Method

Encapsulation of drug with stabilizer avoid separation of drug into external aqueous phase during solvent evaporation in which is external phase of w/o/w emulsion.[24,31]

I. Precipitation Method.

Dissolution of glycerides in an organic solvent and solution will get emulsified in water phase. As evaporation of organic solvent occurs the lipid will get precipitated in the form of nanoparticles.[24]

J. Film Ultra Sound Dispersion

After adding lipid and drug together in organic solution, decompression rotation and evaporation causes lipid film. Then aqueous solution which contains emulsions was mixed using the ultrasound with the probe to diffuser finally the SLN with little and uniform particle size is produced. [24]

Drug	**Part used**	**Method**	**Benefits of formulation**	**References**
Curcumin	Rhizome of curcuma longa	Micro-emulsification technique	Anti-depressant effects	32
Bacoside	Leavesof Bacopa monniera	Microemulsion probe sonicator method	Memory enhancing	33
Capsaicin	Capsaicin is an component ofchilli pepper	High shear homogenization and ultrasonication	Topical delivery carrier to enhance thepenetration of lipophillic drug capsaicin	34
Curcuminoids	curcuminoids from Curcuma longa L.	High-shear homogenizer	Antinflammatory activity in radiodermitis treatment	35
Artemisia arborescens	Artemisia arborescens L leaves	Homogenized at high pressure	Good potential carriers for ecological pesticides in agriculture.	36
Garlic	Bulb belonging to family liliaceae	Hot homogenization method	Antidandruff Shampoo	37
Neem oil	Seed of the Azadirachta indica	Double emulsification method	Treatment of acne	38
Soy isoflavone dermal gels	Whole soybean extract	Microemulsion template technique	Better deposition of the isoflavones in the dermal matrix	39
Frankincense and myrrh essential oils	Boswellia and Commiphora,	High-pressure homogenization	Increased the antitumor efficacy of FMO Reduction in Evaporation loss of the active components in FMO	40

Table 1: Examples of Herbal Solid Lipid Nanoparticles

V. CONCLUSION

Herbal medicines have been accepted worldwide as a alternative system of medicines. Conventional drug delivery system for herbal drugs limits the use of it due to some remarkable disadvantages like instability, poor bioavailability, poor solubility. To overcome such problems and to enhance the therapeutic effect of phytoconstituents various novel drug delivery systems are exploring their research in this area. Among these, SLN for various plant constituents with diversity in their structure can be incorporated in it by various different techniques. The use of SLN for various life saving drugs has been adopted at an industrial scale.

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