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A COMPREHENSIVE REVIEW ON NOVEL HERBAL DRUG DELIVERY SYSTEMS

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ABSTRACT

Herbal medicines have been increasingly recognized for their therapeutic potential, but their efficacy is often hindered by poor bioavailability and limited delivery options. Recent advancements in drug delivery technologies have led to the development of novel herbal drug delivery systems, offering improved pharmacokinetics and enhanced therapeutic outcomes. This review provides a comprehensive overview of innovative herbal drug delivery systems, including nanoparticles, liposomes, microspheres, hydrogels, and transdermal patches. We discuss the advantages, limitations, and potential applications of these systems, highlighting their ability to overcome traditional delivery challenges. Furthermore, we examine recent advances, regulatory considerations, and future research directions. Our analysis underscores the promise of novel herbal drug delivery systems in revolutionizing the field of herbal medicine, and we provide recommendations for future investigations.

KEYWORDS– herbal drug, liposome, Microspheres, novel drug delivery,

1.INTRODUCTION

The delivery of drugs involves administering the right amount of medication to the patient so that it reaches the specific target area and begins to take effect immediately. The goal of novel drug delivery systems is to address the drawbacks of traditional methods of drug delivery. Several methods can be employed to achieve novel drug delivery.(1) Over the years, there have been advancements in formulations and techniques, advancing the field of medication delivery. The effective administration of medication is often hindered by the chemical and physical properties of the drug, as well as biological obstacles such as the skin and membranes covering different human organs.(2) The qualities of drugs may differ significantly based on their size, chemical structure, ability to bind to specific receptors, and hydrophilicity, even when they are used to treat the same symptoms. Many medications have limited bioavailability due to their insolubility in physiological fluids and restricted permeability in organs. Furthermore, certain medications only exhibit therapeutic effects when they are present at a specific concentration; at concentrations above or below that level, they may cause toxic side effects or have no therapeutic effect at all.(3)

The popularity of herbal medicine is due to three main reasons:

1) Concerns about safety and addiction to drugs and surgery are increasing.
2) Most medical conditions are not fully cured by modern drugs.
3) Many natural remedies have been found to work better than drugs or surgery without side effects.(4)

1.2.Current tendencies

Inside the brand new years, nanostructured provider device like polymeric nanoparticles, liposomes, SLNs, polymeric micelles, nanoemulsions, and so forth., have been investigated for their functionality to supply anticancer tablets via manner of oral course. Moreover, the oral route gives terrific potential For delivery of cytotoxic retailers and therefore The eye has focused at the improvement of Oral chemotherapy in oncology.(5)

1.3. NEW DRUG DELIVERY POTENTIAL FOR HERBAL DRUGS:

Phytopharmaceuticals are medications that use traditional components derived from plants instead of chemicals. Natural substances are more easily and quickly metabolized by the body. They therefore improve bloodstream absorption and have fewer, if any, side

effects, which results in more thorough and effective treatments. Negative side effects are possible with chemical substances used to create medications. The human body frequently rejects chemicals that are not found in nature. These denials show up as negative reactions, which can range in intensity from minor headaches to potentially lethal ones. Lipid-based drug delivery systems have been the subject of numerous studies, which have shown promise for controlled and targeted drug delivery. Pharmacosomes are amphophilic phospholipid complexes that bind to phospholipids and contain drugs.(6)

1.4. Ideal Features:

1)Targeted medication delivery framework.

2)Biochemically inert and non-immunogenic.

3)Drug distribution should remain consistent and limited to the intended cell or organ.

4)Ensure that the pace of medication delivery remains controlled and predictable. The efficacy of medications remains unaffected by their method of release.

5)Drugs release a therapeutic amount.

6)Drug leakage during travel is minimal.

7)The carriers in use do not create issues or result in mediated illness modifications if they are biodegradable or easily removable from the body.

8)An efficient system in place for rapid (or relatively straightforward) reproduction and cost-effective distribution.(7)

2. TYPES OF NDHDDS

2.1.Nanoparticles

Nanoparticles, which can be either unformed or liquid, are in the solid form and include nanospheres and nano capsules with sizes ranging from 10 to 200 nm. They retain the capability to synopsize and/ or adsorb the medicine, shielding it from enzymatic and chemical breakdown. Biodegradable polymeric nanoparticles have garnered significant interest as possible medicine delivery agents in recent times due to their implicit uses in controlled medicine release, targeting specific organs or apkins, acting as DNA carriers in gene remedy, and delivering proteins, peptides, and genes via the peroral route.(8)

2.1.1. Method of preparation

A. Mechanical Methods

1) High Energy Ball Milling

2) Melt Mixing

B. Methods Based on Evaporation

1) Physical Vapour Deposition
2) Laser Ablation

C. Chemical Methods

1) Colloids synthesis
2) Synthesis of Metal Nanoparticles by Colloidal Method
3) Sol-Gel Method

D. Biological Methods

1) Synthesis using Plant Extracts
2) Synthesis using DNA(9)

2.1.2.Classification of herbal excipient

Classification according to their application and

Function in the drug

- Binder
- Diluents
- Lubricants

- Colidants
- Disintegrants
- Polishing film-forming & coating agent
- Plasticizers
- Coloring agent
- Suspending agent
- preservatives
- antioxidants etc.(10)

2.1.3. Advantages of nanoparticles

1.The controlled release and degradation properties of the particles can be easily tuned by selecting the matrix components.

2. Site-specific targeting can be achieved by attaching targeting ligands to the surface of the particles or by using magnetic guidance.

3. Liposome- and polymer-based nanoparticles are generally biodegradable, do not accumulate in the body, and are therefore considered safe.

4. Smaller sized nanoparticles can penetrate smaller capillaries, which may allow for effective drug accumulation at target sites.

5. There are various routes of administration, including oral, nasal, injectable, intraocular, etc.

2.1.4. Disadvantages of nanoparticles

1. The smaller the particle size, the larger the surface area, and this property makes nanoparticles very reactive in the cellular environment.

2.The small particle size results in limited drug loading and explosive drug release.

These practical issues must be addressed before nanoparticles can be used clinically or commercially.(11)

2.2. Liposomes

Liposomes are condensed double-layered vesicles containing a volume of water entirely contained, with a lipid bilayer membrane composed primarily of natural or synthetic phospholipids.Liposomes are spherical particles that contain some solvent inside, where it diffuses or floats freely.They may have one, several, or more condensed membranes.Polar lipids, which are composed of lipophilic and hydrophilic groups on the same molecule, are what make up liposomes.Simple examples include detergents, whose components form micelles; polar lipids, in contrast, have a larger hydrophobic portion that cannot associate into micelles with a high radius of curvature but instead form bilayers that can self-assemble into liposomes or lipid vesicles.Polar lipids self-assemble and form self-organizing colloidal particles upon interaction with water.(12)The term “liposome” originates from the fusion of two Greek words: “Lipos,” representing fat, and “Soma,” signifying body. Liposomes can come in a variety of sizes as either single or multi-lamellar structures. Their name is derived from their constituent phospholipids, rather than solely from their dimensions. They do not have lipophobic substances, like water. Yet, they usually do not include them. Liposomes are synthetic vesicles composed of bilayer lipid membranes. They can be filled with medications and used for administering treatments for cancer and other illnesses. Liposomes can be created from biological membranes using techniques such as sonic disruption. They act as microparticulate or colloidal carriers, usually ranging in diameter from 0. 05 to 5. 0 ?m, and naturally form in aqueous media as the lipids hydrate. Liposomes are composed of a biocompatible, biodegradable, and aqueous material containing a mix of natural and/or synthetic lipids arranged in one or more bilayers. A wide range of medications can be contained within liposomes, either within the phospholipid bilayer or at the interface of the two layers, depending on their different levels of lipophilicity.(7)

2.2.1.Procedure for preparation

There are four fundamental steps involved in all liposome preparation techniques:

1. Lipids are dried out using an organic solvent.

2. Lipid dispersion in watery media.

3. Cleaning the liposome that is produced.

4. Examining the finished item.(13)

2.2.2Benefits of Liposomes (14)

1. Offers liposomal doxorubicin, a selective passive targeting agent for tumor tissues.

2. A higher therapeutic index and efficacy.

3. Encapsulation results in increased stability.

4. A decrease in the encapsulated compounds’ toxicity.

5. The effect of site avoidance.

6. Better pharmacokinetic outcomes (longer circulation durations, decreased elimination).

7. The ability to pair with ligands unique to a spot to accomplish active targeting

8. Flexible and biodegradable

9. Capable of combining macro and micromolecules

10. Able to transport medications that are soluble in both water and lipids

2.3.PHYTOSOME

"Some" implies cell-like, and "Phyto" signifies plant. The phyto components of herb extract encircle and are bound by lipids (one phyto-constituent molecule coupled with at least one phospholipid molecule) in a vesicular drug delivery system called a phytosome. Because phytosomes shield important components of herbal extracts from being broken down by gut bacteria and digestive secretions, they exhibit superior absorption, leading to increased bioavailability and better pharmacological and pharmacokinetic characteristics than traditional herbal extracts.(15)

2.3.1. Procedure for preparation

Phosphatidylcholine and cholesterol were precisely weighed, diluted in 10 milliliters of chloroform, and then sonicated for 10 minutes using a bath sonicator in a round bottom flask (RBF). Organic solvents are eliminated using rotary evaporators set between 45 and 50°C. After the solvent was totally eliminated, the phospholipid combination formed a thin layer. For one hour, this film was wet at 37 to 40 degrees Celsius in a revolving evaporator. A lipid and plant extract mixture was sonicated for 20 minutes after hydration, with an ice bath close by to aid in heat dissipation. After that, the phytosomes were prepared, put in amber-colored bottles, and stored between 2 and 8 degrees Celsius in the freezer until they were needed.(16)

2.3.2. PHYTOSOME BENEFITS

1.Increased phospholipid complex bioavailability.

2.Improved GIT absorption.

3.Better therapeutic results are believed to be a result of higher bioavailability.

4.Because of its great absorption, a low dose is required.

5.More stability.

6.More stability.

7.Because of its excellent penetrating capabilities, strong lipophilicity is chosen over liposomes in cosmetics.

8. notable therapeutic advantages.

9. Instead of functioning as a carrier, phosphatidylcholine shields the liver.(7)

2.4. Niosomes

Niosomes are multilamellar vesicles composed of nonionic surfactants belonging to the dialkyl or alkyl polyglycerol ether family and cholesterol. Previous studies carried out in partnership with L'Oreal have shown that the general characteristics of niosomes as potential drug carriers are similar to those of liposomes. Niosomes differ from liposomes in that they have certain benefits over liposomes. One of the components of liposomes, phospholipids, are chemically delicate due to their susceptibility to oxidative degradation. As a result, they need special attention and memory, and the purity of natural phospholipids varies. All these problems do not affect niosomes.(17,18)

2.4.1.Benefits:

1.They are osmotically active and stable.

2. They increase the drug's stability while it is entrapped.

3. Surfactants don't require any particular handling or storage.

4.They can improve the way medications are administered topically, parenterally, and orally.

5.The surfactants are non-immunogenic, biodegradable, and biocompatible.(19)

2.5.Microsphere

The introductory description of microspheres is" monolithic spheres or remedial agents circulated throughout the matrix, either as a molecular structure composed of a nonstop phase of one or further miscible polymers, whereby drug patches are distributed on a macroscopic or molecular scale." Microspheres are bitsy, globular patches that generally range in size from one to a thousand micrometers. Another name for microspheres is" micro patches." Microspheres ameliorate patient compliance by taking smaller tablets to be administered. Effective medicine use will reduce side goods and boost bioavailability due to the harmonious and long- lasting remedial benefits of microspheres and their shape, which permits controlled inflexibility in drug release and breakdown.(20)

2.5.1. Benefits of formulations for microspheres

1. The use of microparticulate systems for medicine administration is beneficial since microspheres can be injected or consumed, can be customized for desired release profiles, and can be utilized to transport pharmaceuticals to specific sites or, in certain situations, to offer organ-targeted release.

2. The composition allows for easy drug release.(21)

2.6. Dendrimers

Dendrimers are polymeric polymers with globular or spheroid nanostructures. These are monodisperse, highly branched nanoparticles that either entrap the medicine inside their inner cores or bind it to their surface. Branching around the interior area is a special feature that greatly influences the physical and chemical characteristics. These particles are created using either divergent or convergent techniques. As more surface groups are added, the size increases linearly. They range in dimension increment by 1–10 nm in a stepwise manner and have an extremely low polydisparity index. Dendrimers' unique characteristics and performance might differ significantly from their linear complements. Dendrimers' extremely low polydispersity adds to their effectiveness as a medication delivery method.(22)

2.6.1. Drug Delivery Mechanism Using Dendrimers

Drug molecules can be loaded into the inside of the dendrimers as well as attached to the surface groups (as seen in the picture) thanks to the well-defined 3D structure and numerous functional surface groups. Drugs can be transported by dendrimers either by encasing them in their dendritic structure or by interacting with them at their terminal functional groups through covalent or electrostatic interactions (prodrug).

In general, there are two ways that drugs are delivered.

A) The first is by in vivo drug-dendrimer conjugate degradation (covalent drug-dendrimer bonding), which is dependent on the existence of appropriate enzymes or a bond-degrading environment.

B) The second is when the medication is released as a result of modifications to the physical environment, like temperature or pH. This method occurs in the cavities of the receptor's core (endo-receptor) or outer shell (exo-receptor) and is unaffected by outside variables.(23)

2.6.2. Benefits of Dendrimer

1.Administering medication directly to the affected area inside a patient's body.

2.In the realm of targeted drug delivery, dendrimers prove ideal for pinpointing solid tumors.

3.This is because of their enhanced permeability, as well as the limited drainage in tumor vasculature.

4.These factors culminate in the accumulation of macromolecules within the tumor, thus boosting the permeation rate effectively.

5.Reduction in the quantity of drug utilized can also be achieved through targeted delivery methods such as attaching site-specific ligands to the surface or using magnetic guidance, leading to decreased systemic toxicity.

6.Controlled and sustained drug release can also be achieved.

7.Drugs have the capability to be effectively retained within the layers of the skin without entering the bloodstream.

8.By avoiding the stomach environment, you can also eliminate any variations caused by gastric secretions.

9.Drug loading is on the higher side.Preservation of drug activity is possible as drugs can be seamlessly integrated into the systems without triggering any chemical reactions.(24)

2.7. Ethosomes

Ethosomes represent a slight modification of the familiar liposome delivery system. Ethosomes are lipid vesicles filled with water, phospholipids, and higher levels of alcohol such as ethanol and isopropyl alcohol. Ethersomes, delicate vesicles, consist of water, phospholipids, and a larger quantity of ethanol. Ethamomes vary in size from tens of nanometers (nm) to microns (μ). They enter the layers of the skin rapidly and exhibit a considerably greater transdermal permeation.(25)

2.7.1.Ethosome Benefits

1. Large molecules, such as peptides and protein molecules, can be delivered.

2. Its formulation includes non-toxic raw materials

3. Improved medication penetration via the skin for transdermal administration.

4. Ethosomal drug delivery systems are widely applicable in the sectors of cosmetics, veterinary medicine, and pharmaceuticals

5. A straightforward drug delivery technique as opposed to iontophoresis, phonophoresis, and other intricate techniques

6. The Ethosomal system is ready for immediate commercialization and is passive and non-invasive.(26)

3. India's Prospects and Opportunities for the Future

One of the most important areas for the pharmaceutical industry is India. As a result, numerous global behemoths have expressed a strong desire to invest and expand in this industry. The use and development of a wide range of excipients will be greatly impacted by advancements in the new and sophisticated NDDS procedures. India is renowned for being able to quickly adopt novel excipients and related technology. Therefore, the Indian excipient market will expand in two ways: first, by exporting new organic excipients, and second, by using new excipients in a variety of cutting-edge delivery technologies. The vast majority of the nation's pharmaceutical firms have been submitting and being granted new patents in the area of innovative drug delivery methods. This ultimately results in a significant demand for the goods and services provided by pharmaceutical companies and related enterprises in the near future. Numerous contemporary uses of nanotechnology in innovative drug delivery systems have the potential to enhance diagnosis, therapy, and post-administration monitoring of changes in drug composition within bodily systems. Computer-aided drug design is another significant turning point that deserves recognition because it provides a great deal of opportunity for the creation of such innovative and cutting-edge systems. Compared to traditional approaches, computer-aided drug design helps design and develop medications and delivery systems more accurately and with higher quality while using less time and resources.(26)

4.1. The significance of innovative drug delivery methods in herbal remedies

A unique drug delivery system is an innovative method of delivering drugs that overcomes the drawbacks of conventional drug delivery systems.(27) The innovative drug delivery technology is being utilized.Herbal medicine could potentially assist in enhancing.Enhancing effectiveness while minimizing the adverse effects of different treatments.Botanical extracts and plants. This represents the fundamental essence.The concept of integrating a new approach to drug administration.The distribution of herbal remedies is being carried out smoothly. Therefore it is.It is crucial to incorporate innovative drug delivery methods.Blend the system with Indian Ayurvedic medicines.Addressing more severe illnesses. For an extended period of time Herbal remedies were not taken into consideration.Novel formulations have emerged due to advancements in development.Absence of scientific validation and procedures.Challenges like standardization and extraction may arise.The discernment of each specific drug.(28) Nonetheless, contemporary phytopharmaceutical research can address the scientific requirements (e.g., pharmacokinetics, mechanism of action, site of action, precise dosage needed, etc.) for herbal medicines to be integrated into innovative drug delivery systems, including solid dispersions, liposomes, solid lipid nanoparticles, microemulsions, matrix systems, nanoparticles, and so forth.(29)

5. Creation of dosage forms and formulations offered as a cutting-edge method of medication delivery

5.1. Herbal formulations

A novel approach to medicine delivery due to their ability to treat a variety of disorders with less toxicity and better therapeutic results the use of herbal remedies is becoming more and more common in modern culture the development of nano dose forms is a primary focus of phyto-formulation research solid lipid nanoparticles liposomes polymeric nanoparticles and nanocapsules among them are nanoemulsion and phytosomes.(30)have several benefits for herbal medications, such as improved solubility and bioavailability, protection against toxicity, increased pharmacological activity, improved stability, improved tissue macrophage distribution, sustained delivery, and defense against chemical and physical deterioration, among others. Therefore, there may be a future for improving the effectiveness and resolving issues with plant medicines using nanoscale new drug delivery systems for herbal medications. Whole plants, broken or chopped plants, or plant parts are treated with extraction, distillation, expression fractionation, purification, concentration, or fermentation to create herbal medicines. This includes extracts, essential oils, expressed juices, and ground or powdered plant materials.(31)

5.2. Methods in Formulation (32)

The following methods are frequently employed in the formulation:

1 High-pressure homogenization method

By pushing the lipid through a very high shear stress at high pressures (100–2,000 bar). A very dependable and effective method for producing parenteral emulsions, lipid drug conjugates, SLNs, and nanostructured lipid carriers on a large scale is the high-pressure homogenization process.

2 The approach of complex coacervation

The interaction of two oppositely charged polyelectrolytes after mixing in an aqueous solution causes the spontaneous phase separation of two liquid phases in colloidal systems.

3.The method of co-precipitation

This technique for creating nananoscale core-shell particles is a variation of the complicated coacervation process. It has been claimed that this technique gives poorly water-soluble medications good dispersion stability.

4. The salting-out technique

This approach is predicated on the observation that adding an electrolyte reduces a non-electrolyte's solubility in water.

5.The solvent displacement approach or nanoprecipitation method

The basis of this technique is the displacement of a semipolar solvent that is miscible with water from a lipophilic solution. This increases the surface area, and even in the absence of mechanical stirring, tiny droplets of organic solvent are subsequently formed.

6.The diffusion-emulsification technique of solvents

The process entails creating an o/w emulsion using an oil phase that contains oil and polymer in an organic solvent. This is then combined with an aqueous phase that contains stabilizer in a high shear mixer. Water is then added to cause the organic solvent to diffuse, which leads to the formation of nanoparticles.

7. Fluid methods

that are supercritical Submicrometer and nanoscale formulations can be made with this technique. Supercritical fluids (SCFs) are employed above their thermodynamic critical point of temperature and pressure. They can be either liquids or gases. Water and carbon dioxide are the most widely used SCFs.

8. Techniques for self-assemble

The physical process by which previously disorganized atoms, molecules, or components reorganize themselves is known as self-assembly.

6. DIFFICULTIES IN FORMING HERBAL DRUGS

Formulating biomolecules derived from herbs remains a difficult task. The development of an appropriate delivery system presents certain difficulties. Research on delivery methods to transfer bioactive compounds derived from herbal sources to their site of action with improved efficacy and bioavailability is an ongoing endeavor. Some strategies for increasing the bioavailability of new herbal drug delivery systems include: balancing out natural molecules and promoting intestinal assimilation; improving pharmacokinetic profile by formulating with dietary constituents like soy lecithin; mixing dynamic molecules with different mixes as assistants advancing the dynamic particle's ingestion; and chemically derivatizing active biomolecules to increase bioavailability, which nevertheless produces various chemical analogs that should be appropriately screened.(33,34,35)

The majority of herbal plants have not yet had their sufficiency or security fully confirmed. Due to many factors, herbal medications, whether they are made from a single herb or a combination of herbs, suffer from inconsistent chemical properties. The traditional medicinal cases have been consistently supported by a large number of nonclinical in vitro and in vivo analyses of herbal details. However, there is a lack of effective information translation and examination convention approval. Examining the pharmacokinetics and bioavailability of herbal preparations presents a similar problem. These are driven by their dynamic chemical ingredients, which are opaque or possibly unidentifiable. (36)

The quality of the herbal products can influence clinical outcomes and their successful incorporation into evidence-based medicine, in addition to preclinical pharmacological concerns. The quality of plant-based medications might vary greatly depending on external and natural factors. Examples of natural variables that can affect the subjective and quantitative aggregation of the pharmacologically dynamic biomolecules produced by the plants include species differences, organ explicitness, and sporadic variations. Environmental factors, field assortment and development practices, post-harvest care, capacity, production, contamination, replacement, and anticipated adulteration are examples of external factors affecting the character of the herbal remedy.(37,38)

As a result, the quality of an item can differ from one country to another, from one brand to another within a comparable country, and even from one group to another within a similar brand. The 1940 Drugs and Cosmetics Act and the 1945 Drugs and Cosmetics Regulations serve as representatives for conventional medications. The guidelines established by a specialized panel in 1993

regarding the safety and effectiveness of natural medicines stipulated that all herbal and traditional remedies must adhere to the guidelines established by the Drug Controller General of India for allopathic medications in order to proceed with clinical preliminary testing for any restorative condition.The World Health Organization (WHO) has disseminated a number of guidelines for the clinical evaluation of both conventional and natural drugs.(39, 40)

7. Conclusion

In conclusion, novel herbal drug delivery systems have demonstrated remarkable potential in optimizing the therapeutic potential of herbal bioactives. Advances in nanotechnology, liposomes, and hydrogels have improved bioavailability, targeted delivery, and controlled release. Future research should focus on combination therapies, novel biomaterials, and comprehensive clinical trials. As the field continues to evolve, novel herbal drug delivery systems hold promise for transforming the prevention and treatment of complex diseases.

Clinical Implications

1. Personalized medicine approaches using novel herbal drug delivery systems.

2. Potential for improved patient compliance and reduced side effects.

3. Enhanced treatment outcomes for complex diseases..

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