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A Comparative Study on Applications of Novel Drug Delivery System for Herbal Formulations

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Abstract: ***For plant actives and extracts, novel drug delivery systems (NDDS) have made great strides in the past few years. Bioactive and plant extracts have been used to create a variety of novel herbal formulations, including polymeric nanoparticles, nanocapsules, liposomes, phytosomes, nanoemulsions, microspheres, transferosomes, and ethosomes. There are a number of advantages that the novel formulations have over conventional formulations, including improved solubility, bioavailability, protection from toxicity, enhancement of pharmacological activity, improved tissue distribution of macrophages, sustained delivery, and protection from physical or chemical degradation, among others. A review of the current state of herbal formulation development, including preparation method, active ingredient type, size, entrapment efficiency, route of administration and biological activity is highlighted in the present work.***

I. INTRODUCTION

Recent decades have seen a great deal of attention focused on new drug delivery systems for herbal drugs. Ideally, the novel carriers should meet two requirements. Erstens: The drug delivery rate should be determined by the body's needs during a treatment period. As a second goal, it should direct active constituents of herbal drugs to their target sites. These requirements are not met by conventional dosage forms, including those with the prolonged release. The development of nano dosage forms (polymeric nanoparticles, liposomes, solid lipid nanoparticles, phytosomes and nano-emulsions, etc.) has many advantages for herbal drugs, including enhanced solubility and bioavailability, protection from toxicity, enhancement of pharmacological activity, enhancement of stability, and improving tissue macroplasia (the amount of drug that reaches the tissue in the body).

Plant medicines could benefit from the use of nano-sized drug delivery systems to improve their efficacy and overcome common problems. It has been shown that hydrophilic and hydrophobic materials can be enclosed in biodegradable liposomes [1]. It is possible to increase the therapeutic index of anticancer agents by increasing drug concentration in tumour cells and/or decreasing exposure in normal tissues by exploiting the enhanced permeability and retention effect phenomenon as well as by using targeting strategies with liposome-based drug delivery systems [2]. In addition to their high biocompatibility, liposomes are easy to prepare and offer chemical versatility that allows the loading of hydrophilic, amphiphilic and lipophilic compounds [3]. Most conventional liposomes are trapped by the reticuloendothelial system (RES), making the delivery of agents to the RES easy. Herbal cosmetic formulations can also be made more effective by using novel approaches [4]. Some of these advantages are summarized here for the other vesicular systems such as nanoemulsions, ethosomes, and transferosomes as well.

A number of different aspects of the development of novel herbal formulations are discussed in this article, including the method of preparation, the type of active ingredient, entrapment efficiency, and applications, among others.

II. LIPOSOME

In their interior, the liposomes are spherical particles that contain a fraction of the solvent. They can have a single concentric membrane, or they can have several or many. Polymeric liposomes are composed of lipophilic and hydrophilic polar lipids [5]. Polar lipids self-assemble and form self-organized colloidal particles upon interaction with water. In the case of detergents, the hydrophobic components form micelles, while the bulkier hydrophobic parts of polar lipids cannot form micelles with high curvature radii, but instead form bilayers that can self-close into liposomes or lipid vesicles. According to a cross-section of a liposome (Fig. 1), the amphiphile's water-loving heads are facing the compartment of water, while its lipophilic tails are facing away from the compartment of water and towards the centre of the liposome. Aquatic compounds are therefore confined to the water compartment, while lipid-soluble substances accumulate in the lipid compartment. Water- and fat-loving materials can be enclosed in liposomes, which is unique. The pharmacokinetic profile of drugs, herbs, vitamins, and enzymes has been altered using liposomes, which are usually formed from phospholipids.

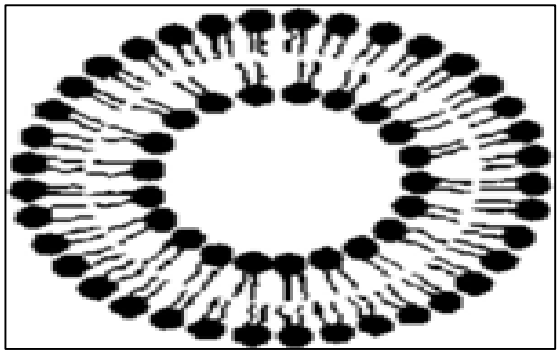

Figure 1 Cross-section of liposome

By increasing ingredient solubility, improving ingredient bioavailability, enhancing intracellular uptake, and altering pharmacokinetics and biodistribution [6], liposomes can improve the performance of products in vitro as well as in vivo. Since drugs are delivered to their target sites via liposomes, they are more effective and safer [7–9]. One of the few herbal drugs with an excellent pharmacological profile that readily lends itself to clinical efficacy testing is milk thistle (Silybum marianum). Due to the poor absorption of silymarin from the gastrointestinal tract (between 20 and 50 percent), silybin - one of the main active flavonoids found in dried silymarin fruit - has greater effects after parenteral than oral administration [10].

Silymarin's bioavailability can be improved by incorporating it into a liposomal dosage form that is administered buccally. Improving the bioavailability of silymarin through the incorporation of commercially available soybean lecithin into a stable liposomal buccal dosage form is one approach. Liposomes encapsulating silymarin were prepared by El- Samaligy et al. [11]. In a (1:1) ratio, silymarin-loaded hybrid liposomes were mixed with unloaded ones to prevent liposomal aggregate formation. After 3 months of storage at 4 °C or ambient temperature, M50 showed good stability in terms of encapsulation efficiency, turbidity measurement, and particle size analysis. Better stability can be achieved by refrigerating the food. As a result of the presence of Tween 20 as an edge activator, the liposomal silymarin formulation for buccal administration has the advantage of exerting a mucoadhesive effect [12]. The rat buccal mucosa was also shown to be safe when exposed to the substance.

III. NANOPARTICLES

Recent media attention has focused on the nanonization of herbal medicines. A nanoparticle and nanoemulsions (Fig. 2) is a colloidal system with particles ranging in size from 10 nanometers to one thousand nanometers [13, 14]. This includes curcuminoids [15], paclitaxel [16], and praziquantel [17], which are all nanonized and have particles that are larger than 100 nanometers in size. Submicronic colloidal systems could also be used to define nanoparticles. A matrix-like structure surrounds the active ingredient in nanospheres, whereas a polymeric membrane surrounds an active ingredient core in the nanocapsules. Herbal medicines absorb better when nanonized compared to their crude preparations [18]. Compound solubility increases, dosages are reduced, and herbal medicines absorb better when nanonized.

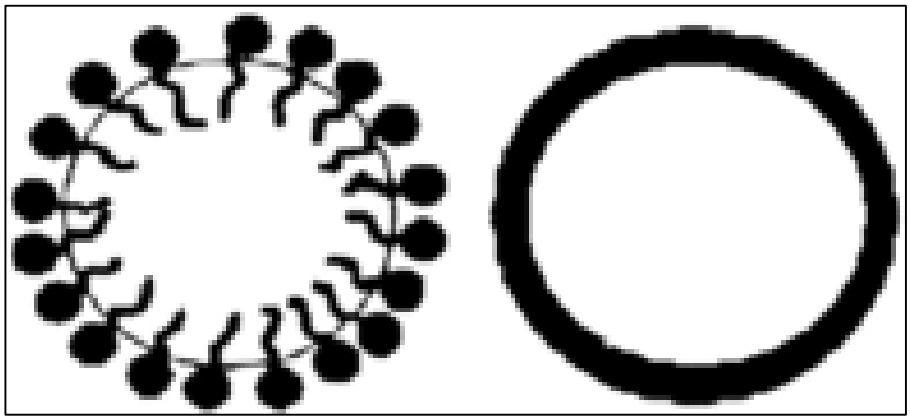

Figure 2 Cross-section of (a) nanoemulsion and (b) biopolymeric nanoparticle [4].

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IV. PHYTOSOME

Many plant products have been studied for their compositions, biological activities, and health-promoting benefits over the past century by phytochemical and phytopharmacological sciences. Pollutants and water-soluble molecules make up the majority of plants' biologically active constituents. Although some phytonutrients (such as flavonoids, tannins, terpenoids and others) are poorly absorbed due to their large molecular size, or because of their poor lipid solubility, they have a low bioavailability [19]. When constituents of a plant extract are isolated and purified, they lose some or all of their specific bioactivity — the natural constituent synergy is lost. Very often, it appears that the chemical complexity of the crude or partially purified extract is crucial to the bioavailability of the active constituents present. Some constituents of oral extracts may be destroyed in the stomach. As standardized extracts are developed, their clinical utility is often limited by their low bioavailability due to the reasons mentioned above in this article.

The bioavailability of such extracts and their constituents has been found to be significantly improved by complexation with certain clinically useful nutrients. The phospholipids are the nutrients that are most helpful in enhancing absorption. To improve absorption and bioavailability, a leading drug and nutraceutical manufacturer has developed a patent-pending technology called phytosomes, which incorporates plant extracts or water-soluble phytoconstituents into phospholipids to form lipid-compatible molecular complexes known as phytosomes. [20]

Phosphatidylcholine molecules surround the water-soluble substance in liposomes, where no chemical bond is established. Phosphatidylcholine molecules may surround the water-soluble compound by hundreds or even thousands. According to the substance(s) complexed, the phosphatidylcholine and plant components actually form a 1:1 or 2:1 molecular complex (Fig. 3).

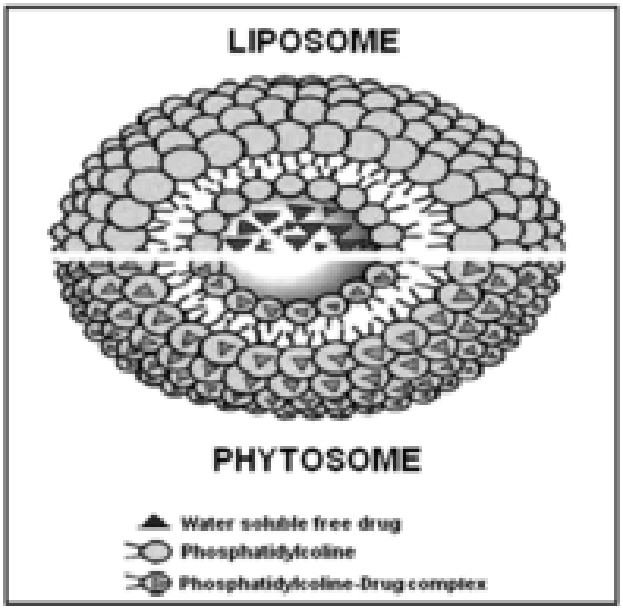

Figure 3 Difference between liposome and phytosome [21].

It is a complex chemical compound that is used in the construction of cell membranes in all known life forms. People and other higher animals use phospholipids as natural digestive aids and carriers of fat-miscible and water-miscible nutrients, respectively. In water and lipid environments, they are miscible. Oral absorption is good. As opposed to conventional herbal extracts, phytosomes are more bioavailable due to their increased ability to cross the lipoidal biomembrane and reach the systemic circulation. Nutraceuticals and herbal drugs are increasingly being delivered via phytosomes.

V. EMULSIONS

This system of non-homogeneous dispersion is made up of two liquids unable to dissolve each other, one of which disperses in the other as droplets [22]. It is composed of an oily and a watery phase, a surfactant and subsurfactant in general. Translucent to transparent liquid is its appearance. There are several types of emulsion, including ordinary emulsion (0.1–100 m), micro-emulsion (10–100 nm), and sub-micro-emulsion (100–600 nm). In addition to microemulsions, submicron emulsions are also known as lipid

emulsions. Due to its affinity for the lymphatic system, emulsions deliver drugs in vivo in a targeted manner. Additionally, the drug can be released over a long period of time because it is packaged in an inner phase and is not in direct contact with the body or tissue fluid [23]. oily or lipophilic drugs are made into O/W/O emulsions, and the oil droplets are then phagocytosed by macrophage, resulting in high levels of dissolved drug concentration in the liver, spleen or kidney. It is possible to concentrate water-soluble drugs in the lymphatic system by injecting them intramuscularly or subcutaneously. On its target distribution depends on the emulsion particle size.

Aside from the targeted sustained release, emulsifying the herbal drug improves the stability of the hydrolyzed materials, improves drug penetrability to the skin and mucous, and reduces the drugs' stimulus to tissues. So far, emulsions have been created from herbal drugs such as camptothecin, Brucea javanica oil, coixenolide oil, and zedoary oil. Zhou et al. [24] investigated the effect of elemenum emulsion on the human lung adenocarcinoma cell line A549 and protein expression. The results showed that the elemenum emulsion inhibited the growth and proliferation of A549 cells in vitro, with a time and dose-dependent relationship. Elemenum emulsion is a novel anti-cancer drug with broad application potential. It also has no marrow inhibition and causes no harm to the heart or liver.

VI. OTHER NOVEL VESICULAR HERBAL FORMULATIONS

Transferosomes are applied to the skin in an unoccluded manner, and they permeate through the stratum corneum lipid lamellar regions as a result of hydration or osmotic force in the skin. It has the potential to be used as a drug carrier for a variety of small molecules, peptides, proteins, and herbal ingredients. Transferosomes can penetrate the stratum corneum and supply nutrients locally to maintain its functions, resulting in skin maintenance [25]. In this regard, Xiao-Ying et al. [26] prepared transferosomes of capsaicin, which show better topical absorption than pure capsaicin. It is particularly suitable for topical or transdermal administration as a novel liposome [27, 28]. Drug delivery through the skin is improved by ethosomes because of their high deformability and entrapment efficiency. Its physical and chemical properties, compared to those of other liposomes, enable it to deliver drugs efficiently to a deeper skin layer or even the bloodstream [29]. As a topical drug carrier and transdermal delivery system, this property is critical. Furthermore, the ethosomes carrier can provide efficient intracellular delivery of both hydrophilic and lipophilic drugs [30], increasing percutaneous absorption of matrine, an anti-inflammatory herbal drug [31], and allowing the antibacterial peptide to easily penetrate the fibrocyte [32].

VII. MICROSPHERES

Medication administration via microparticulate systems is advantageous because microspheres can be ingested or injected; they can be tailored for desired release profiles and used for site-specific drug delivery; and in some cases, they can even provide organ-targeted release [33]. So far, microspheres have been created from plant active ingredients such as rutin, camptothecin, zedoary oil, tetrandrine, quercetine, and Cynara scolymus extract. Furthermore, reports on immune microspheres and magnetic microspheres have become more common in recent years. Immune microspheres have immune competence because antibodies and antigens were coated or adsorbed on polymer microspheres.

VIII. CONCLUSION

Plant actives and extracts are the subjects of extensive research in the area of novel drug delivery and targeting. Researchers are only at the exploratory stage of their work. Es must be resolved a number of issues in research, production and application. Research on carrier materials should also receive more attention in order to develop better carriers that can reduce drug toxicity, enhance their activity, and improve the agents' overall quality. Drug delivery systems with added value should be investigated for the therapeutic potential of herbal drugs. Following oral or topical administration, drug molecules' lipid solubility and molecular size are the major limiting factors in their ability to cross the biochemical membrane and be absorbed. As a result of their poor lipid solubility or improper molecular size or a combination of the two, several plant extracts and phytomolecules, despite excellent bioactivity in vitro, show little or no action when administered in vivo. Through the use of a novel drug delivery system, standardized plant extracts or polar phytoconstituents such as flavonoids, tannins, and xanthones have a much better absorption profile, which allows them to cross the biological membrane, resulting in increased bioavailability. The site of action (liver, brain, heart, kidney, etc.) is, therefore, more active when compared to the conventional plant extract or Phyto molecule. Consequently, the therapeutic effect is enhanced, detectable, and extended. NDDS has been successfully used to deliver a number of excellent phytoconstituents. As a result, there is significant potential for the development of novel drug delivery systems for plant actives and extracts.

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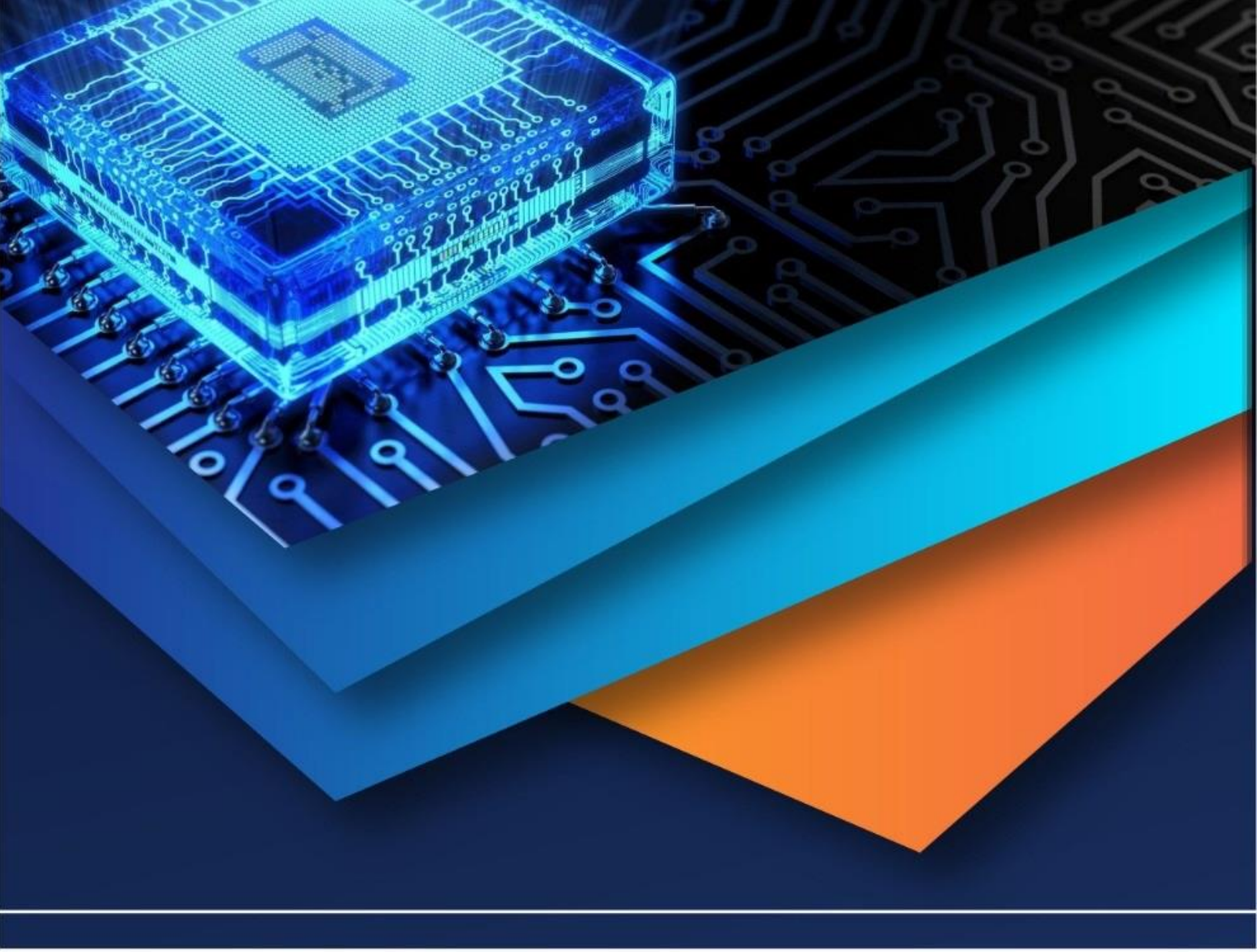

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