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REVIEW ARTICLE

A Promising Approach in Modern Drug Delivery: Vesicular Drug Delivery System

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ABSTRACT

Plants are the medicines of nature and have been used for food and medicine since ancient times by human beings on earth. Today, there are global trends towards the discovery of herbal medicines in plants to bring them to the market through an effective human drug delivery method. The basic idea behind it is that each disease's cure is concealed in nature. The distribution of herbal products, however, also needs to be changed in order to achieve sustained release, improve patient compliance, etc. Due to packaging, standardization, extraction and detection difficulties, previous herbal drugs could not attract scientists to the modifications of novel drug delivery systems. But now, with advances in technology, modern drug delivery systems (NDDS) are opening the door to the development of a new herbal drug delivery system. Using advanced toxicity safety methods, stability improvement, enhanced bioavailability of herbal formulations, physical and chemical degradation protection can be achieved. In order to achieve modified delivery of herbal drugs by increasing the therapeutic benefit as well as reducing toxicity, novel drug delivery technologies have gained significance. The existing reviews include information on different novel approaches used to enhance the safety and efficacy of phytomedicines and to apply novel formulations.

INTRODUCTION

In the past few decades, considerable attention has been paid on the development of novel drug delivery system (NDDS) [1]. Evolution of an existing drug molecule from a conventional form to a novel delivery system can significantly improve its performance in terms of patient compliance, safety and efficacy. In the form of a novel drug delivery system an existing drug molecule can get a new life. An appropriately designed novel drug delivery System can be a major advance for solving the problems related towards the release of the drug at specific site with specific rate. The need for delivering drugs to patients efficiently and with fewer side effects has prompted pharmaceutical companies to engage in the development of new drug delivery system [2].

➢ Merits of Novel Drug Delivery System

1. Reduction in the total amount of drug administered over the period of drug treatment. This contributes to the reduced incidence of systemic and local side effects.
2. Devoid of first pass metabolism and gastrointestinal tract degradation.
3. Improved patient compliance resulting from the reduction in the frequency of doses required to maintain the desired therapeutic response.
4. Targeting of the drug molecule towards the tissue (or) organ reduces the toxicity to the normal tissues [3].

➢ Targeted Drug Delivery System

Drug targeting can be defined as the ability to direct a therapeutic agent specifically to desired site of action with little or no interaction with

non-target tissue. Targeted drug delivery system means accumulation of pharmacologically active moiety at desired target site in therapeutic concentration at the same restricting its access to normal cellular lining, thus minimizing therapeutic index. Minimum distribution of the parent drug to the non-target sites with higher and effective concentration at the targeted site certainly maximize the benefits of targeted drug delivery [4].

➢ **Properties of Ideal Targeted Drug Delivery**

- It should possess controllable and predictable rate of drug release.
- Carriers used should be inert or should have zero therapeutic value.
- Carriers should be biodegradable and easily eliminated from the body.
- Should be nontoxic and physicochemical stable in vivo and in vitro.
- Drug release should not affect the drug distribution [5].

➢ **Types of Drug Targeting**

i. Passive Targeting

In this type of targeting the particle system is captured by physiological mechanism such as filtration or macrophage (Reticuloendothelial system) sequestration. (i.e.) drug targeting occurs because of the body's natural response to physicochemical characteristics of the drug or drug carrier system. It is concentration dependent, so external energy is not necessary [6].

ii. Inverse Targeting:

To achieve inverse targeting, RES normal function is suppressed by preinjecting large amount of blank colloidal carriers or macromolecules like dextran sulphate. This approach leads to saturation of RES and suppression of defense mechanism. This type of targeting is an effective approach to target drug(s) to non-RES organs [7].

iii. Active targeting:

Surface modification technique is used to achieve active targeting. In this approach active ingredient is attached with the surface of carrier system such as monoclonal antibodies or carbohydrates like glucose and galactose. The drug reaches to specific site on the basis of modification made on its surface rather than natural uptake by RES. Active targeting is classified into three [8].

a. First order targeting:

It involves distribution of drug carrier system to capillary bed of target site or organ. For example lymphatic's, peritoneal cavity, plural cavity, cerebral ventricles, etc.

b. Second order targeting:

It involves delivery of drug to special cells such as tumor cells or kupffer cells in lives.

c. Third order targeting:

Third order targeting is essential for gene delivery and exogenous DNA to the nucleus. Targeting is based on the structure with in a cell.sThe active targeting more specific for kupffer cells of the liver and parenchyma cells like hepatocytes [9, 10].

iv. Dual Targeting:

In this targeting approach carrier molecule itself have its own therapeutic activity and thus increase the therapeutic effect of drug. For example, a carrier molecule having its own antiviral activity can be loaded with antiviral drug and the net synergistic effect of drug conjugate was observed [11-14].

v. Double Targeting:

When temporal and spatial methodologies are combined to target a carrier system, then targeting may be called double targeting. Spatial placement relates to targeting drugs to specific organs.

vi. Combinations Targeting:

Combination targeting is for site specific delivery of proteins and peptides. The targeting systems are equipped with carrier and polymer. This method is more specific for gene therapy [15].

➢ **Drug Delivery Carriers**

Carrier is one of the special molecule or system essentially required for effective transportation of loaded drug up to the preselected sites. Some carrier based drug delivery systems are:

- Microspheres and micro capsules
- Nanoparticles
- Monoclonal antibodies
- Prodrugs
- Resealed erythrocytes
- Artificial cells
- Neutrophils
- Vesicular carriers [16]

➢ **Vesicular System – Carrier For Drug Delivery**

Vesicles act as the vehicle of choice in drug delivery. Vesicles play a major role in modeling biological membranes and in the transport and targeting of active agents. Vesicular drug delivery system has some of the advantages:

- Like other targeted drug delivery systems, it prolongs the existence of the drug in systemic circulation and perhaps, reduces the toxicity due to the delivery of drug directly to the site of infection.
- Both hydrophilic and lipophilic drugs can be incorporated.
- Delays elimination of rapidly metabolizable drugs and thus function as sustained release systems [17].

Some important vesicular drug delivery systems are:

I. Niosomes
II. Liposomes
III. Sphingosomes
IV. Transferosomes
V. Pharmacosomes
VI. Virosomes
VII. Proteasomes
VIII. Archaesome
IX. Ethosomes
X. Proniosomes

I. Niosomes

A niosome is a non-ionic surfactant vesicle. Niosomesis formed mostly by cholesterol incorporation as an excipient. Niosomes have more penetrating capability than the previous preparations of emulsions. They are structurally similar to liposomes in having a bilayer; however, the materials used to prepare niosomes make them more stable and thus niosomes offer many more advantages over liposomes.

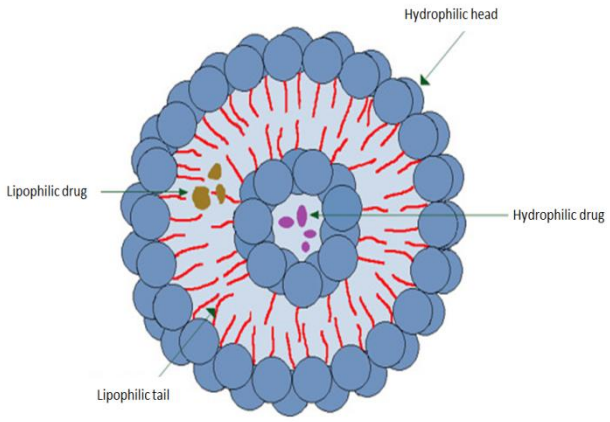

Figure 1: Niosomes

II. Liposomes

Liposomes are simple microscopic vesicles in which lipid bilayer structures are present with an aqueous volume entirely enclosed by a membrane, composed of lipid molecule. There are a number of components present in liposomes, with phospholipid and cholesterol being the main ingredients.

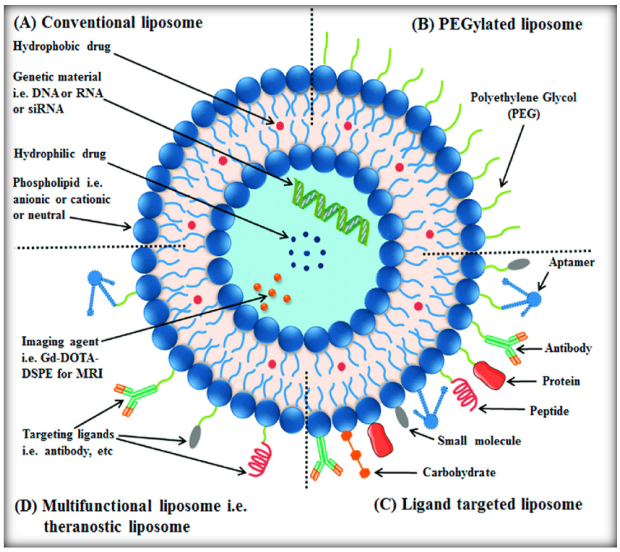

Figure 2: Liposomes

III. Sphingosomes

Sphingosomes is bilayered vesicles in which an aqueous volume is entirely enclosed by membrane lipid bilayer mainly composed of natural or synthetic sphingolipid. Sphingosomes solve the major drawback of vesicle system (liposomes, niosomes) such as less stability, less in vivo circulation time, low tumor loading efficacy in case of cancer therapy. Sphingosomes are clinically used delivery system for chemotherapeutic agent, biological macromolecule and diagnostics [18].

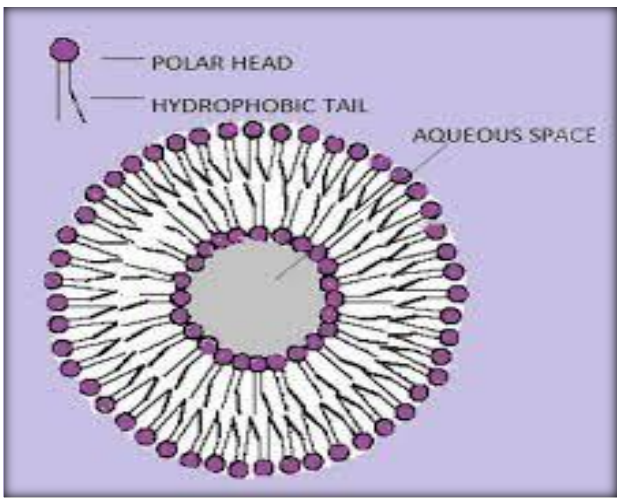

Figure 3: Sphingosomes

IV. Transferosomes

It consist of both hydrophilic and hydrophobic properties,highdeformability gives better penetration of intact vesicles. A transferosomes, in functional terms, may be described as lipid droplets of such deformability that permits its easy penetration through the pores much smaller than the droplets size. They protect the encapsulated drug from metabolic degradation. A transferosomes carrier is an artificial vesicle designed to be such as a cell vesicle or a cell engaged in exocytosis and thus suitable for controlled and potentially targeted drug delivery.

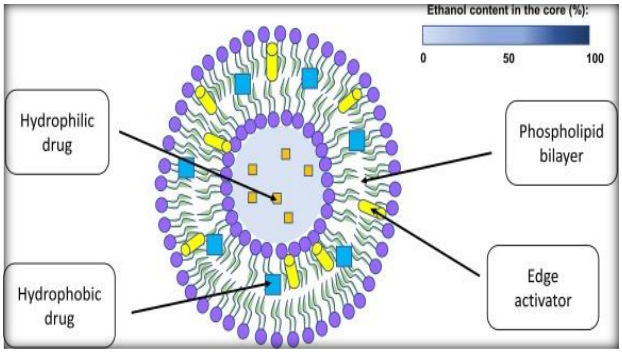

Figure 4: Transferosomes

V. Pharmacosomes

The term pharmacosome comprises of two main parts - Pharmacon (active principle) and some carriers (Vaizogle and Speiser 1986, Goymann and Hamann, 1991) postulated that amphipathic drug can self-assemble to form vesicle and these vesicles are termed as pharmacosomes. Drug covalently bound to lipid may exist in a colloidal dispersion as ultrafine, micelles or hexagonal aggregates which are known as pharmacosomes [19].

VI. Virosomes

Virosomes are drug or vaccine delivery mechanism consisting of unilamellar phospholipid membrane, which is either a mono or bi-layer vesicle incorporating virus derived proteins to allow the virosomes to fuse with target cells.

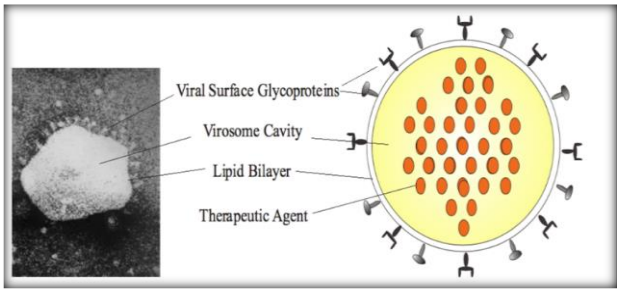

Figure 5: Virosomes

VII. Proteasomes

Proteasomes are cytoplasmic organelle, composed of a cylindrical core particle bound by two regulatory particles at each end, responsible for degrading endogenous proteins. Proteins to be destroyed are recognized by proteasomes because of the presence of ubiquitin conjugated to the targeted protein's lysine residue.

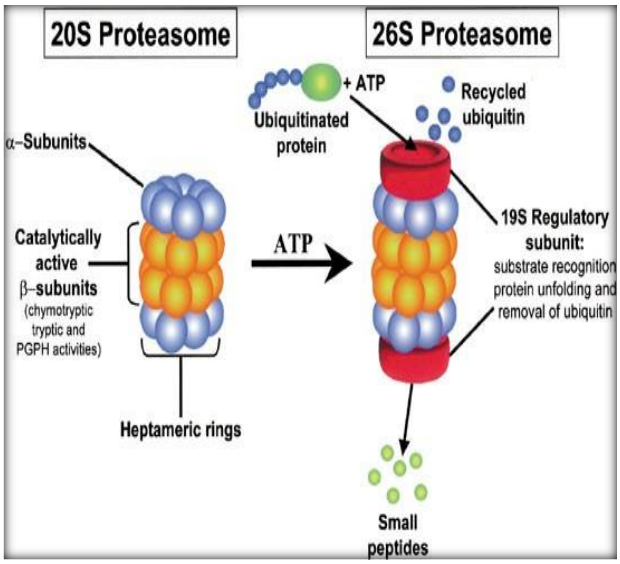

Figure 6: Proteasomes

VIII. Archaesome

Archaeosomes are liposomes made from the polar ether lipids of Archaea. These lipids are unique and distinct in structure from the ester lipids found in Eukaryote and Bacteria.

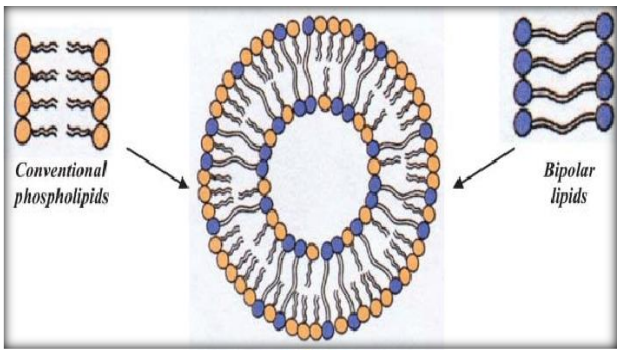

Figure 7: Archaesome

IX. Ethosomes

Ethosomes are soft, malleable vesicles tailored for enhanced delivery of active agents. It has been shown that the physicochemical characteristics of ethosomes allow this vesicular carrier to transport active substances more efficaciously through the stratum conium into the deeper layers of the skin than conventional liposomes [20].

X. Proniosomes

Proniosomes are dry formulation of water soluble carrier particles that are coated with surfactant. They are rehydrated to form niosomal dispersion immediately before use on agitation in hot aqueous media within minutes. Proniosomes are physically stable during storage and transport. It enhances the penetration into target tissue and reduces toxicity [21].

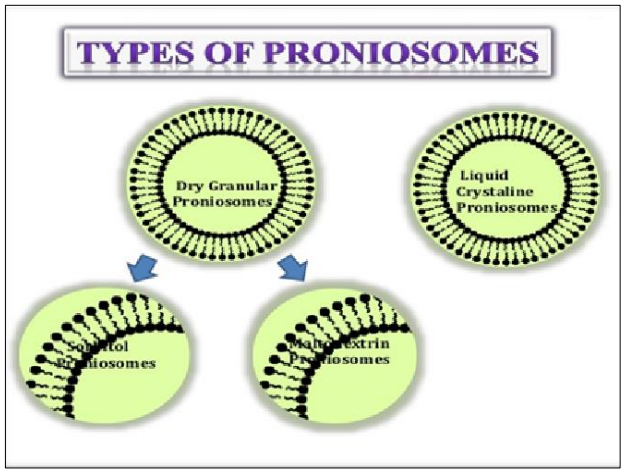

Figure 8: Proniosomes

CONCLUSION

In addition to minimizing repeated administration to resolve non-compliance, the innovative drug delivery system also helps to improve therapeutic value by reducing toxicity and increasing bioavailability, etc. Herbal medicines are being thoroughly studied to integrate them into novel drug delivery systems. Increased bioavailability, reduced toxicity, sustained release action, safety from GI degradation that cannot be accomplished via traditional drug delivery system due to large molecular size, low solubility, degradation of herbal medicines in Gastrointestinal media will benefit from the application of these novel techniques to natural medicines.

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