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Cryptosomes: A Novel Promising Drug Delivery System

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ABSTRACT

Vesicular drug delivery systems might be a solution to the problem of limited bioavailability and rapid clearance of medications from the body. The four kinds of lipid-based drug delivery techniques include solid-lipid particle system, emulsion-based system, solid lipid tablet, and vesicular system. Cryptosomes are a novel vesicular drug delivery system that may solve some of the shortcomings of classic drug delivery methods, such as high stability, enhanced bioavailability, longer release, and decreased elimination of fast metabolizable drugs, among others. Cryptosome is derived from the Greek terms "Crypto," which means "hidden," and "Soma," which means "body." It's made up of phospholipids like distearoylphosphatidylethanolamine-polyethylene glycol and distearoylphosphatidylcholine (DSPE-PEG). Vesicular systems refer to the use of vesicles as a carrier or adjuvant in a variety of applications. This research looks at several vesicular drug delivery technologies and emphasises cryptosome's accomplishments in this area. This review will be useful to researchers working in the field of vesicular drug delivery.

Key Words: Vesicular system, Drug Delivery, Cryptosome, Formulation, Composition, Preparation

INTRODUCTION

Cryptosomes are one kind of drug delivery system that is being created in the present drug discovery system to increase therapeutic activity and reduce negative effects of many new drugs. It's a liposome, which is a lipid-based medication delivery system. Over the past three years, many liposomes have been explored in the aim of utilizing them to deliver medicine to people and animals. As a consequence of this approach, drug discovery, development, and use have all grown considerably. Lipid-based drug delivery systems (LDDS) provide a wide range of formulations with different structural and functional features dependent on the lipid and other additional components. LDDS has moved from micro to nano-scale by boosting the efficacy and therapeutic application of these systems. The four types of LDDS include solid lipid particle dosage form, emulsion-based system, solid lipid tablets, and vesicular systems. Cryptosomes are a kind of vesicular drug delivery mechanism [1].

CRYPTOSOMES

The vesicular system is essential for NDD, particularly for sorting ill cells, diagnostics, gene and genetic materials, and guaranteeing safe, effective, and targeted medication administration in vivo. They function as a long-acting delivery system, lowering the quantity of drug that is immediately digested. In recent decades, they've been widely used as medicine carriers. Cryptosomes (Figure 1) are derived from the Greek words Crypto (hidden) and Soma (body or carrier). These lipid vesicles circulate in the blood for a long period after systemic delivery, reducing phagocyte mononuclear uptake. They have a phosphatidylcholine and polyoxyethylene surface coating, both of which are phosphatidylethanolamine derivatives. Distearoylphosphatidylcholine and phospholipids such as distearoylphosphatidylethanolamine-polyethylene glycol make up cryptosomes (DSPE-PEG). Cryptosomes, also known as immune-liposomes, are a kind of cryptosome that

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may evade detection by the immune system. Cryptosome characteristics may be affected by how the polyethylene glycol (PEG) is linked to the lipid. The rigidity of the phospholipid bilayer and surface hydrophilicity, both of which are essential to keep the vesicles in the circulation, explain why cryptosomes have such a long lifetime. Another key factor regulating the lifespan of Cryptosomes circulation in vivo is the prevention of macromolecule adsorption on the surface of such vesicles. This adsorption may be hampered by mobile steric hindrances at the lipid surface [2,3].

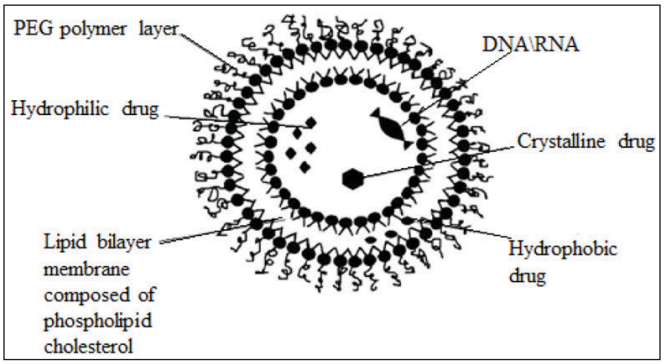

Figure 1: Basic structure of an Aquasome system.

COMPOSITION OF CRYPTOSOMES

Cryptosomes are liposomal compositions that include one or more delivery agents and are built up of poloxamer molecules (polymers) and liposomes. Poloxamer is also known as pluronics. The most often used poloxamers are polyethylene oxide (PEO), polypropylene oxide (PPO), and PEO-triblocks co-polymers of different molecular weights (Figure 2). The hydrophobic Polypropyleneoxide groups in the centre are connected by two hydrophilic polyethylene oxide groups. Polymers having hydrophilic PEO groups on either side of the PPO units may provide steric hindrance and hence protection to the bilayer surface. They may be utilized as emulsifiers and stabilisers as a result of this [4].

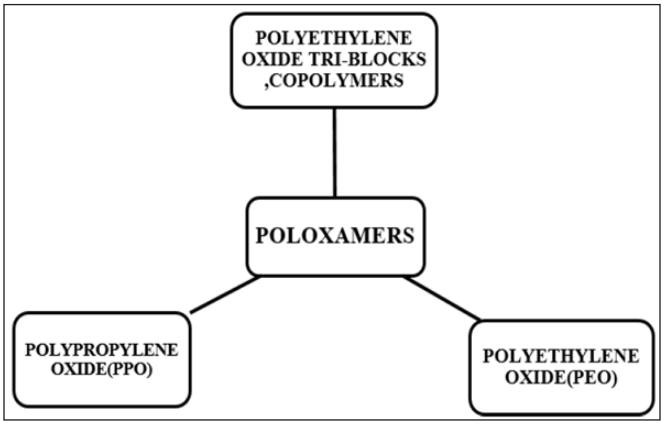

Figure 2: Types of poloxamers.

Cryptosomes are liposomal compositions made up of poloxamer molecules (polymers) and liposomes that incorporate one or more delivery agents. Pluronics is another name for poloxamer. Polyethylene oxide (PEO), polypropylene oxide (PPO), and PEO-triblocks co-polymers of various molecular weights are the most often utilised poloxamers (Figure 2). Two hydrophilic polyethylene oxide groups join the hydrophobic Polypropyleneoxide groups in the centre. Steric hindrance and hence protection of the bilayer surface may be provided by polymers with hydrophilic PEO groups on each side of the PPO units. As a consequence, they may be used as emulsifiers and stabilizers [4].

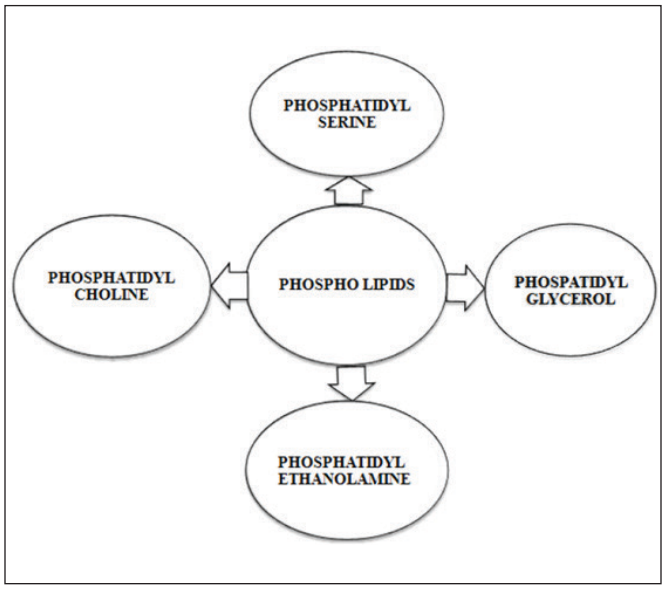

Figure 3: Types of phospholipid.

Cholesterol

Cholesterol, an important component of vesicles, is present. The inclusion of cholesterol boosts the vesicle's stability substantially. Cholesterol composition influences drug trapping in vesicles. As cholesterol levels grow, vesicles' ability to entrap medicines increases. The entrapment efficiency is greatly diminished if the cholesterol concentration is particularly high. This is because the bilayer gets broken once a certain quantity of cholesterol is added, reducing drug entrapment [6].

Lipid core

This material is made up of lipids. Naturally occurring substances include fat, wax, sterols, and fat-soluble vitamins [such as A, D, E, and K]. Lipids are used in immunology, membrane biology, and diagnostics. One or more lipids may be used to make the lipid core. The nature of lipids, which are generally hydrophobic, is defined by their fatty acid content, melting point, and hydrophilic-lipophilic balance (HLB). To provide medications a longer shelf life, lipids with a lower HLB and a higher melting point are used. Lipids with a greater HLB have a faster drug release and better bioavailability [7].

Negatively charged particles

Phosphatidylinositol is a negatively charged phospholipid. Particle aggregation, as well as coalescence, flocculation, and fusion, are all inhibited by negatively charged particles [8].

Phosphatidylcholine

The major component of lecithin is phosphatidylcholine. It has a poor solubility in water. Depending on temperature and hydration, phospholipid in an aqueous medium forms bilayer sheets, micelles, or lamellar structures. This kind of surfactant is classified as amphipathic. It's found in a variety of biological membranes, including egg yolk and soya bean. Depending on where they originate from, egg lecithin and soya lecithin are two distinct forms of lecithin. When lecithin is introduced, the quantity of drug entrapment in the vesicle increases considerably [9].

Surfactants

Surfactants are selected based on their characteristics (HLB). It is used to assess a surfactant's ability to form vesicles. Vesicle production is aided by HLBs in the 4-8 range. The drug's entrapment in the vesicle is affected by the temperature of the surfactant. In the spans with the highest phase transition temperature, drug entrapment is greater. Because of the high phase transition temperature and limited permeability, the drug is leached from the lipid vesicle. High HLB values of span-40 and span-60 result in lower surface free energy, larger vesicles, and hence greater surface area exposed to the dissolving liquid [10].

FORMULATION

Cryptosomes are made up of liposomes and poloxamer molecules. Above the critical micellar temperature, the poloxamer molecules form micelles, and a part of them is injected into the surface of the liposome, blocking their attachment to the cells. Below their critical micellar temperature, poloxamer molecules break down into monomers, enabling the liposome to adhere to surrounding cells and impacting the liposome's capacity to stick to neighboring cells. The targeted release of pharmaceuticals necessitates the incorporation of components into monomers as well as the freezing of the target region, which keeps liposomes at or near the targeted place. Liposomes may be created in a number of methods (Figure 4). To make lipid vesicles, standard procedures like sonication and extrusion may be utilized. They may also be made by reverse-phase evaporation, detergent dialysis, and freeze-thawing. To make Cryptosomes, the poloxamer molecules are incorporated into the liposome at various phases of the liposome formation process [11].

After being treated with poloxamer molecules, the liposomes are implanted in it. Polyethylene glycol and poloxamer or polymer is mostly used to make liposomes stealthy. As a result of this, cryptosomes are generated. PEGs with molecular weights between 1000 and 5000 have a longer circulation and are less absorbed by the mononuclear phagocytic system (MPS). The most often used phospholipid in formulations is phosphatidylcholine, which is the fundamental unit of the plasma membrane, preserves polyphenolics, and possesses both lipophilic and hydrophilic analogues, with the phosphatidyl moiety being lipophilic and the choline moiety being hydrophilic [12].

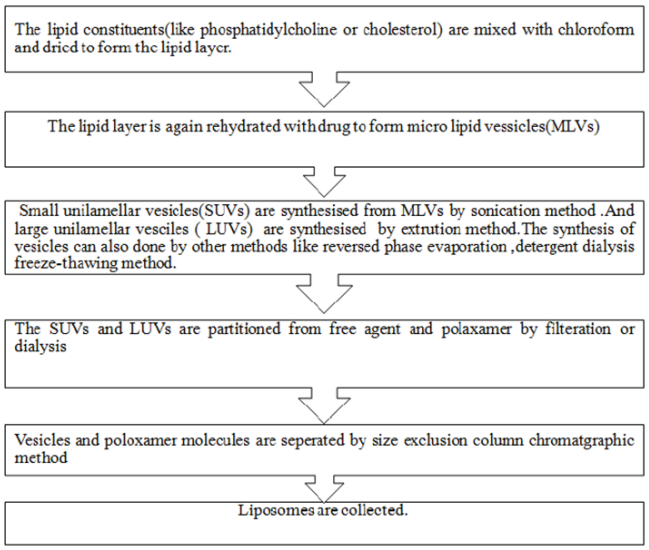

Figure 4: Preparation method.

METHODS OF PREPARATION

Detergent removal technique

To produce the micellar combination, the phospholipid and detergent are combined. Adsorption or column chromatography is then used to remove the detergent from the mixture. The micelle's phospholipid concentration increases, pushing the lipids closer together and forming a single bilayer vesicle [13].

Reversed-phase evaporation

It is divided into two phases. The phospholipid and buffer are used to create a water-in-oil emulsion. After that, the organic layer is separated and removed at a lower pressure. Both the water and the phospholipid layer are emulsified using sonication or other mechanical processes. The organic layer is removed under vacuum as the phospholipid-coated water droplets draw closer, creating a gel-like matrix. Under vacuum, the organic phase is lost even further, resulting in the production of a smooth paste. In this paste, the LUVs are suspended. This method can provide 60-65 percent drug

integration efficiency. As a consequence, it may be used to join together both small and large molecules [14].

Sonication method

In a round bottom flask with varied molar ratios, phosphatidylcholine, cholesterol, and lipids were dissolved in chloroform with 3-4 drops of methanol. The right amount of medicine was weighed and added to the mixture. Using a rotary evaporator, the organic layer was then evaporated until dry in a low-pressure atmosphere. As a result of this process, a lipid coating formed on the borders of the circular bottom container [15].

DRUG RELEASE FROM CRYPTOSOMES

The phospholipid bilayer of cryptosomes mixes with other bilayer membranes (such as cell membranes) to release the liposomal contents. Two mechanisms for doing this are endocytosis and adsorption to the cell surface. During endocytosis, the lipid bilayer fuses with the plasma membrane, enabling the contents to be released. Adsorption to the cell surface causes transfer of liposomal contents [16].

USES AND APPLICATIONS OF CRYPTOSOMES

- Cryptosomes have the potential to carry physiologically active molecules.
- Ciprofloxacin therapy of Klebsiella pneumoniae pneumonia is improved by long-circulating sustained-release liposomes coated with polyethylene glycols (PEG).
- In mouse tumors, Doxil, a liposomal formulation of doxorubicin including polyethylene glycols, outperforms free (unencapsulated) doxorubicin in terms of therapeutic effectiveness, circulation time, and accumulation time (DOX). In malignant effusions, improved drug accumulation is associated to longer liposome longevity.
- It has the potential to be used for drug delivery, tumor imaging, and therapy.
- It has enhanced medicine delivery in solid tumors and breast cancer.
- Cryptosomes are used as a ligand-gated drug delivery mechanism [17].

CONCLUSION

Enhancing dose formulations in order to increase their half-life or duration of action is one of the most challenging problems for scientists. Because of their great stability, longer circulation, increased half-life, and reduced recognition and absorption by macrophages, cryptosomes are one of the most efficient vesicular drug delivery modalities. This is a lipid vesicle with a surface coat that circulates in the blood for a long period after systemic delivery. As a consequence of this approach, drug discovery, development, and use have all grown considerably. They've piqued interest in a range of innovative vesicular drug delivery systems using a phospholipid bilayer and lipid core. Vesicular systems refer to the use of vesicles as carriers or additives in a variety of applications. It may operate as a transporter for substances that are physiologically active. It has been shown to be beneficial in the realms of tumor imaging and therapy. In the future, cryptosome-like vesicles, in concert with other technologies, will play a vital role in innovative drug delivery in diagnostics and targeted medicine administration.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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AUTHOR'S CONTRIBUTION

All authors have equally contributed to this manuscript. All authors did the literature survey from standard databases, collected all essential elements, and wrote this manuscript collectively.

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