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A Review on Liposomes

Ms. Supriya B Chavan[1], Ms. Harshada S Shelke[2], Dr. Nitin M Gawai[3], Rushali S Bedjawalge[4]
B.Pharmacy Department, Mahadev Kanchan College Of Pharmaceutical Education and Research , Uruli Kanchan , Pune , Maharashtra , India

***Abstract:** In the latter part of the 1960s, liposomes sphere-shaped vesicles composed up of one or more membrane bilayers were first identified. In many scientific fields currently, including as mathematics and theoretical physics, biophysics, chemistry, colloid science, biochemistry, and biology, they serve as an immensely helpful reproduction, reagent, and tool. Ever since, liposomes have entered the market. Liposomes are an incredibly successful novel drug delivery system that uses cutting-edge technology to transfer active molecules to the site of action. Currently, a number of formulations of liposomes are being used in clinical settings. Research on liposome technology is moving from traditional vesicles to "second-generation liposomes," which produce long-circulating liposomes by altering the vesicle's size, charge, and lipid composition.[1]*

I. INTRODUCTION

Liposomes have long been regarded as promising options for effective drug delivery and transportation systems. They provide a potential way to deliver therapeutic drugs locally to the site of interest while lowering systemic toxicity because of their vast aqueous interior and biocompatible lipid coating. Chemotherapeutic drugs encapsulating in conventional and sterically stabilised liposomes have been recently developed with improved pharmacological efficacy over free treatments against specific tumour models.

Circulation liposomes can release their contents near cancer cells or be absorbed by the cells if they manage to get to a tumour site. In the latter instance, it seems that the liposome and endosomal membranes must fuse in order for the chemotherapeutic agent to be transported efficiently. appeared to be important for the chemotherapy medicine to move from the liposome to the cell in an effective way.

In order to better design photosensitive liposomes for cell interaction, we are currently studying the uptake of liposomes with cells in tissue culture as part of our investigations on the photoactivated fusion of liposomes [2,3]. The method of liposome elimination by cells and the way liposomes carry drugs are still being understood [4,5,6].

A. The Advantageous Properties of Liposomes

1) If it involves delivering genes to cells, liposomes has numerous of advantage.
2) Both positively and negatively charged substances may develop compounds with liposomes.
3) The DNA is partially insulated from damaging processes by liposomes.
4) Large fragments of DNA, theoretically as large as a chromosome, can be transported by liposomes.
5) Delivering liposomes to individual cells or tissues is available. [7]

B. The Disadvantageous Properties of Liposomes

1) The expense of production is serious.
2) The protected medicine or molecules may leak or fuse.
3) Phospholipids are substances that occasionally experience reactions like oxidation and hydrolysis.
4) Reduced stability, low solubility, and short half-life. [7]

II. LIPOSOMES FUNCTION MECHANISM:

As established in the previous section, liposomes differ from free drug particles in terms of their pharmacokinetics and biodistribution. This may be applied to improve the encapsulated medicine molecules' effectiveness in therapy. Seven categories can be used to group the many benefits of drug-loaded liposomes, which can be used as aerosols, (colloidal) solutions, or in (semi)solid structures like gels and creams:

A. Improved Solubility Of Amphiphilic And Lipophilic Drugs

Additionally, hydrophilic medicines, such the anticancer medicine doxorubicin or acyclovir, are occasionally encapsulated in the liposomal interior at concentrations that are frequently higher than their solubility in water. The drug or gel structure occurring inside the liposome with the proper substances included make this possible.

B. Inactive Drugs Affecting Immune System

Cells contain vaccines, immune modulators, and (immune) suppressors, along with antioxidants, porphyrins, and amphotericin B.

C. Maintained Free System Of Liposomes Provided Locally Or Systemically

Effects contain biological proteins or peptides involving vasopressin, doxorubicin, cortisones, cytosine, or arabinose.

D. Site-avoidance Mechanism

Liposomes reduce cardio-, nephro-, and neuro-toxicity by avoiding the disposal of themselves through specific organs, particularly the heart, kidneys, brain, and nervous system. Amphotericin B's reduced nephrotoxicity and doxorubicin liposomes' reduced cardiotoxicity are two such instances.

E. Precise Targeting of Location

In certain cases, liposomes with surface attached ligands can bind to target cells, or can be delivered into the target tissue by local anatomical conditions such as leaky and badly formed blood vessels, their capillaries and basal lamina. Instances include anti-cancer, anti-disease and anti-provocative drugs.

F. Improved Transfer of Hydrophilic

Electric molecules such as antibiotics, chelators, plasmids and genes, into cells.

G. Improved Penetration Into Tissues, Particularly In The Case Of Dermally Functional Liposomal Dosage Forms

Usually, liposome encapsulation is done carefully when the drugs are very potent, toxic and have very short life times in the blood circulation or at the sites of local (subcutaneous, intramuscular or intrapulmonary) administration.[8,9]

III. LIPOSOMES OF CLASSIFICATIONS

A. Conventionally Created Liposomes

The level liposome-based concept was the first liposome invention to be utilised for use in medicine. The most important natural phospholipids or lipids discovered in conventional liposome formulations are monosialoganglioside, 1,2-distearoryl-sn-glycero-3-phosphatidylcholine (DSPC), egg phosphatidylcholine, and sphingomyelin. [10]

B. Sensitive to pH Liposomes

Cell membranes can effectively bind to many types of liposome substances. When it involves gene transport during in vitro gene transfection, dioleoyl phosphatidyl ethanolamine (DOPE) has long been recognised as the most efficient lipid for cationic liposomes or as a lipid helper in pH-sensitive liposomes. It has been anticipated that phosphatidylethanolamine enhances membrane formation in its native state because this lipid undergoing transformations prior to acidification. After binding to the cell surface and entering into contact with a more acidic pH, liposomes are internalised into endosomes. Endosomes usually have an inside pH of 6.50. Conventional liposomes that are insensitive to pH dissolve as they pass on to lysosomes. Plasmid liposomes must mainly avoid forming up in particular cell divisions, such as lysosomes, following cell penetration. pH-sensitive liposomes showed effectiveness in preventing this. pH-sensitive liposomes were created in reaction to the notion that viruses could attach to the endosomal membrane and pass gene material to the cytosol before accessing the lysosomes. [11]

C. Cationic Liposome

It can frequently basic to introduce cationic lipids inside cells after they have become paired with DNA. Collectives formed by cationic lipids and DNA are thus generated. First, the cationic lipid DOTMA is produced and analysed by the cationic liposomes. To determine the composite properties, cationic lipids mixed with DOPE and varying amounts of three distinct cationic surfactants have been analysed using cryo transmission electron microscopy.

The results of the cryoTEM study show that excessive amounts of charged lipids in collections of aggregated multilamellar forms could cause DNA molecules to become trapped between lamellae. The complexes' structure is not impacted by the inclusion of a surfactant.[12]

D. Immune liposome

Another prospective use in medicine for liposomes is their ability of working as an immunological adjuvant, enhancing the immune response. Antigens that have been reconstituted into liposomal membranes or inserted into the liposome's aqueous core will boost the immune response by triggering macrophage stimulation, generation of antibodies, cytotoxic cell induction, and anticancer activity. Liposomes are useful as immunological adjuvants because they are biodegradable, lower in toxicity, not immunogenic, and may target particular cells in vivo. [13] When considered multiple other possible targeted uses, such as injection in various body cavities, immune liposomes present a viable substitute in immunoassays and diagnostic tests. [14]

E. Long stretching liposomes

The findings indicate that liposomal disposition, including intrahepatic consumption, can be altered, in particular within the mononuclear system of phagocytic (MPS). Both lipids are substituted with synthetic lipids that contain polymers to enable to get the optimum results. The covalent interaction between the phospholipid and polyethylene glycol resulted in prolonged circulation. [15] A reduction in the union and adsorption of blood products, which identify anomalous particles for later macrophage consumption, is linked to the presence of a steric shield. It has recently been established that the Alexander-de-Gennes hypothesis can qualitatively affirm the lifetime of liposomes in living systems. Here is a brief list of all the different kinds of liposomes. [16]

IV. LIPOSOMES STRUCTUREAL COMPONENTS

Liposomes, which are globular lipid bilayers with a size range of 50 to 1,000 nm, serve as excellent delivery vehicles for biologically active substances. In dermatology, liposomes can be applied topically to provide anticancer drugs that decrease toxicity when taken alone or to enhance the half-life of medications and boost their effectiveness. Liposomes can be used to precisely target cells by connecting pertinent amino acid fragments that target specific receptor sites or antibodies, proteins, or other acceptable elements. 6. Both structural and non-structural elements make up liposomes. These are the main component structures of liposomes.

A. Phospholipids

Phosphodiglycerides and sphingolipids are the two forms of phospholipids that are the main structural components of biological coverings. The most typical phospholipid is the phosphatidylcholine (PC) molecule. In order to reduce the toxic contact between the long hydrocarbon fatty chain and the bulk aqueous phase in planar bilayer sheets, phosphatidylcholine particles tightly arrange themselves since they are insoluble in water and aqueous conditions. Most liposome formulations contain glycerols, primarily phospholipids, which make up more than half of the lipid in the membranes. [17, 18].

B. Cholesterol

Cholesterol could exist in membranes in extremely high concentrations without forming a bilayer structure on its own; for illustration, a 1:1 or even 2:1 molar ratio of cholesterol to phosphatidylcholine. With the hydroxyl group towards the aqueous region, cholesterol is situated in the middle of the bilayer of the membrane, similar to the acyl chains. It is uncertain how cholesterol is organised in the bilayer, considering the fact that interactions between hydrophobic and specific head groups have also been linked to improved cholesterol solubility in phospholipid liposomes [19].

V. METHODS OF PREPARATION

A. Thin Film Method

This method of production creates liposomes by hydrating an extremely thin film of lipids in an organic solvent, which is further extracted by a vacuum. Aqueous buffer is used to hydrate the solid lipid mixture once the solvent has been completely fully removed. Lipids hydrate and swell on their own to produce the liposomes. The encapsulation efficiency of this approach is low [22].

B. Reverse Phase Evaporation

This process involves transferring the lipid mixture to a round-bottom flask and using a rotary evaporator for extracting the organic solvent (diethyl ether and isopropyl ether) under low pressure. The used method may achieve excellent encapsulation efficiency (up to 65%) in a low-ionic-strength media, such as 0.01M NaCl. Large macromolecules can be effectively contained using this technique. [20,21,22].

C. Freeze-thaw Technique

The FT methodology includes vortexing the liposomes created by the film method with the solute to be trapped until the entire film is suspended. After that, liposomes are frozen in liquid nitrogen or dry ice-ethanol (-80 ˚C), thawed, and vortexed one more. The cycles of cooling and heating are repeated. This approach is used frequently for for protein encapsulation [22, 23, 24].

D. Ultrasonic Method

SUV liposomes are manufactured using this method of production. Sonication Two types of sonicators are used to disperse phospholipids in water: bath sonicators for large quantities and probe sonicators for very small amounts [22].

E. Calcium-induced Fusion Method

This method is used to create LUV liposomes from phospholipids that are acidic. SUV liposomes are provided with calcium, which causes fusion and the development of multilamellar vesicles. With the addition of EDTA to the preparations, LUV liposomes emerge. The calcium-induced fusion approach has an advantage of encapsulated macromolecules, but it also has the drawback of only being able to generated LUV liposomes from acidic phospholipids [21].

VI. CONCLUSION

Liposomes are shown to be a successful medication delivery method for a number of conditions, include managing pain and cancer treatment. The formation of the biocompatible, biodegradable, and low immunogenicity liposomes improved the pharmacokinetic and pharmacodynamic features of the highly hazardous, water-insoluble, and poorly bioavailable medication. To get beyond their initial weaknesses, liposomes undergo a number of changes in terms of the elements and manufacture method. Several liposomes formulation is now approved in the market to treat various conditions and more than five hundred liposomal formulations are now in different phases of clinical manufacturing.

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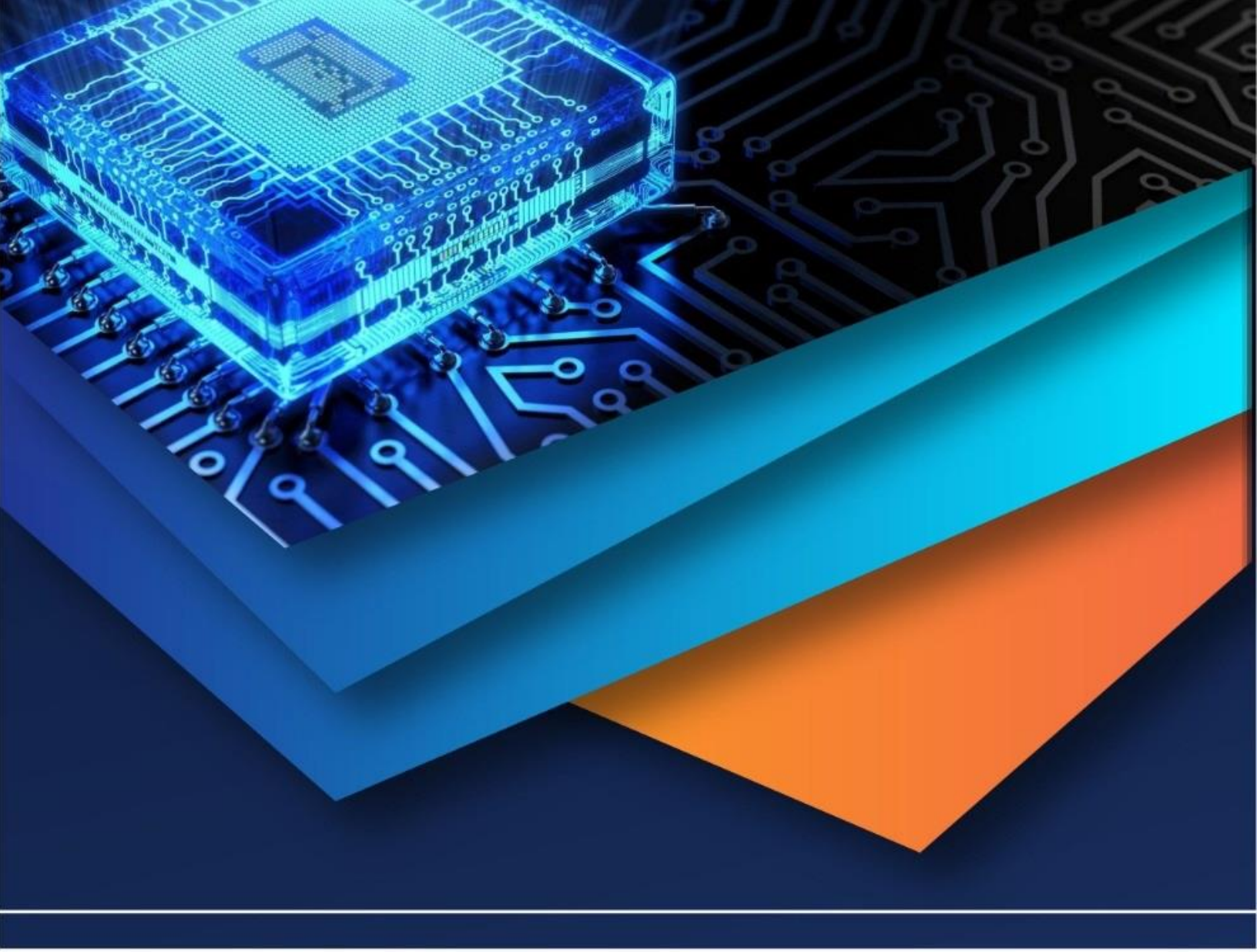

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