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LIPOSOMES AS SMART NANOCARRIERS FOR DELIVERY OF POTENT DRUGS

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ABSTRACT

Liposomes have wide range of applications in pharmaceutical and biotechnology. To eliminate the adverse effects associated with conventional treatments, smart nanostructured materials can deliver medications to the intended site with reduced dosage frequency and in a (spatial/temporal) controlled manner. Topical therapy in dermatology has improved due to liposomal carriers' ability to deliver active agents to the skin. The motivation behind interest in these carriers is their capacity to transport different biological materials to different cell types and to enclose them. These benefits include reduced risk of toxicity and side effects (because of the high topical concentrations of drugs); longer retention of high drug loads at the site of action and controlled drug release, guaranteeing prolonged therapeutic effect; and enhanced protection of drugs from potentially harsh environments at the site of action. They specifically enable overcoming the most important problems with conventional pharmaceutical therapies, including nonspecific distribution, fast clearance, unpredictable drug release, and inadequate bioavailability. Liposomes are nanoparticle drug-delivery systems that can release the drug in response to particular physiological signals, at the right time, and at the right target place. Smart nanoparticles are those that combine all two delivery methods: targeting that is passive targeting and active targeting. In this review paper applications of liposomes are specified and also their role as smart nanoparticles is clearly defined.

Keyword: Liposome, Nanocarrier, Skin, Nanoparticle, Targeted drug delivery

1. INTRODUCTION

The Greek terms "lipo" (meaning their fatty structure) and "soma" (meaning their structure) are the origin of the word "liposome." At the macroscopic level, liposomes are sphere-shaped vesicles made up of one or more phospholipid bilayers that are stabilized by cholesterol and whose aqueous volume is completely surrounded by a lipidic membrane [1]. Because of its structural similarity to the cell membrane, the liposome bilayer interacts with the skin more effectively when applied topically. Because of their diverse forms, liposomes have been studied more than any other system as a carrier system [2]. Liposomes were first described as small, spherical vesicles with phospholipids, cholesterol, non-toxic surfactants, and even membrane proteins, by Bangham and colleagues approximately forty years ago [3]. This group's investigations led to the idea that liposomes, which are known for containing a variety of compounds in their core section, could be used as delivery systems. These structures have the ability to afflictively encapsulate and deliver both hydrophilic and hydrophobic substances [4, 5]. Furthermore, liposomes are an emerging drug delivery carrier system due to their biocompatibility, biodegradability, and lack of potential tissue toxicity when compared to other colloidal carriers. Enhancing liposomal drug formulations' drug loading

and release qualities while optimizing their delivery system may be the best way to create medications for this class of nanoparticle drugs. The drug delivery research community needs to make the most of liposomes because they have a wide range of applications [6, 7]. This will help them develop new drugs that can treat serious illnesses. Drug delivery systems referred to as smart drug delivery systems (SDDSs) have the ability to autonomously send a signal, react, distribute the drug, and stop distributing it. The distribution of the drug in the expected quantity at the anticipated time in the appropriate location is the specific goal of all smart drug delivery methods. The control signals of SDDSs include exterior signals like light of various wavelengths, magnetic fields, electric fields, and ultrasound in addition to interior signals like redox, pH, concentration of particular biomolecules, and enzyme activity. There are various carriers for smart nanoparticles (NPs) such as polymers, hydrogels, liposomes, nanosheets, micelles etc. From conventional tablets and granules to microparticles and nanoparticles, pharmaceutical particles come in a range of sizes and forms [8]. A wide range of biotechnology applications can be achieved through the development of novel methods for creating nano formulations (nanocarriers) for the effective transport of

medicinal molecules. One novel way to use nanomaterials in the size range of 1-100 nm for various reasons, such as the therapeutic management of various diseases, is through the remarkable field of research known as nanotechnology [9, 10].

2. LIPOSOMES AS SMART NANOPARTICLES

Smart NPs play a crucial role in synergism and attenuation by increasing the drug concentration in the target tissues or cells and lowering the drug release in the healthy tissues or cells [11, 12]. Smart NPs exhibit dramatic conformational changes in their physical/chemical properties in response to mild changes in environmental physical and/or chemical signals [13, 14]. To lessen the adverse effects associated with conventional medicines, smart nanostructured materials can deliver medications to the target locations with reduced dosage frequency and in a (spatial/temporal) regulated manner. They specifically enable addressing the most

important problems with conventional pharmaceutical therapies, such as nonspecific distribution, quick elimination, unpredictable drug release, and inadequate bioavailability. A significant reduction in toxicity and/or negative reactions is the overall result [15]. But despite the impressive advancements of recent techniques, the majority of nanocarriers' actions are linked to a number of undesirable side effects that reduce their effectiveness in nanomedicine. Modern smart nanostructured systems can be broadly divided into organic and inorganic nanocarriers, and their physiochemical properties can be tuned by changing their compositions—organic, inorganic, or hybrid dimensions small or large sizes shapes sphere, rod, hyperbranched, multilamellar, or multi-layered structures—and surface characteristics (functional groups, surface charge, PEGylation, coating processes, or attachment of targeting moieties) [16].

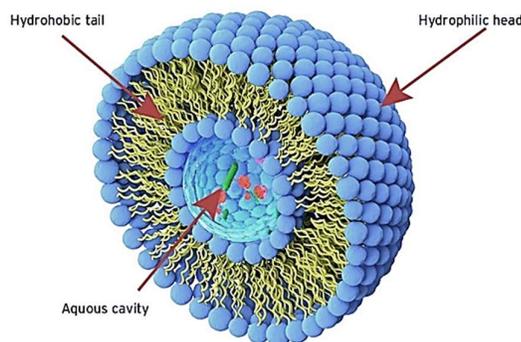


Figure 1: Structure of Liposome

Lipid based NPs

Liposomes constitutes of phospholipid bilayer that assumes as a spherical shaped structure consisting of an aqueous core of 50-1000 nm diameter. Small unilamellar vesicles (SUVs) (20-100nm), large unilamellar vesicles (LUVs) (>100 nm), giant unilamellar vesicles (GUVs), multivesicular vesicles (MVs), and multilamellar vesicles (MLVs) (>500nm) are potential subtypes of bilayers based on the number of layers. Due to its advantages over other NP types, such as their efficiency in production, biocompatibility, and ability to carry molecules of various types, lipid-based nanoparticles (LNPs) are the most frequently used NP type to receive FDA approval [17, 18]. Liposomes are primarily made of cholesterol and a variety of phospholipids, whose chemical composition ultimately determines the liposomal characteristics [19]. Lipid nanoparticles (LNPs) were shown to be preferable to polymeric nanoparticles through the development of nanoparticle-based delivery systems, and they have since been employed extensively for drug delivery. These lipid-based carrier systems are even referred to as "nano safe" carriers because LNPs are made from physiologic and/or biodegradable lipids [20]. Because they can merge with the plasmatic membrane and release the medication inside the cell, they are largely used in the DDS. The qualities that set SLNs

apart from liposomes and polymeric nanoparticles include the feasibility of the preparation processes and scaling-up procedure, the GRAS (generally recognized as safe) status of all formulation ingredients, and the lack of the usage of organic solvents. More easily opsonized and cleared by the reticuloendothelial system are particles less than 100 nm [21]. Furthermore, the amount of drug contained in liposomes is influenced by the size and amount of lipid bilayers. The four types of lipids nanocarriers are liposomes, niosomes, SLNs, and NLCs. The drawbacks of the conventional colloidal carrier systems, such as liposomes, niosomes, nanoemulsions, and polymeric nanoparticles, are overcome by SLNs and NLCs [22, 23]. Lipid nanoparticles enhances the solubility, bioavailability, intestinal absorption, pharmacokinetic parameters, skin permeation, and ocular residence time of drugs along with reduced side effects. It is possible to divide the lipid particle drug delivery system into SLNs and NLCs. According to reports, with low drug loading, SLNs release drugs more slowly than NLCs. However, with high drug loading, there is no noticeable difference in the drug release from SLNs and NLCs. At 25 °C, NLCs are more stable than SLNs [24].

3. SKIN DELIVERY MECHANISM OF LIPOSOMES

There are two main strategies by which liposomes target skin i.e., active targeting and passive targeting. These help to improve therapeutic efficacy of drug. The field of oncology has been the primary application of passive targeting approaches because of the pathophysiological characteristics of cancers and their surroundings. Liposomes are passively targeted to specific tissues or cells by transporting them into the tumour interstitium through leaky tumour vasculature using molecular drive-in fluids. The development of a liposomal formulation for passive targeting entails avoiding their quick removal by organism defence mechanisms like phagocytic uptake or clearance by MPS cells. Targeting solely on the basis of the EPR effect is insufficient to completely mitigate the side effects of cytotoxic medications. The effectiveness of medications administered passively can also be impacted by the heterogeneity of the EPR effect within tumours and their restriction to specific solid tumours. On the other hand, active targeting entails attaching a targeting ligand to the liposome surface in order to improve liposomal system delivery [25, 26]. A wide range of targeting ligands, including peptides, small molecules like vitamins, nucleic acids (aptamers), whole proteins like

transferrin, and antibodies, have been used for active targeting. The relative degree of overexpression or selective expression on the target, target cell uptake of the ligand-targeted formulation, and degree of covering of the target molecule are some of the factors taken into consideration when choosing target ligands. There exist three primary methods for functionalizing liposomes. The first step in the preparation of liposomes is attaching the target ligand to a lipid before combining it with other lipid components [27].

In the second method, the necessary targeting ligand is added to liposomes right after they are prepared. Options for this strategy include head group modified lipids with a PEG spacer functionalized at the end with amine, carboxylic acid, thiol, or maleimide groups. A different approach suggested inserting the functionalized lipid into liposomes that had already been formed. The foundation of this technique is the spontaneous integration of drug-loaded liposomes and even preformed liposomes with functionalized lipids from the micellar phase. To avoid activated lipids interfering with other liposomal components, like those in the buffer, derivatization of the targeting molecule takes place in a separate step.

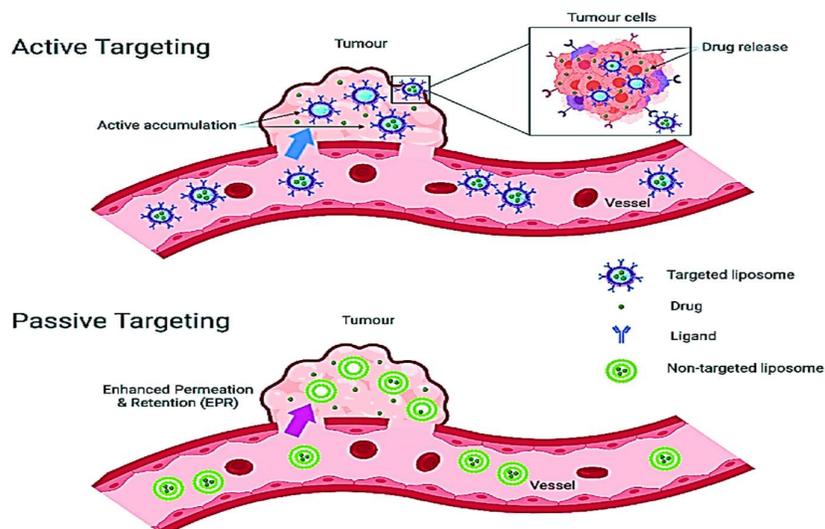


Figure 2: Schematic Representation of Active and Passive Transportation of Liposomes

4. APPLICATIONS OF LIPID BASED NPS

In cosmeceuticals:

A category of cosmetic items termed as cosmeceuticals serves as a connection between cosmetic and pharmaceutical products. It is a rapidly expanding segment of the cosmetics industry, especially in light of the introduction of cutting-edge formulation and production methods like lipid nanoparticles (LNPs). LNPs-based cosmeceutical products provide a number of benefits, including enhanced visual appeal, stability of the finished products, and increased bioavailability of the cosmeceutical active ingredients (CAIs). Among the suggested technologies for developing unique, secure, potent, and elegant cosmeceuticals, cosmetic nanotechnology is emerging as a standout [28]. Due to their small size, nanoparticles can be absorbed onto the skin and supply the

active ingredient to mend the skin's damaged areas, increasing the effectiveness of the treatment. Lipid nanoparticles adhere well to the skin when they come into contact with it. This characteristic results from a reduction in the surface free energy caused by the adsorption of these particles on a skin, which directly lowers the thermodynamic driving force of the resulting system. Liposomes have been proved to show good adherence effects. Liposomes are known to have excellent skin permeation properties. Different bleaching agents have issues with poor water solubility, poor stability, or inadequate skin penetration. To address the aforementioned issues, various research teams have created whitening agents enclosed in lipidic nanoparticles [29, 30].

- Different issues with topical application affect the many chemicals that are utilized as antioxidants or anti-aging. They might have weak stability, poor

skin penetration, or low water solubility. The above difficulties might be overcome by encapsulating these compounds in various kinds of lipid nanoparticles.

- Isotretinoin is most commonly used agent for the treatment of acne, but its topical application can lead to various problems such as erythema, skin peeling, and skin irritation. Employing the formulation by design (FbD) method, solid nanoparticles containing isotretinoin have been formulated, which overcame the side effects associated with conventional method of drug delivery.
- The application of sunscreen products is actually recommended by numerous health organizations to protect the skin from harm or sunburns. Different kinds of chemical UV filters, such as octyl methoxycinnamate (OMC), zinc oxide, and titanium dioxide, are employed as sunscreen protectors. They might, however, result in some skin allergies or rashes [31]. Therefore, these compounds could have less adverse effects and less photodegradation if they were encapsulated in lipid nanoparticles.

In CNS Disorders:

Numerous nanotechnological techniques are used to aid drug transport over the BBB since the BBB hinders the access of

pharmacological compounds to the brain. Among these methods, NLC stands out as a promising carrier system that, in part, because of its reduced size, biocompatible lipodic structure, and high drug loading capacity, claims to increase the drug concentration in the brain. Additionally, it promotes medication absorption through the blood-brain barrier (BBB) using a variety of transport modes, such as passive diffusion via paracellular and transcellular pathways and active diffusion via receptor- and carrier-mediated transport [32].

Alzheimer's disease is a chronic neurological disorder, a reason for dementia. It is commonly seen in older age usually after 65 years of age. In previous research, various unique approaches for efficient brain targeting of bioactive for the treatment of AD, including liposome-based systems, nanoparticle-based carrier systems, and novel carriers via direct nose-to-brain administration. Pioglitazone-loaded NLC was developed for nose to brain drug delivery. In comparison to the prior drug solution, the prepared NLV demonstrated superior drug penetration and sustained drug administration. Nasal epithelial toxicity was remarkably low. The entire study provides successful preclinical evidence supporting pioglitazone's role in the treatment of Alzheimer's disease [33].

Targeted drug delivery:

LNPs that have been drug-loaded have been applied to other drug delivery systems. To combat tuberculosis, one of the main causes of death worldwide, a mucoadhesive chitosan-incorporated, rifampicin-loaded LNPs system was created. The chitosan-incorporated LNPs showed improved cellular uptake and mucoadhesive strength with mucin, indicating a viable delivery strategy for drugs that are aimed for the lungs [34, 35].

Ocular drug delivery:

The intracameral injection is a technique of administering medication directly to the eye's anterior chamber, although it is sometimes limited by the need to administer general anaesthesia first and the risk of damaging intraocular structures [36-42]. Lipid nanoparticles provide a number of advantages, including modified release, enhanced absorption, high stability, minimal degradation, in vivo compatibility, and adaptability to different delivery methods [43-47]. Lipid nanoparticles have many advantages over polymeric nanoparticles, including modified release, high stability, minimal lipid decomposition, in vivo tolerability, and flexibility to varied delivery systems, making them an effective drug delivery vehicle in a variety of delivery systems. In comparison to other colloidal carriers, SLNs have demonstrated a number of advantages, including modified drug release, site-specific drug delivery, long-

term stability, high entrapment efficiency, biocompatibility, sterilizability, formulation as self-administering eye drops, ease of scale-up, and simple production procedures. The ability to administer these nanocarriers via parenteral, peroral, transdermal, pulmonary, nasal, ophthalmic, rectal, and vaginal routes has proved to have great potential [36, 48].

6. CONCLUSION

Nanotechnology offers a completely new concept and fresh approaches in numerous disciplines of contemporary science and medicine, with a particular focus on nanomedicine. Because they are governed by physical principles that fall between classical and quantum physics, NPs' small size confers upon them special features. The liposome project is crucial in this situation since the material, size, shape, and functionalization all need to be selected and optimized in order to accomplish the desired goal. The basic goal of effective liposomal delivery systems is to prevent drug from degradation from external environment, lower drug dose required to provide a particular therapeutic effect, hence lowering costs and minimizing adverse effects. Liposomes has also shown remarkable applications in various field.

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