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Liposomes- A Nanocarrier System for Pulmonary Infection

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ABSTRACT: This review studied the efficacy of liposomal dry powder inhalation for pulmonary infections. The lungs are primary organ of pulmonary system in human and most other animals The lung infection caused by various bacterias, viruses and fungus. The pneumonia is major pulmonary infection caused by some bacterias like *Streptococcus pneumoniae, Staphylococcus aureus*, *Bacillus subtilis*, *E. coli*, etc. The antibiotics can be administered orally, intravenously, or in other ways. On their approach to the infection site and the disease, they travel through numerous layers of tissue. Drugs can fail to perform as intended because of diverse metabolic breakdown. Because they include both hydrophilic and hydrophobic antibiotics, liposomes are amphiphilic. The Liposomes have better features than conventional drug delivery methods, including site-targeting, sustained and regulated release, protection of the drug against degradation and removal, then superior therapeutic effectiveness, and fewer harmful side effects. The size, integrity, and number of charges of liposomes are just a few of the variables that affect their stability. Several polymers are used to prevent liposome leaking.

Keywords: Antibacterial, drug delivery system, nanoliposomes, pulmonary system, vesicles.

INTRODUCTION

The bacterias causes various diseases. The Streptococcus, staphylococcus, classes bacteria are causes major diseases, for treat this bacterial infection antibiotics drugs are taken. way (Chennakesavulu *et al.,* 2018). This antibiotic drug are taken by various route like oral, Intravenous route, etc. The antibacterial drug treat bacterial infection by various mechanism like inhibition of nucleic acid synthesis, inhibition of protein synthesis, alterations in cell wall synthesis, etc. (Mishra *et al.,* 2018).

In recent days the antibiotic drug are deliver via the advance delivery system which is liposomes. The liposomes are tiny vesicles made up from the one or more phospholipid layers. Scientists at the Babraham Institute in Cambridge, led by British haematologist Dr. Alec D. Bangham FRS, originally described liposomes in 1961 (published in 1964) (Alexandre *et al.,* 2013). Abangham and R. W. Horne made the discovery while experimenting with the Institute's brand-new electron microscope by mixing negative stain with dried phospholipid. The similarities to the plasmalemma were evident, and this image from a microscope provides the first concrete proof that cell membranes had a bilayer lipid structure (Wu *et al.,* 2020). Liposomes are derived from the Greek words "lipo" and "soma," which both refer to lipo means fat and soma means body (i.e. bodily fat). The Phospholipids, which are molecules with a hydrophilic head and a hydrophobic tail, which form the membrane of liposomes.

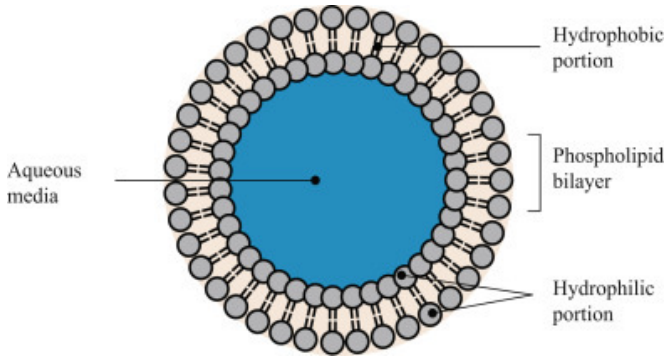

Fig. 1. Structure of liposomes.

Water is drawn to the hydrophilic head group and repelled by the hydrophobic tail group, which is composed of a long hydrocarbon chain (Shashi *et al.,* 2012).

STRUCTURAL COMPONENTS

The liposomes are made up from various components like phospholipid, sphingolipid, sterols, synthetic phospholipid, polymeric material, polymer bearing lipids, cationics lipids and other substances. The ingredients improve drug entrapment and stabilise liposomes (Skwarczynski *et al.,* 2022). Fig.1 shows the structure of liposomes.

1) Phospholipid

e.g. Phosphatidyl glycerol and phosphatidyl choline (Lecithin) (Holmes *et al.,* 2016).

2) Sphingolipid

e.g. Sphingomyelin (Nainu *et al.,* 2021).

3) Sterol

Liposomes frequently contain cholesterol and there derivatives to reduce the fluidity of the bilayer (Canaparo *et al.,* 2019).

4) Examples of synthetic materials

Distearoyl phosphatidyl choline (DSPC), also known as dipalmitoyl phosphatidyl choline (DPPC), (Holmes *et al.,* 2016).

5) Polymeric materials, such as those containing conjugated diene, methacrylate, and other lipids that can be polymerized. Moreover, several polymerisable surfactants are created (Prasad *et al.,* 2006).
6) Lipid-containing polymers

For instance, the PEG polymer is connected to the diacyl phosphatidyl ethanolamine (DPE) by a carbon at or succinate bond (El-Nesr *et al.,* 2010).

7) Cationic lipids, such as DODAB/C (dioctadecyl dimethyl ammonium chloride), Eight)
8) Other Drugs different polyglycerol and polyethoxylated mono and dialkyl amphiphiles that are mostly employed in cosmetic preparations (Feng *et al.,* 2004).

Advantages

1) Biodegradable and biocompatible liposomes are available.
2) They are not immunogenic or harmful.

They distributed the hydrophilic, hydrophobic, and amphipathic medications.

4) Liposomes shield the medicine from the environment outside (Fan *et al.,* 2013).

Disadvantages

1) Production costs is high.
2) The encapsulated drug leakage is possible.
3) Short half-life (Misra *et al.,* 2009).

Liposome classification

Liposomes are categorised on the basis of

A) Structural Characteristics

1) Unilamellar vesicles
2) Oligolamellar vesicles /(OLV)
3. Multilamellar vesicles/ (MLC) (Holmes *et al.,* 2016)

B) Depending on the preparation procedure

1) REV-Single or oligolamellar vesicles, produced using techniques for reverse phase evaporation
2) MLV-REV: Multilamellar vesicles are produced using the reverse phase evaporation technique.
3) Stable Plurilamellar Vesicles (SPLV)
4) Frozen and thawed MLV (FATMLV)
5) VET: Vesicles made via the extrusion method
6) DRV: The dehydration-rehydration technique. (Meenach *et al.,* 2013).

C) Depending on application and composition

1) Conventional liposomes
2) Fusogenic liposomes
3) Cationic liposomes (Moeller *et al.,* 2008).

Bacterial pulmonary infection

The pulmonary system is susceptible to numerous infections brought on by bacteria, including bacterial pneumonia. bacteria including *Staphylococcus aureus*, *Streptococcus pneumoniae, E. coli,* and *H. influenza*, among others (Moeller *et al.,* 2008). The three ways that germs enter the lung are as follows:

1) Via the tracheobronchial tree, where it most frequently occurs as a result of inhaling droplets from an infected person (Yadav *et al.,* 2017).
2) Direct injection via pulmonary vas culture. (Kapoor *et al.,* 2017).
3) The infection in the mediastinum, chest wall, and upper abdomen can also spread directly. (Kapoor *et al.,* 2017).

The lungs become infected with dangerous microorganisms when this happens. Therefore, air sacs swell up. (Kapoor *et al.,* 2017).

Current treatment of pulmonary bacterial infection

The infection of the lungs is treated with a variety of drugs, including antibiotics and fever-reducers. Nowadays, targeted drug delivery systems like nanoparticles, liposomes, microspheres, ethosomes, etc. are used to treat a variety of ailments (Chalmers *et al.,* 2012). This customised drug delivery system carries the medication to the desired or infected spot, avoiding unwanted or harmful effects, and enhancing the therapeutic benefit (Chalmers, e*t al.,* 2012). The vesicle-shaped structures known as liposomes are comprised of phospholipids, cholesterol, and other polymers. They are a type of targeted drug delivery system that reduces the toxicity of the medicine to other tissues while delivering the drug to the infection site, or the targeted site. These liposomes are improving the therapeutic effects and bioavailability of the medicine (Bassetti *et al.,* 2020).

Pharmaceutical development of liposomal formulation

One of the effective drug delivery systems using nanotechnology to target infection locations, reduce the toxicities of conventional medications, and enhance therapeutic efficacy is liposomes (Zhan *et al.,* (2018). Since the first doxorubicin-loaded liposome hit the market a decade ago, numerous studies have been conducted to create novel liposomal formulations, giving rise to a number of commercial goods. The aqueous core or lipid bilayers of liposomes are used to encapsulate therapeutic medicines, the majority of which are anti-cancer medications, to improve their transport to the targeted area and boost their effectiveness (Drulis-Kawa

et al., 2010). Many liposomal formulations, including Lipoplatin (cisplatin-loaded long circulating liposomes), EndoTAG-1 (paclitaxel-loaded cationic liposomes), and Stimuvax (cancer vaccine), have demonstrated good therapeutic benefit in clinical tests. New designs, such as ecologically friendly liposomes, drug-combination liposomes, and liposomal vaccines, are currently being investigated in clinical studies (Drulis-Kawa *et al.,* 2010).

Mechanism of action of liposomes

A area of aqueous solution enclosed in a hydrophobic membrane makes up the liposome. Due to the ease with which hydrophobic substances can be dissolved into lipid membranes, both hydrophilic and hydrophobic molecules can be transported via liposomes (Drulis-Kawa *et al.,* 2010). Although the drug's physiochemical properties and lipid composition will determine the drug's location and extent. The lipid bilayers fuse with other bilayers of the cell (i.e., the cell membrane) to release the liposomal content or liposomal drug, allowing for the transport of essential drug molecules to the targeted sites.

The lipid bilayer protects the drug molecules from the body's aqueous environment after they are implanted into the liposome's aqueous core. The liposomes' internal drug content is released as the bilayer deteriorates over time (Chennakesavulu *et al.,* 2018).

Steps involved in mechanism of action of liposomes drug delivery:

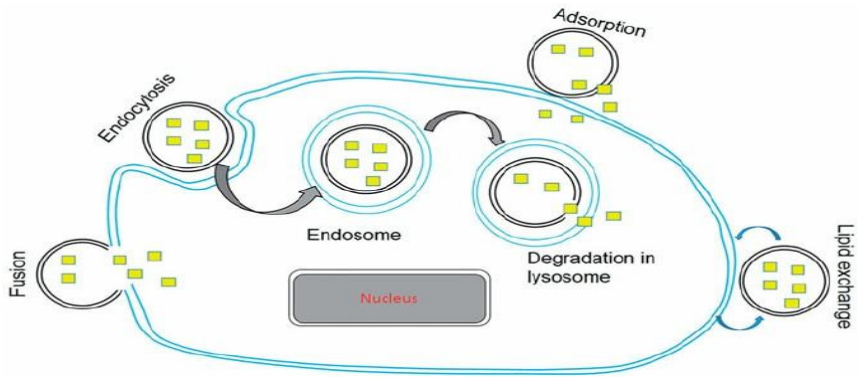

Fig. 2. Mechanism of action of liposomes.

1. Adsorption: Liposomes come into touch with cell membranes by their adsorption to them. It starts to leak and the medicine comes out. This increases the drug concentration near the cell membrane and makes it easier for the drug to be taken up by the cell by passive diffusion or transport (Chennakesavulu *et al.,* 2018).

2. Endocytosis: The process by which liposomes adhere to the cell membrane surface before being engulfed and internalised into the liposomes. Liposomes are delivered to the lysosomes by endosomes. The medication that was trapped in the lipids is released into the cytoplasm as a result of the lysosomal enzymes degrading the lipids (Chennakesavulu *et al.,* 2018).

3. Fusion: Direct distribution of the contents of the liposomes occurs when their lipid bilayers fuse with the lipoidal cell membrane through lateral diffusion and lipid mixing or drug in cytoplasm (Shirley *et al.,* 2019).

4. Lipid exchange: Lipid transfer proteins in the cell membrane readily recognise liposomes and initiate lipid exchange as a result of the liposomal lipid membrane's similarity to the phospholipids of the cell membrane. Liposomal membranes deteriorate as a result, and medication contents are released intracellularly (Schreier *et al.,* 1993). Fig. 2's illustration of the liposomes' mechanism of action.

Lungs targeting

• The liposomal drug carrier decreases drug exposure to normal cells while enabling delivery of a large fraction of the drug to the desired site of action. To obtain a secure and effective drug therapy under disease conditions, it is possible to target pharmaceuticals actively or passively by encasing them in liposomal vesicles (Ding *et al.,* 2006).

1) Cellular targeting in lungs

The therapeutic goal in the management of infectious, immunologic, genetic, and neoplastic disorders is the cellular targeting of drugs. Depending on the type of cells involved, there are two main methods for cellular targeting which are as follows:

i) Alveolar macrophages are an example of phagocytic cells

ii) nonphagocytic cells such as pulmonary epithelial cells (Ding *et al.,* 2006).

2) Targeting to alveolar macrophages

The diseased or immunologically compromised macrophage becomes a natural target for liposomes due to the reticuloendothelial system's (RES) which is highly efficient clearance of the liposomes (Han *et al.,* 2014).

3) Targeting to pulmonary epithelial cell

The Liposomes' more difficult purpose of targeting nonphagocytic pulmonary epithelial cells necessitates membrane modification. The ability of the liposome to bind to and deliver its content into the cytosol of epithelial cells allows it to do so selectively. A tailored formulation with dramatically increased or improved efficacy that can penetrate the respiratory epithelial ceiling (Han *et al.,* 2014).

Evaluation

Following the creation of liposomes, the following evaluation techniques were used (Schreier *et al.,* 1993).

1) Size of liposomes and Size Distribution

When liposomes are employed for pulmonary medication administration, size and size distribution are the key factors. The variety of techniques, including optical microscopy, scanning electron microscopy, the laser light scattering method, and photon correlation spectroscopy are used for particle size determination (Schreier *et al.,* 1993).

2). Percent Drug Encapsulation

The percentage of drug encapsulation determines how much of the drug is contained within the vesicles of liposomes. The medication is both free and encapsulated in the liposomal formulation. entrapped (He *et al.,* 2019).

3) Surface charge

The free-flow electrophoresis and zeta potential define the surface charge of liposomes (Riaz *et al.,* 1995).

4) Vesicle shape and lamellarity

The form of the liposomal vesicles can be determined using a variety of electron microscopy techniques. The number of bilayers a liposome has determines its lamellarity. Freeze-fracture electron microscopy and 31P-Nuclear magnetic resonance studies also used to determine it (Riaz *et al.,* 1995).

5) Stability of Liposomes

The produced formulation's stability is a crucial consideration while formulating liposomal products. The liposome formulation's stability throughout the preparation or formulation process, storage, and delivery is correlated with the medicinal substance's therapeutic effect (Riaz *et al.,* 1995).

CONCLUSION

The liposomes are nanocarrier system which carry the encapsulated drug safely and effectively. Due to this system metabolic degradation of drug is avoids. The antibacterial drugs are encapsulate into the liposomes due to this bioavailability and drug retention time in blood is increase. The evaluation tests confirmed that the medication delivery method using carrier-based liposomes for treating pulmonary infections resulted in prolonged drug retention at the desired region and also decreased the systemic exposure. It increase the therapeutic index, decrease systemic adverse effects, lower dosage and frequency, and also reduce the cost of therapy. This work shows the liposomes can improve the treatment of the disease and prevent the emergence of drug resistance. However, research on at least two animal species, followed by clinical trials, are necessary to determine the function of liposomal formulations in the treatment of lung infection.

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