Liposomes - properties and bursting

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Introduction

Liposomes are synthetically constructed phospholipid vesicles that consist of at least one phospholipid bilayer. These are obtained by methods based on lipid diffusion in water.

Because of their characteristic bilayered structure, liposomes have the ability to cross cell membranes and therefore, can be used as a means of transport for the administration of nutrients as well as certain types of drugs. Upon reaching a specific pre-determined site within the body, the liposomes can burst or be broken down to release potentially lifesaving drugs.

The name liposome is derived from two Greek words: 'Lipos' meaning fat and 'Soma' meaning body. Liposomal vesicles are made up of a lipid bilayer surrounding the inner volume, that contains an aqueous solution. The vesicle membrane allows water to be exchanged between the outer and inner parts of the liposome. As the liposome is of enormous theoretical interest, being based around the simplest figure of a biological cell, they also play an important role in drug delivery.

Why Liposomes are Important in Clinical Medicine

Currently, clinical medicine contains a vast range of drug molecules in use, and the clinical usefulness of most of these therapeutics is limited by the inability of these drugs to reach their target tissues or by the harmful effects that are caused on healthy tissues and organs. Although various approaches have been tried to surmount these problems by attempting to create site-specific drugs that incorporate the idea of “selective delivery”; the real idyllic solution would be to create medication that targets only those cells or tissues that are affected by disease (1).

The study of liposomes has been particularly fascinating in the field of drug delivery and the reason lies in the liposomes’ characteristic properties, which makes them both biocompatible as well as biodegradable. The structure of a liposome consists of an aqueous core encapsulated by one or several bilayers that are composed of either natural or synthetic phospholipids. Liposomes that are composed of naturally occurring phospholipids are biologically unreactive and indistinguishably immunogenic, and possess a low intrinsic toxicity. As a result of this, drugs with different lipophilicities can be entrapped into liposomes - strongly lipophilic drugs are incorporated almost completely into the lipid bilayer, whereas strongly hydrophilic drugs are incorporated completely in the aqueous interior (2).

Literature Relating to the Properties of Liposomes

Type of Liposome	Size of Liposome	Number of Layers
Small Unilamellar Vesicles	20nm - 100nm	Single
Large Unilamellar Vesicles	100nm - 400nm	Single
Giant Unilamellar Vesicles	1µm and larger	Single
Large Multilamellar Vesicles	200nm - 3µm	Multiple
Multivesicular Vesicles	200nm - 3µm	Multiple

Table 1 shows the classification of different liposomes (3)

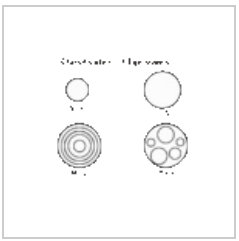

Diagram 1 shows a visual representation of the different classifications of liposomes.

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Advantages of the Use of Liposomes	Disadvantages of the Use of Liposomes
Liposomes are biocompatible, biodegradable, not toxic, supple, and non-immunogenic	Liposomes and encapsulated drugs are costly to produce
Liposomes have both a lipophilic and lipophobic environment. Therefore these are useful for delivering hydrophobic and hydrophilic drugs	Liposomes may have accidental leakage and may lead to the fusion of the encapsulated drugs
Liposomes have layers that can encapsulate a drug and serve to protect the drug from the environment as well as act as a slow release mechanism. This encapsulation also helps to protect sensitive areas from the drug as well	The liposome phospholipid may undergo oxidation and hydrolysis which will lead to degradation of the liposomal structure
Liposomes are versatile in the form which they may be delivered. These forms include suspension, cream, and powder which can then be given through most traditional routes of medicinal administration	Liposomes have a short half-life
Liposomes assist with active targeting as they have flexibility in binding with site-specific ligands	Liposomes have a low solubility in water

Table 2 shows the advantages and disadvantages in the use of liposomes (4)

Bursting

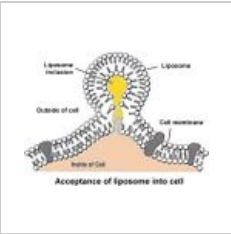
The bursting of liposomes can be referred or described like the bursting of soap bubbles in air. This action will be accomplished within tens of milliseconds independently of the size of the liposomes; and in what was observed in some rare cases, the liposome membrane changes or fluxes immediately before the burst. The liposomal burst happens when the liposomes are made of mixed phospholipids holding an inhomogeneous acyl chain. The acyl chain length of lipid molecules is known as one of the aspects that controls or affects membrane fluidity, which makes membrane fluidity a strong factor in the bursting of liposomes.

The burst happens depending on the membrane elasticity and depends on the inner concentration of the liposomes. Bursting of liposomes is the outcome or formation of pores. This will create stress of the membrane and in addition to this will increase the exposure of the hydrophobic membrane or the lipid tail to water. Therefore, when the pore appears, the internal matter or substance of the organelle will start to leak out, which in turn leads to decrease the membrane tension.

Liposomes Delivery System

Liposomes can enclose water-soluble drugs in their aqueous spaces and lipid-soluble drugs within their membrane. Liposomes let off their contents by interacting with cells in one of four ways:

1. Adsorption: To gather a liquid or dissolved substance on the surface in a condensed layer
2. Endocytosis: The transport of solid matter or liquids into a cell by means of a coated vesicle
3. Lipid Exchange: The exchange of lipid molecules between a vesicle's bilayer in water and a nanolayer
4. Fusion: The process of joining two or more things together to form a single entity



Liposome-entrapped drugs are divided within the body in a different way than free drugs. In most living organisms, vesicles accumulate in the liver, spleen, lung, bone marrow and lymph nodes when they are injected. This is unlike liposomes, which accumulate at the sites of inflammation and infection and in some solid tumors.

Prospects in the Use of Liposomes

New research in the field of liposomes has allowed liposomes the ability to avoid detection by the immune system. These are now known as stealth liposomes.

Liposomes can have various molecules attached to their surface. The most common surface modification is PEGylation; in which the polymer polyethylene glycol is covalently linked to the surface of a liposome. Small PEGylated liposomes have a longer circulatory life in the bloodstream than plain liposomes as the PEG coating is unreactive in the body.

In addition to the PEG, stealth liposomes may also have a biological species attached to them, thus allowing site-specific drug delivery. One such example could be antibodies, which can then be attached to these liposomes for targeting purposes. Many studies now show that targeting is more effective if the antibody is attached to a spacer (like PEG) rather than directly to the liposome surface. Another advantage of this is that naturally toxic drugs may be less toxic if they are delivered only to the sites of disease (5).

Conclusion

In conclusion, the studies into the properties and further uses of liposomes will continue to grow. As more advances are made into the use of liposomes as drug carriers, we will slowly but surely begin to see the use of this method of drug delivery to target even the most difficult of diseases. There is research into the use of liposomes in the treatment of tumours as well as the possibility of using liposomes containing positively charged lipids (such as the DOTAP liposome) as transport vehicles for negatively charged DNA and RNA through electrostatic interactions in the form of lipoplexes to cells both in vitro and in vivo.

The way in which liposomes enclose drugs represents a new drug delivery system that appears to offer important, therapeutic advantages over pre-existing methods of drug delivery.

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