Liposomes And Lipid Nanoparticles As Delivery Vehicles For Personalized Medicine

WHAT ARE LIPOSOMES, AND HOW ARE THEY USED IN DRUG DELIVERY?

Liposomes are specialized delivery vehicles that serve two main roles in enhancing the capabilities of active pharmaceutical ingredients (APIs). First, they can shield a drug from detection by the body's immune system, mimicking biological membranes and giving the drug more time to reach its intended destination. Second, they serve to help solubilize highly lipophilic drug molecules or modulate the distribution of the API throughout the body – minimizing side effects and enhancing the product safety profile.

Liposomes possess a unique vesicular structure, composed of a lipid bilayer that forms in the shape of a hollow sphere encompassing an aqueous phase. As such, any "cargo" of interest can be encapsulated within either the aqueous compartment (if it is water-soluble/hydrophilic) or within the lipid bilayer (if fat-soluble/lipophilic).

Some of the primary lipids used to make liposomes are phospholipids and sphingolipids. These two categories of lipids are unique in terms of a head group that is water-loving/hydrophilic and a tail group that is water-hating/lipophilic. Due to their amphiphilic nature, these molecules spontaneously self-assemble to form liposomes and other unique 3D structures when added to aqueous solutions. The shape or morphology of the 3D structures is dependent on a variety of different factors – for example, lipid composition, temperature, pH or the presence of other buffers, salts and sugars in the water.

HOW DOES A DRUG INTERACT WITH THE BODY AND BECOME AVAILABLE FOR USE WHEN IT IS FORMULATED AS A LIPOSOMAL DRUG PRODUCT?

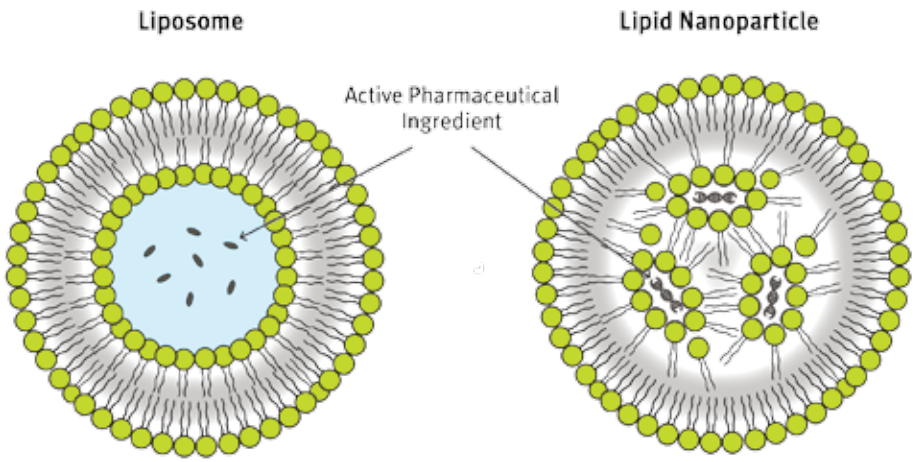
In recent years, liposomes have attracted significant attention as a trusted class of drug delivery vehicles. Their self-closed structures can encapsulate multiple drugs at once, protecting enclosed cargo from hydrolysis and breakdown. Additionally, targeting proteins and surface functional ligands on the outer shell of the lipid bilayer can add novel functionality – enabling targeted entry of liposomes into cells, either via antibodies or receptor-targeted ligands.

Typically, liposomes are manufactured as sterile injectables for delivery to the bloodstream, and release of the drug takes place when lipid envelopes break down – which can happen in extracellular or intracellular environments. Various strategies have been employed to design conventional liposomes with triggered-release capabilities, causing the liposomes to release the encapsulated API or "cargo" based on a stimulus response.

Formulations geared for release in intracellular environments can include pH-sensitive lipids that change the liposomal structure or degrade within acidic compartments, enabling the release of the encapsulated drug. Alternatively, thermosensitive or photosensitive components are sometimes included to enable breakdown and structure modulation due to changes in temperature or reaction to light of certain wavelengths.

LIPOSOMES VERSUS LIPID NANOPARTICLES

Liposomes and lipid nanoparticles (LNPs) are similar by design, but slightly different in composition and function. Both are lipid nanoformulations and excellent drug delivery vehicles, transporting "cargo" of interest within a protective, outer layer of lipids. In application, however, LNPs can take a variety of forms.

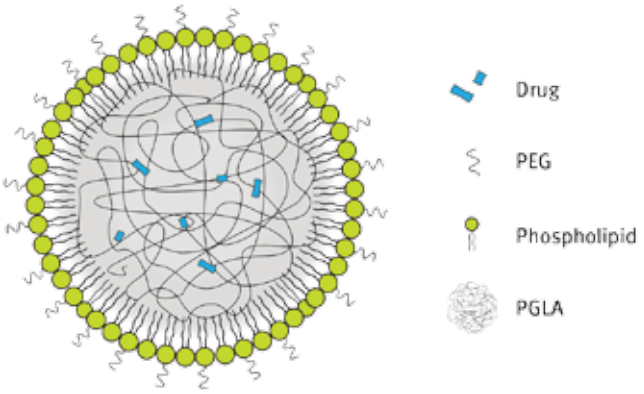


LNPs are liposome-like structures especially geared toward encapsulating a broad variety of nucleic acids (RNA and DNA), and as such, they are the most popular non-viral gene delivery system. Exelead develops and manufactures LNPs to encapsulate different types of genetic payloads including siRNA, mRNA and saRNA.

Traditional liposomes include one or more rings of lipid bilayer surrounding an aqueous pocket, but not all LNPs have a contiguous bilayer that would qualify them as lipid vesicles or liposomes. Some LNPs assume a micelle-like structure, encapsulating drug molecules in a non-aqueous core.

PEGYLATION OF LNPS AND LIPOSOME-LIKE DRUG DELIVERY STRUCTURES

PEGylated phospholipids – which consist of a polyethylene glycol (PEG) polymer covalently attached to the head-group of a phospholipid – are used in many lipid-based drug carriers primarily because they offer what is known as a stealth effect to the drug product as it circulates within the body. The human immune system is driven to protect the body from any foreign object, and medicinal nanoparticles are no exception. To allow more circulation time for cargo molecules to reach intended diseases sites, PEG is added to shield these nanoparticles by preventing blood plasma proteins from absorbing into the liposome surface.



The second benefit of PEGylation is a boost in stability for liposome-like nanostructures. Conventional liposomes, particularly those smaller than 200 nm in size, can be unstable on their own and tend to fuse with each other to reduce surface tension. One way drug manufacturers have learned to overcome this problem is by covering the exterior of liposomes with polymers such as PEG.

These stealth-equipped nanoparticles have resulted in a new generation of liposomal formulations and multiple clinically-approved products. PEGylated liposomes and LNPs are currently the new paradigm for most cancer therapeutics.

LNPS IN GENE THERAPY

For a long time, the most effective way to deliver gene-based therapeutics to human cells was to use a virus that had been modified to carry medicinal cargo rather than harmful, self-replicating genes. This method is still occasionally used today, and is referred to as viral gene delivery. Non-viral gene delivery, however, has become popular over the last 20 years due to enhanced safety profiles, lower rates of adverse immunogenic reactions and ease of manufacturing. One of the primary drivers of this movement has been the development of lipid and polymer-based carriers, of which LNPs are the most popular.

LNPs used to deliver genes are primarily synthesized using cationic, or positively-charged, lipids that associate with anionic, or negatively-charged, nucleic acids. Other lipid-based components can also be added to modulate the delivery efficiency and location release of the genetic cargo.

AN EXPANDING FIELD

While there is significant work ongoing in the development of controlled-release, nano-compartmentalized medicinal agents, liposomes and LNPs are especially promising options. These structures provide a unique, naturally stable, cell-like morphology for nanomedicines, and are poised to progress toward more advanced therapeutic strategies.

Since liposomes were first proposed as a drug delivery system in the late 1960s, variations in structure and functionality have emerged, providing valuable advancements in terms of disease targeting. LNP drugs have cropped up across the pharmaceutical industry as therapies designed to deliver anticancer agents, antibiotics, gene medicines, anesthetics and anti-inflammatory drugs.

APPLICATIONS IN PERSONALIZED MEDICINE – A NEW ERA IN THERAPEUTIC STRATEGIES

With the advent of personalized genetic therapies, doctors and scientists can effectively tailor an active pharmaceutical ingredient – often RNA or DNA – to match the specific disease profile of a particular patient or small group of patients. This approach to hyper-specific disease targeting increases efficacy and decreases unwanted side effects for groups of similar patients.

LNPS AS DELIVERY VEHICLES FOR OLIGONUCLEOTIDES

Because so much of the growing field of personalized medicine is focused on genetic therapies, LNPs have become particularly useful as a drug delivery platform. Any oligonucleotide could theoretically be encapsulated within a liposome or LNP, but siRNA are currently the most common cargo.

In theory, segments of siRNA can be designed to silence any gene, which is an exciting concept for both doctors and researchers. Unfortunately, delivery of free, unencapsulated RNA into human cells is difficult, as they are large, unstable in serum and prone to nuclease degradation.

LNPs have provided a solution to this problem by providing flexible and easy means of encapsulation, protecting the siRNA segments until they reach their intended destination and facilitating their delivery into target cells.

Read the full white paper at https://www.exeleadbiopharma.com/articles (Full link: https://www.exeleadbiopharma.com/articles/liposomes-and-lipid-nanoparticles-as-delivery-vehicles-for-personalized-medicine)