LIPID NANOPARTICLES FOR DRUG DELIVERY

Lipid nanoparticles (LNPs) are vesicle composed of lipids that are used to deliver a wide range of therapeutic modalities including nucleic acids (DNA, mRNA, siRNA), antibiotics and small molecules (such as doxorubicin)[1]. The most well-known application of LNP drug delivery are the mRNA COVID-19 vaccines developed by Pfizer/BioNTech and Moderna. Fundamentally, LNPs are spherical vesicles composed of ionizable lipids whose charge changes in response to pH[2]. LNPs have neutral charge at physiological pH, which facilitates entry into cells but have positive charge at acidic pH to promote complex formation with negatively charged nucleic acids. LNPs are internalized into cells via endocytosis and release the payload in the cytoplasm upon exposure to low pH2. LNPs can take various forms including liposomes, nano-emulsions, solid lipid nanoparticles, nanostructured lipid carriers, and lipid polymer hybrid nanoparticles[1]. Liposomes are best known for delivering chemotherapies such as doxorubicin and paclitaxel for cancer treatment and lipid polymer hybrid particles have also been used to deliver docetaxel for treatment of various cancers1. The nanostructured lipid carriers and solid nanoparticles have been used to deliver nucleic acid therapies. Apart from therapies, LNPs are gaining interest in cosmeceuticals which is an unregulated space that primarily consists of skin and hair care products[3]. LNPs have desirable properties for topical applications as they adhere well to the skin and easily disperse across the tissues. However, since this space is not overseen by regulatory agencies like the FDA or EMA[3], it is important for manufacturers to manufacture and test the LNPs to ensure high quality standards.

Various types of LNPs have been used to deliver different therapeutics, antibiotics and sedatives since the 1990s. A majority of the therapies use liposomes[4], and the first LNP based siRNA (Patisiran) therapy was approved in 2018 for the treatment of hereditary transthyretin amyloidosis[2]. The mRNA based COVID-19 vaccines that were approved in 2021 also used LNPs to deliver mRNA targeting the spike protein of the SARS-CoV2 virus. However, it is important to note that LNPs have pros and cons. One of the key advantages of LNPs is the low toxicity rate since the lipids are biocompatible and do not trigger significant toxicity. Structurally, LNPs are very stable and are amenable to tissue targeting. Depending on the target tissue or organ, LNPs can be directly administered via nebulization to the lung or direct injection into the eye[5]. LNPs have natural tropism to the liver so they are well-suited to target hepatic diseases and this property is being used to engineer LNPs to deliver payloads to the liver at high efficiency. Additionally, LNPs can be targeted to immune cells such as T-cells via specific antibodies such as anti-CD4[5]. Currently, there is active research to develop next-generation LNPs that have specific tissue targeting properties. LNPs also have certain disadvantages and the major challenge is the low drug loading and delivery efficiency. While this is not a major issue for vaccines, it is of concern to deliver drugs in sufficient quantity to exert a therapeutic effect. LNPs also have short blood circulation time and are susceptible to removal by macrophages causing a low number of LNPs reaching the target tissues. While LNPs are considered to be the most clinically advanced nonviral gene delivery method, the current status of the field restricts LNP use to specific applications but the fields of use are likely to grow with improved next-gen LNPs.

References:

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