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Review Article

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Lipid Nanobiotechnology: An Alternative Strategy to Targeted Drug and Vaccine Delivery System and Its Biomedical Applications as Nanomedicine

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ABSTRACT

Nanobiotechnology has very compelling role in vaccine development. Delivery system orientates toward less immunogenic minimal compositions and formulations that boost antigen effectiveness. Latest advancements in LNPs formulations as targeted vaccine delivery systems, like anticancer and nucleic acid therapeutics. Nanomedicine expel challenges and promote growth opportunities inareas, like biomedical imaging, nutraceuticals, biomedicine, gene technology, and basic sciences. The fundamental understanding regarding the *in-vivo* behavior of nanoparticles explored, which can perform as either a delivery system to enhance antigen processing and/or as an immunostimulant adjuvant to activate or enhance immunity. The utilization of nanoparticles in vaccine development allows targeted delivery, improved antigen stability and immunogenicity.

Keywords: Lipid nanoparticles, Liposome, Immunoliposome, Targeted delivery, Vaccine, Nanomedicine

INTRODUCTION

Lipid nanoparticles (LNPs) have emerged across the biomedical industry as promising vehicles to deliver a variety of therapeutic agents. The application of LNPs has also been extended to fields like biomedical imaging, nutrition, biomedicine, and other innovative sectors such as biotechnology, vaccinology, and nanoreactors. Presently in the spotlight as a major component of the COVID-19 mRNA vaccines, LNPs play a vital role in effectively protecting and transporting mRNA to cells. Liposomes, an advance version of LNPs, are an extremely adaptable nanocarrier and a flexible nanomedicine delivery platform as they can transport hydrophobic or hydrophilic molecules, including small molecules, proteins, and nucleic acids.[1]

Liposomes are the earliest nanomedicine delivery platform, which successfully proceed from concept to biomedical application. The subsequent generations of LNPs, including liposomes, solid-lipid nanoparticles, nanostructured lipid carriers, cubosomes, and cationic-lipid macromolecules complexes (**Fig. 1**), exhibit more complex internal construction and enhanced biophysical stabilities. Ability to manage the location and schedule of drug delivery in the body, LNPs may be used to deliver therapies for a range of diseases. Increasingly, scientists are moving beyond traditional medications to more complex and specialized therapies that can fight disease at the genetic or cellular level.[2]

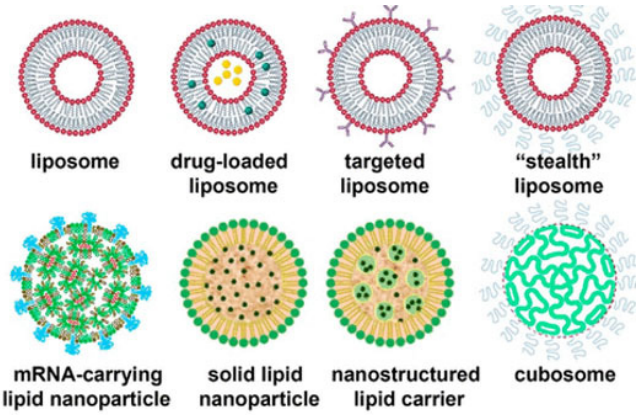

Figure 1: The subsequent generations of LNPs and cationic lipid macromolecules complexes.

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Principle of Lipid Nanoparticles

Liposomes: The Advance Generation of LNPs

"Liposomes" were first describedby British hematologist and biophysicist Alec D. Bangham in the 1961 at University of Cambridge. Liposomesare single or multiple concentric lipid bilayers encapsulating an aqueous compartment. Shortly, after it had been found that closed lipid bilayer vesicles form spontaneously in water (**Fig. 2A**). The term "lipid nanoparticle" came into utilize much later, within the first 1990s, with the birth age of nanotechnology. Therefore, liposomes are commonly nanosized, which made from lipids and they considered as the advance generation of LNPs. The application of liposomes as drug and vaccine delivery systems was presently noticed after their discovery.[3]

Liposomes are the earliest nanomedicine delivery platform to successfully proceed from concept to medical application, with variety of approved remedy preparations. They are utilized in numerous biomedical trials to deliver anticancer, anti-inflammatory, antibiotic, antifungal, anesthetic, and other drugs and gene therapies. Phospholipids like phosphatidylcholines, phosphatidylethanolamines, phosphatidylserines, and phosphatidylglycerols, together with stabilizers like cholesterol, are common liposome substituents.[4]

Hydrophilic drugs are often enclosed within the aqueous interior of liposomes, while they can be entrapped in the hydrocarbon chain region of the lipid bilayer to making liposomes a flexible vaccine delivery platform (**Fig. 2B**). For delivery system, liposomes could be either unilamellaror multilamellar vesicles, in which concentric bilayers form an onion-like multilayer structure. Size could be a critical parameter in determining liposome drug encapsulation and half-life in circulation, with smaller liposomes having more chances of disappearing phagocytic uptake.[5]

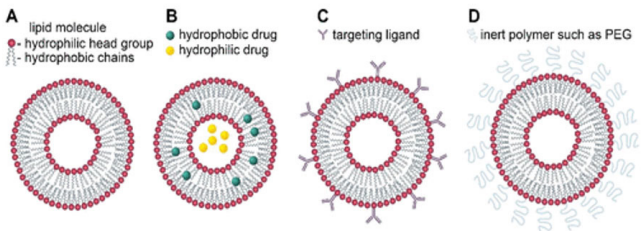

Figure 2: Schematic description of (A) liposome, (B) liposome encapsulating hydrophobic and hydrophilic drugs, (C) immunoliposome functionalized with targeting ligands, and (D) stealth liposome functionalized with inert polymers like PEG.

The dimensions of nanoparticles are often measured employing a various kinds of techniques like light scattering, size exclusion chromatography, nuclear magnetic resonance spectroscopy, and electron microscopy. The particle size distribution of LNPs will be controlled using manufacturing methods like extrusion, sonication, and homogenization. More currently, microfluidic methods are successfully beneficial and utilizable for LNPs manufacture and size control. The lipid head groups generally determine the surface charges of LNPs, which can be either negatively or positively charged or zwitterionic.[6]

The surface potential mainly depends on the surface charge density, which controls the interactions between particles and the adsorption of counterions. Uncharged or low charge particles densities tend to aggregate over time, while more highly charged particles repel each to one another and preventing aggregation. The surface charge of nanoparticles is most frequently demonstrated by their zeta potentials, which vary linearly with the ionic lipids fraction incorporated into the liposomes.[7]

Cationic LNPs Complexes with Nucleic Acids

Nucleic acids have a wide range of roles in biomedicine, including gene therapy agents as well as RNA therapeutics. The association of nucleic acids with their serum proteins uptake by phagocytic cells and degradation by endogenous nucleases interferes with their systematic delivery. Because of this, nucleic acids will require the specific delivery vectors to safeguard them from degradation and to deliver them to the target cells for efficacious uptake. Cationic LNPs comprise stable complexes between synthetic cationic lipids and anionic nucleic acids and hence they are the foremost widely used non-viral vectors delivery system for nucleic acid vaccines.[8]

The molecular architecture of the cationic lipids is comparable to natural lipids, apart from the presence of cationic head group rather than zwitterionic or anionic. They contain a hydrophobic fragment of two alkyl chains or a cholesterol portion, and a linker connecting the positively charged polar head group with the hydrophobic fraction. Ionizable lipids, which are positively charged only inside the cell and uncharged within the bloodstream flow because of a change in pH are preferable, as well as their less toxicity than non-ionizable cationic lipids.[9]

Composition with positively charged lipids stabilizes nucleic acids to increase their resistance against enzymatic degradation for allowing delivery toward desired targeting cells (**Fig. 3**). Other hand the nanoparticle lipids for nucleic acid delivery bear positive charges and their attraction thus drives negatively charged membrane fusion and endocytosis. Once the nucleic acids release from their cationic lipids complexes is fundamental for nucleic acid delivery. The cell's anionic lipids are help to liberate nucleic acids by neutralizing the charge of cationic lipid carriers and disturbing the electrostatic interactions.[10]

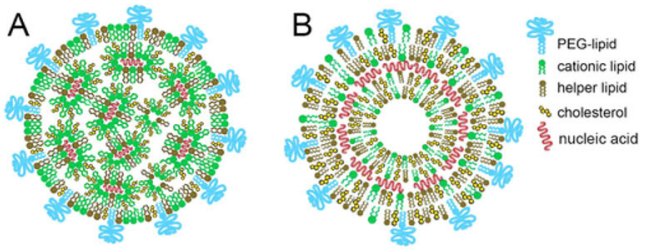

Figure 3: Suggested structures of LNPs nucleic acid carriers (A) nucleic acids organized in inverse lipid micelles inside the nanoparticle, (B) nucleic acids intercalated between the lipid bilayers.

Solid LNPs and Nanostructured Lipid Carriers

Due to liposomes require complex production methods, and exhibit low effectiveness, solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) were developed to handle these shortcomings (**Fig.4**). While conventional liposomes contain liquid-crystalline lipid bilayers, SLN contain solid lipids, and NLC comprise mixtures of both solid and liquid-crystalline lipids. SLN and NLC exhibit enhanced foremost physical stabilities to sterilization than other LNPs; even have higher loading capacities and shipment accessibilities.[11]

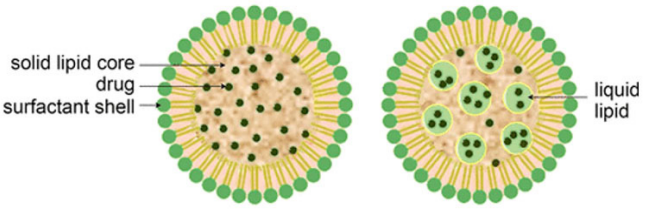

Figure 4: Schematic representation of a solid lipid nanoparticles (left) and a nanostructured lipid carrier (right).

Furthermore, the reduced mobility of molecules within the solid state allows SLN and NLC to manage the discharge of their drug payloads more precisely. Nevertheless, on long-term storage, crystallization of SLN can expel the incorporated drugs into the surrounding media. NLC were designed by introducing small amounts of lipids liquid at room temperature into SLN to reducing the degree of crystallinity of the lipid core. The decreased crystallinity of NLC arrest the drug dispersion from the matrix and enhances the drug-loading capacities and long-term nanoparticles physical stabilities.[12]

SLN and NLC are composed of lipids and stabilizing agents like surfactants and other coating materials (**Fig.4**). Generally,in the LNPs preparation thelipid constituents are commonly includes fatty acids, fatty alcohols, glycerides, and waxes (**Table 1**). Surfactants are located at the lipid-water interface to reduce the interfacial surface tension between the lipid and aqueous phases for improve the stabilities of the resultant formulations. SLN and NLC are usually produced using various organic solvent-free methods including high-pressure homogenization, high-speed stirring, ultrasonication, emulsion/solvent evaporation, double emulsion, phase inversion, and solvent injection.[13]

Table 1: Common ingredients used for the preparation of SLN and NLC

Lipids	Emulsifiers
Triglycerides	Lecithin
Tripalmitin (Dynasan 116)	Poloxamer 407
Tristearin (Dynasan 118)	Tyloxapol
Mono, di, and triglyceride mixtures	Polysorbate 20
Witeposol bases	Polysorbate 60
Glyceryl stearates (Imwitor 900)	Polysorbate 80
Glyceryl palmitostearates (Precirol ATO 5)	Sodium glycocholate
Waxes	Taurodeoxycholic acid sodium
Beeswax	Butanol and Butyric acid
Cetyl palmitate	Cetylpyridinium chloride
Hard fats	Sodium dodecyl sulfate
Stearic acid	Sodium oleate
Palmitic acid	Polyvinyl alcohol
Other lipids	
Miglyol 812	
Paraffin	

Non - Lamellar LNPs

Cubosomes

Cubosomes are highly stable nanoparticles under physiological conditions, formed from lipid-cubic phases and stabilized by polymer-based outer coronas (**Fig. 5**). Liquid-crystalline lipid cubic phases include single lipid bilayers that form a bicontinuous periodic lattice structure with pores formed by two splicing water channels. Cubosomes provide a significantly higher membrane expanse for loading of membrane proteins also tiny-molecule drugs. This complex properties of the cubosomes allows to be employed in a range of applications, likevaccine delivery, membrane bioreactors, artificial cells, and biosensors.[14]

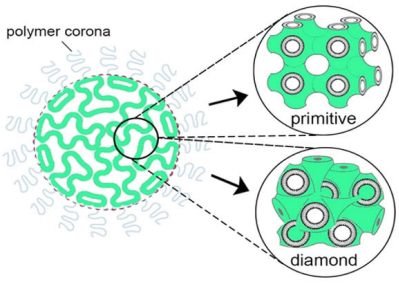

Figure 5: Cubosomes (nanoparticles with lipid in a bicontinuous bilayer cubic phase, either primitive or diamond type).

Cubosomes are composed of the major component amphiphilic lipids with a stabilizer and upon hydration; the lipid spontaneously forms a cubic liquid-crystalline phase. The stabilizer is often a polymer that anticipate the reconstitution of the cubosome into a bulk cubic phase. The foremost compositions of cubosomes use mainly monoolein, because the lipid component with poloxamer 407 as a stabilizing surfactant. The mixture of monoglyceride/surfactant makes up between 2.5% and 10% of the full weight of the dispersion.[15]

Hexosomes

Hexosomes are another kind of LNPs, in which lipids form a non-lamellar phase inverted hexagonal phase. Their compositions are similar to those of cubosomes which containing amphiphilic lipids, a polymeric stabilizer, and water. Micelles are non-lamellar lipid nanosized particles with a hydrophobic core and hydrophilic shell. While theyused to solubilize poorly water-soluble drugs, reverse micelles with hydrophilic core and hydrophobic shell are usual encapsulate hydrophilic molecules in complex lipid vehicles.[16]

Ethosomes

Ethosomes are phospholipid nanoparticles containing a high proportion (20-45%) of ethanol. The added ethanol increases the permeabilities and elasticities of the ethosomes which allowing them to perform transdermal delivery of medicine by squeezing through the outermost layer of skin (corneum pores). This direction offers an alternative method to deliver liposomal formulations to avoid the complications caused by the canal in oral drug delivery mechanism. Commercial products including anticellulite, antiaging agents, hair growth stimulants, and topical creams are using for the treatment of animal herpes virus infections.[17]

Echogenic Liposomes

Echogenic liposomes are considerably active liposomes utilized as ultrasound contrast agents. They have been needs to evolve following the finding that microscopic bubbles of gas reflect diagnostic ultrasound waves. Gas-liquid interfaces provide an oversize discontinuity in density and reflect sound much proficiently. Encapsulated into liposomes the gas microbubbles provide developments in biomedical imaging. Echogenic liposomes offer additional therapeutic applications like ultrasound-controlled drug delivery system and ultrasound-enhanced thrombolysis.[18]

Procedures for LNPs Development

The film hydration method represents the convenient method used for liposome preparation. Lipids are initially dissolved in an organic solvent so dried right down to yield a skinny-film at the underside of a vial, so lipid film is hydrated to provide a liposomal dispersion. The hydration conditions affect vesicles structures are formed by gentle hydration, poor size homogeneity upon intense agitation, and probe or bath sonication. Consecutive extrusion through polycarbonate filters of defined pore sizes may be significant in determining the homogeneity and control liposome diameter.[19]

Another standard method is reverse-phase evaporation which including formation of a water-oil emulsion between an aqueous-organic phase containing lipids. The solvent injection method involves the rapid injection of a lipid solution into an aqueous medium. The detergent removal method involves dissolution of phospholipids with solution containing detergents at their critical micelle concentrations followed by removal of the detergents by dialysis method. The heating method including hydrated lipids heated above the transition temperature of the phospholipids in the presence of a hydrating agent like glycerin or propylene-glycol.[20]

The modern method is microfluidic hydrodynamic focusing, which involves a stream of lipid-alcohol solution is forced to flow in the central channel of a tool, intersected, and sheathed by coaxial stream of an aqueous phase. Reciprocal diffusion of alcohol and water across the focused alcohol-water interface, while the lipid to precipitate and self-assemble into liposomes. Moreover, up-to-dating developed method include cross-flow injection using supercritical fluids. Likewise, preparation of SLN, NLC, and cubosomes including various methods for homogenization, ultrasonication, extrusion, and micro-fluidization mostly useful to control LNPs size.[21]

Functional Variations of LNPs

Targeted Liposomes

Targeted liposomes are designed with surface attached ligands for recognition and bind to specific receptors on cells (**Fig. 2C**). In general, they are prepared by conjugation of small molecule ligands, peptides or monoclonal antibodies to the surface of LNPs. Whereas antibodies initially used to construct actively targeted liposomes (immunoliposomes). For instance, receptors like the folate and transferrin, they are overexpressed on many cancer cells, moreover, their corresponding ligands have been used to direct liposomes to these cell types.[22]

Folate receptors are overexpressed on macrophages, which is present in inflammatory diseases like psoriasis, Crohn's disease, atherosclerosis, rheumatoid arthritis, and autoimmune disorder. Transferrin receptors are over-expressed in rapidly proliferating cancer cells to fulfill the iron increasing demands of tumor cells to making the possible event of transferrin receptor targeted in anticancer therapies (**Table 2**).[23]

Table 2: Examples of ligands and receptors tested as LNPs-targeting agents in cancer therapies

Targeting ligand	Target receptor	Targeted cancer
Folate	Folate receptor	Expressing folate receptor
Transferrin	Transferrin receptor	Expressing transferrin receptor
GM-CSF	GM-CSF receptor	Leukemic blasts
RGD	Integrins	Endothelial cells in solid tumors
NGR	Aminopeptidase N (CD13)	Endothelial cells in solid tumors
Anti-VEGFR antibody	VEGFR (FLK1)	Endothelial cells in solid tumors
Anti-ERBB2 antibody	ERBB2	ERBB2 receptor, breast cancers
Anti-CD20 antibody	CD20, B-cell surface antigen	non-Hodgkin's lymphoma
Anti-CD22 antibody	CD22, B-cell surface antigen	non-Hodgkin's lymphoma
Anti-CD33 antibody	CD33, leukocyte antigen	Acute myeloid leukemia
Anti-CD25 antibody	Interleukin-2 receptor	T-cell lymphoma
Anti-CEA antibody	CEA	Small-cell lung cancers

Stealth Liposomes

Immunoliposomes were rapidly separated from the blood flow by phagocytic cells. Therefore, liposomes were coated with biocompatible inert polymers, commonly polyethylene-glycol (PEG) which making them invisible to phagocytes is called stealth liposomes(**Fig. 2D**). While PEGylation was initially invented to assist the protein drugs to evade the body's immunological response, later found that it was to be a very effective at improving the surface properties of the liposomes through preventing access to their surface by steric hindrance. The increased circulation in half lives of sterically stabilized liposomes also increases their passive gathering in cancer tissues by the improved permeation and retention effect to further increasing their potency.[24]

Stimuli Responsive Liposomes

Liposome improvement includes formulations designed to release encapsulated drugs controllably when exposed to physicochemical or biochemical stimuli known as stimuli responsive liposomes. These drug delivery systems reply to specific triggers to release their cargo where needed for increasing drug efficacy and reducing adverse effects. Liposomes are sensible of temperature, pH, enzymes, light, electromagnetic fields, and ultrasound are deliberate (**Table 3**).[25]

Table 3: Examples of stimuli-responsive liposomes for enhanced anticancer drug delivery

Stimuli	Anticancer Drug	Liposome Composition	Tumor
Temperature	Doxorubicin	DPPC: MSPC: DSPE-PEG2000	Ovarian cancer
		DOPE, DSPE-PEG-H7K(R2)2	
pH	Doxorubicin	Phosphatidylcholine	Glioblastoma
		Soybean phosphatidylcholine	
Magnetic field	5-Fluorouracil		Colon carcinoma
Laser irradiation	AMD3100		Breast cancer

Temperature responsive systems are investigated significantly for anticancer drug delivery. While exposed to mild local hyperthermia, the lipids approach their liquid-crystalline phase transition temperatures to creating disorder between their solid and fluid domains. Becoming more permeable to water-soluble molecules, leads to burst and release of the entrapped drug within the cancer.[26]

Lethality of Lipids Used in LNPs Preparations

LNPs are generally composed of natural lipids and studied pharmacologically inactive and minimally toxic. LNPs are not immunologically inert, whilst their constituents are unnatural compounds, which can be harmful to human cells. For instance, while cationic lipids offer great promise as carriers for the delivery of fragile compounds like nucleic acids, some cationic lipids cause cytotoxicity. In few cases, cationic lipids reduce mitosis in cells, which form vacuoles in the cytoplasm of cells, and cause detrimental effects on key cellular proteins[27].

Amphiphiles with quaternary ammonium head groups are more toxic than those with tertiary amine head groups. While effect of the hydrophobic chains on the toxicity of lipids are not well understood, hindering the look of less toxic lipids. Moreover, the presence of certain lipid phases also correlates to membrane damage and cytotoxicity. PEG-lipid conjugates might also cause undesired toxicity, whilst LNPs containing

PEG-lipid conjugates are known to interact with immune cells to get and generate undesired antibodies against some PEGylated lipids.[28]

Applications of LNPs

Targeted Drug and Vaccine Delivery

Liposomes have capability to encapsulate and deliver therapeutics controllably to specific locations in the body makes them effective for treating a number of diseases. A variety of LNPs drug formulations have been approved and used in biomedical practices (**Fig.6**). The sustainable application of LNPs in drug delivery is in cancer treatment, because of the improved bioavailability as well as selectivity of LNPs encapsulated antitumor agents over the free drugs (**Fig. 6**). Lipid-based nanocarriers lower the toxicity of anticancer drugs to normal tissues; also increase the water solubilities, resident time of hydrophobic drugs, and better drug release control.[29]

Figure 6: Approved LNPs drugs and the diseases they target.

LNPs also improve the efficacy of cancer therapies by the improved enhanced permeability and retention (EPR) effect. Defective angiogenesis in cancers growth results in blood vessels that possess large apertures through which LNPs can freely and quickly pass. Additionally, dysfunctional lymphatic drainage in tumors reduces the speed at which LNPs leave tumors with improves their retention. The proliferation of LNPs in tumors because of the EPR effect allows the nanoparticles to release the antitumor drugs selectively in the vicinity of tumor cells.[30]

Controlling the aggregation state of the drug may enhance its efficacy in therapeutic effect and lower its toxicity. For instance, nucleic acid therapeutics is an emerging class of drugs displaying potential for treating various diseases. However, nucleic acids are polyvalent anionic and extremely hydrophilic molecules, hence they are scarcely taken up into cells. They are also easily degraded by nucleases enzyme in the blood and therefore they require effective delivery vector in order to enter cells[31].

COVID-19 mRNA Vaccines

The current successful implementation of LNPs is the delivery vehicle in the two recently approved mRNA vaccines by Pfizer and Moderna, which are developed with unparalleled speed and they have shown notable effectiveness against viral infection and in disease prevention. The vaccines distribute mRNA encoding for the SARS-CoV-2 spike protein into the cytoplasm of targeting host cells. The mRNA translated into spike protein, performs as an antigen and results inthe development of an immune response against viruses.[32]

They also contain a PEGylated lipid to opsonization by serum proteins and clearance by phagocytosis thus consulting longer and regular circulation. Those nanoparticles are 80-100 nm in diameter and contain nearly about 100 mRNA molecules per lipid nanoparticle. Proprietary cationic lipids ALC-0315 (Pfizer) and SM-102 (Moderna) (**Fig. 7**) are utilized in the COVID-19 vaccine nanoparticles and both lipids are tertiary amines, which are positively charged. Their hydrocarbon chains are connected through biodegradable ester groups, allowing safe clearance after mRNA delivery.[33]

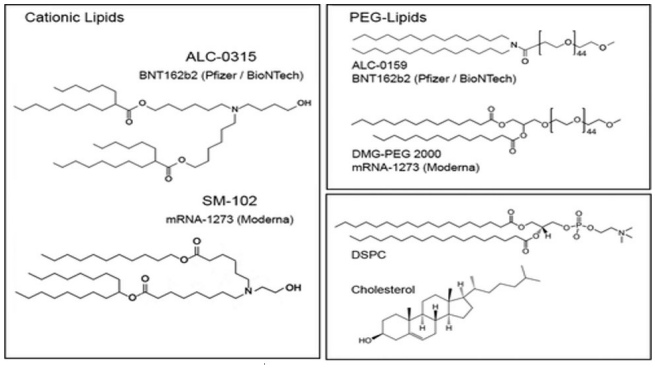

Figure 7: Structures of the lipid constituents of the LNPs of COVID-19 mRNA vaccines.

The cationic lipids applied in the mRNA vaccines contain branched hydrocarbon chains (**Fig.7**), which increase the formation of non-lamellar phases and mRNA delivery efficiency. Whilethe LNPs are prepared at low pH (4.0), at which the ionizable lipid is positively charged, in order they can easily form complex with mRNA[34].

LNPs-based mRNA Vaccines

A significant feature of mRNA-based therapeutics comparing to DNA therapies is that low risk level of mutagenesis, and mRNA does not need the machinery of the nucleus to perform its work. While mRNA does not integrate into the host genome, the threat of carcinogenesis and mutagenesis from mRNA-based therapeutics is decreased, thus, improving their safety. The manufacture of mRNA is more readily standardized than the production of DNA and affordable to better reproducibility. The mRNA vaccines

have revolutionized vaccine due to their high efficiency, accelerated cycles, and low-cost manufacturing possibility.[35]

LNPs-based mRNA vaccines have infiltrate clinical trials against a range of infections, like modified nucleoside mRNA vaccines for Zika virus, cytomegalovirus (CMV), tuberculosis, and influenza virus (**Table 4**). The mRNA therapeutic vaccines have substantial in cancer immunotherapy against melanoma, carcinoma, and other solid tumors (**Table 4**). LNPs vectors are crucial for the successful intracellular mRNA delivery towards the cytosol of antigen presenting immune cells, which are responsible for triggering the desired immune response. LNPs are the well-organized vehicle to deliver the mRNA drugs towardsthe cells, whilst typically require repetitive dosing by prolonged time periods and hence need careful safety analysis and tests.[36]

Table 4: Clinical trials of LNPs-formulated mRNA drugs and vaccines

Disease	mRNA	NCT Number/Phase
	Infectious disease vaccines	
Rabies	mRNA	NCT03713086/Phase I
Zika Virus	mRNA-1893	NCT04064905/Phase I
Cytomegalovirus	mRNA-1647/mRNA-1443	NCT03382405/Phase I
Tuberculosis	GSK 692,342	NCT01669096/Phase II
Influenza	VAL-506440	NCT03076385/Phase I
	VAL-339851	NCT03345043/Phase I
COVID-19	ChulaCov19 mRNA	NCT04566276/Phase I/II
	SAM platform	NCT04758962/Phase I
	ChAd	NCT04776317/Phase I
	Cancer immunotherapy	
Melanoma	mRNA-4157-	NCT03897881/Phase II
	RBL001.1-RBL1004.1	NCT02410733/Phase I
Solid tumors	mRNA-4157	NCT03313778/Phase I
	Protein-replacement therapies	
Propionic Acidemia	mRNA-392	NCT04159103/Phase I & II
Cystic Fibrosis	MRT5005	NCT03375047/Phase I & II

Biomedical Imaging

Biomedical imaging plays a significant role in enhance disease diagnosis, monitor drug delivery, verify response to therapy, and guide minimally invasive procedures. Conventional methods like positron emission tomography (PET), single photon emission computed tomography (SPECT), and magnetic resonance imaging (MRI) have limited specificity as well asresolution. Nanoparticles delivery systems like LNPs and their versatile surface functionalization provide opportunities to strengthen the imaging resolution and specificity.[37]

The application of the radiolabeled liposomes is in early detection of cancer metastasis. Various PET and SPECT radioisotopes are conjugated with liposome to be used as imaging agents. The notable radionuclide for radiolabel liposome is Technetium^{99}, Indium^{111}, and Gallium^{67}. These radionuclides have different half live and photon energy, therefore they could also be applied to meet the requirements of a specific applications. "Theranostics" is the combine medicinal therapeutic and diagnostic techniques to either simultaneously or sequentially diagnose and treat diseases at their premature stages.[38]

Nutrition

LNPs are employed to manage the delivery of functional constituents like proteins, enzymes, vitamins, and flavors in various food and nutritional applications. The term "nutraceutical" is employed to explain formulations potentially providing medicinal and nutritional benefits. These formulations can involve nutrients, dietary supplements, herbal medicines, and genetically engineered processed foods. Recently, the utilization of SLN and NLC in food and dietary supplements has noticeably increased because of their advantages in higher loading capacities.[39]

Nanoreactors

Themodern application of LNPs including nanoscale chemical reactors, which appealed to nanobiotechnology. For instance, LNPs have been used as nanoreactors for the size-controlled synthesis of metal and nonmetal nanoparticles. Metal nanoparticles are employed in biosensors, and catalysis as well as biomedical applications such as imaging, drug delivery, and photo-thermal therapy. The nanoparticles size determined their numerous properties, whilst control over metal nanoparticle size is

important in controlling their properties and determining their acceptability for use[40].

Synthesized monodisperse nanocrystals of liposome cores used as nanoreactors for precipitation or crystallization. Nanoreactors have also been not only proposed as tools for treatment of disease but also eliminating harmful substances by permit the production of therapeutic agents in situ. In addition, liposome based nanoreactors may be beneficial for delivering enzymes for eliminating toxic substances[41].

Modeling of Biological Membranes

Lipid-based models have been used for decades to investigate membranes related processes and its characteristics. Biological membranes are heterogeneous multicomponent structures with sophisticated molecular organization, whilst model LNPs systems are much simpler and more stable, hence amenable to study of the structure and function of biological membranes. Effectively our recent understanding of membrane lipid phase behavior consequences from the use of lipid membranes as model systems.[42]

DISCUSSION

Nanomedicine has showed impressive progress in modern targeted therapy against many diseases. Applications of nanotechnological strategies to drug and vaccine delivery has improved not only the effectiveness, selectivity, duration, but also biodistribution of conventional drug carrier systems. Furthermore, the continual efforts in synthesis and screening of functionalized LNPs by chemically optimizing their molecular structures and *in vivo* biodegradability would promote the development of more versatile, highly efficient, and biocompatible delivery vehicles.[43]

LNPs with complex structures are being designed to overcome biological barriers specific to individual patient as demanded by precision medicine. Modified nanocarrier designs are adapted by patient data and engineered to permeate particular barriers may enhance the delivery and response to precision therapies. LNPs hold great promise ingene therapy and editing, vaccine development, oncology, and other genetic medicine.[44]

CONCLUSION

Nucleic acid therapeutics is an emerging class of drugs showing capability for treating disease and LNPs have become evident as successful efficient carriers for such drugs. The successful use of LNPs as a delivery pathway for the COVID-19 mRNA vaccines will likely broaden the horizons for research in mRNA-based vaccines. The use of LNPsin the controlled synthesis of metal nanoparticles are very important in widening their use in display technologies. Areas like biomedical engineering, gene editing, and oncology are exploring the advantages of lipid-based nanoencapsulation. Besides, of this, LNPs may have environmental applications like metal detoxification and membrane nano-purifier.[45]

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Conflict of interest

The authors declare no competing interest.

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Author Contribution

The author has alone responsible for writingthis article.

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