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Lipomer: An Advanced Drug Delivery

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ABSTRACT

Over the past ten years, tremendous research has been done on nanotechnology. Lipomers are also known as Lipid Polymer Hybrid Nanoparticles (LNPs). Recently a lipid Polymer hybrid nanoparticle has gained prominence as an ideal drug delivery strategy that combines the benefits of polymeric and liposomal nanoparticles. These nanoparticles exhibit complementary propertis of both polymeric nanoparticles and liposome mainly in stability and biocompatibility. The use of lipid-polymer hybrid nanoparticles in effective drug delivery to address cancer treatment resistance has great promises. In this article contain classification of Monolithic hybrid Nano systems, core shell Nano systems, Hollow core shell nanoparticles, Biomimetic lipid polymer hybrid nano-systems, Polymer caged liposome's as well as Their preparation method which are single step and two step methods. In two step methods there are conventional and non-conventional methods are present for preparation of lipomer in the conventional method preparations done by using Emulsification solvent evaporation and in non-conventional method by using spray drying. Lipomers are used in cancer therapy, gene delivery, anti-microbial drug delivery and imaging drug delivery. These are widely used in antimicrobial drug delivery as well as in drug and vaccine delivery.

Keywords- *Lipomer, Nanoparticles, Lipid -polymer hybrid nanoparticles,*

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INTRODUCTION

Nanoparticles are solid, colloid particles with the diameter of 1 to 100 nanometers [1]. Nanoparticles are effective at delivering drug molecules in a controlled way over an extended period of time, ranging from hours to days. They also assist in increasing the drug's patient compliance and stability inside the body, and even its efficacy, by increasing their hydrophilic solubility of the poorly solubilized drugs, their own bioavailability is increased [2].

Introducing a pharmaceutical ingredient into the human body in order to produce or optimize the targeted therapeutic effects while limiting drug degradation, minimizing any side effects [3]. Traditional medication administration methods have various drawbacks, including higher odds of missed doses, drug level variations, a lack of bioavailability, lack of patient compliance, and an adverse side effect, drug toxicity, and quick metabolism. However, Target-specific Nano carrier systems, such as solid lipid Nanoparticles, liposome's, niosomes, ethosomes, transferosomes, bilosomes, sphingosomes, colloidal Nanoparticles and Polymeric nanoparticles, can overcome these practical limits. Nanomaterial development for medication delivery and biological applications is advancing at an incredible rate [4].

Lipomer (Lipid -polymer hybrid nanoparticles) (LPN) are a new type of nanoparticle drug delivery system that combines polymers with lipids to take use of the both materials. At body temperature, PLN are solid, similar to solid lipid nanoparticles [5]. However, it's different from normally referred as lipid base nanoparticles, Liposome consists of the water- soluble core encased by one or more bilayers comprising

natural or synthesized lipids [6]. Liposomes are widely regarded as a very good biocompatible vesicular system that resembles a biological membrane. The key concerns for vesicular systems are low drug entrapment, stability, and concussive drug release. Polymer-based nanoparticles, on the other hand, are more stable than liposome's and provide drug release that is continuous over a long period of time [7]

LIPID POLYMER HYBRID NANOPARTICLES (LNPs)

Lipid and polymer base nanoparticles are the two most common types of nanoparticles, but One of every has its own set of drug delivery limitations. It has an uncertain physicochemical state, insufficient drug loading, and rapid drug release, similar to liposomes, whereas polymers are prone to cytotoxicity of polymer, degradation of polymer, and the emergence of toxic solvents during processing steps. As a result, they've been coupled and merged to showcase positive characteristics and minimize disadvantages in the form of lipid polymer hybrid nanoparticles (LNPs). The lipid polymeric hybrid nanoparticle system combines the physical advantages of bio-degradable polymers with the pluses of lipid-based nanoparticles such as good drug loading capacity and biomimetic attributes to just provide increased targeting and then a desirable drug release profile [8]. Lipid and polymer are a relatively common lipid–polymer. The core shell structure is seen in hybrid nanoparticles. The polymer-based core is utilized to carry a wide range of small-molecule drug substances and diagnostics agents, whereas the lipid coating adds bio-compatibility and stability. Poly (lactic-co-glycolic acid) (PLGA) is by far the most often utilized polymer in this scenario, owing to its superior biodegradability and biocompatibility. The one-of-a-kind Core is extremely fine-tuneable, allowing it to be modified to load a broad range of drugs [9]. Van der Waal as well as hydrophobic interactions exist between the polymer-based core and the lipid shell. In comparison to liposomes and polymeric Micelles, the biodegradable polymeric matrix core provides stability, the controlled release, and a wide surface area [10, 11]. LPNs combine the properties of polymeric NPs with liposomes, as their name suggests. They are made up of three building blocks, a) the polymer-based core encasing the drug, b) a lipid monolayer encircling the polymer-based core, and last c) an outside lipid polyethylene glycol layer, and the steric stabilizers that prolongs the LPN's systemic circulation by preventing immune destruction [12, 13].

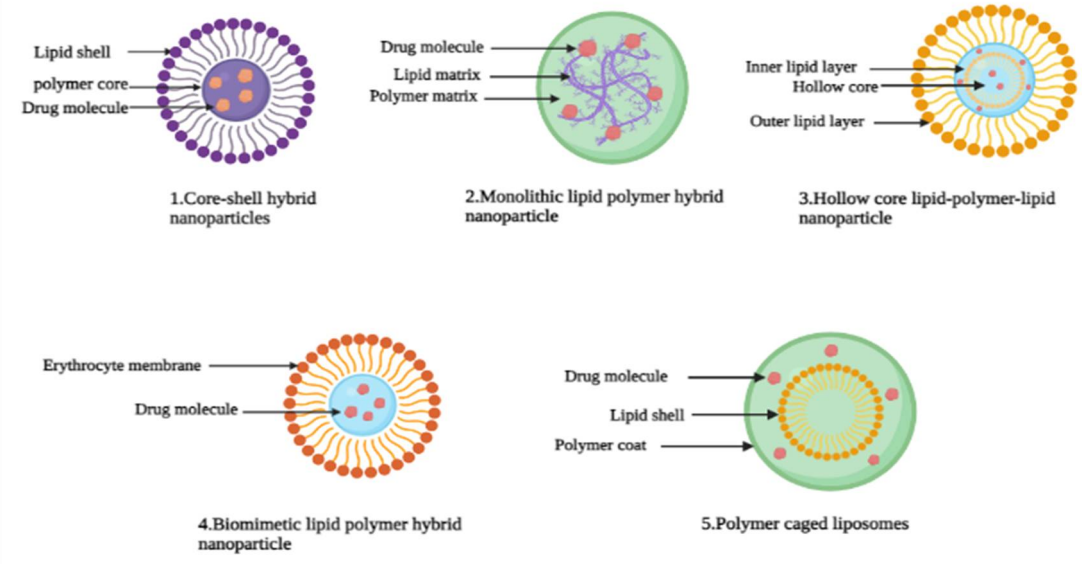

Figure 1: Diagrammatic representation of lipid-polymer hybrid nanoparticles: 1. Core shell hybrid nanoparticle 2. Monolithic lipids polymer hybrid nanoparticle 3. Hollow core lipid polymer nanoparticle 4. Biomimetic lipid polymer hybrid nanoparticle 5. Polymers caged liposome

CLASSIFICATION

LPHNPs can be classified on the basis of their structure as follows:

1. Monolithic hybrid Nano systems
2. Core shell Nano systems
3. Hollow core shell nanoparticles
4. Biomimetic lipid polymer hybrid nano-systems
5. Polymer caged Liposomes [14].

Monolithic hybrid nano-systems

Mixed lipid-polymer hybrid Nanoparticles are another term for monolithic LPHNs [15]. PEG molecules are widely dispersed. Drug particles throughout this type of lipid nanoparticles are contained in a polymeric core matrix. A system like this one could be compared to something like a colloidal drug carrier. Phospholipids are also an important component of their structure, but they aren't adaptable enough yet to allow high-density PEGylation to change their structure [16]. As shown in fig.1(2), Monolithic systems have a polymer-based matrix with lipids that are evenly distributed and form a core around which insoluble in water drug molecules can also be filled in [17].

Core shell nano-systems

Core shell lipid polymer hybrid Nanoparticles have been recently considered as a potential delivery system. The bio-degradable polymer core is enclosed by the Lipids shell inside this system, Greater drug-loading capabilities, easily controlled particle size, surface features, and controllable drug release profile are some of the benefits of hybrid structures [18, 19]. Moreover, core shell lipid polymer hybrid Nanoparticles, which of these incorporates the physical benefits of bio-degradable polymer-based nanoparticles with the benefits of lipid-based nanoparticles, have established themselves as a reliable as well as enticing delivery platform. In the hybrid system, drugs, proteins, genes, as well as targeting ligands can also be entangled, adsorb, and otherwise covalently linked [20, 21]. When comparison to lipid or polymeric Nanoparticles, enhanced entrapment and drug loading of hydrophobic drugs has also been observed for a number of drugs. Furthermore, the lipid shell that surrounds the core seems to be biocompatible, resulting in improved cellular uptake [22, 23].

Hollow core / lipid-polymer-lipid nanoparticles

These systems differ from simple LPNs in that they exhibit the characteristics of both PEGylated lipid complexes and PLGA Nanoparticles. The dual emulsification solvents evaporation process can possibly use to make hollow core lipid-polymer hybrid Nanoparticles. The X-Y-X kind of nanostructure matrix is generated by multilayers of something like the outer surface lipid coat in a circular direction, enclosing the polymer layer that the intrinsic hollow lipid layer is covered in hollow core lipid polymer lipid nanoparticles [13, 24]. The many layers of such nanoparticles help to improve effectiveness of encapsulation and effectively shield the medicine from the environment consists of factors. The most extreme outer lipid utilized could be readily PEGylated, resulting in a prolonged circulation period and improved plasma matrices stability. The many layers also aid in the drug release's long-term stability. Anionic drugs and nucleic acids could be embedded in cationic lipids employed an inside of the hollow core [25, 26].

Biomimetic lipid-polymer hybrid nanosystems

Biomimetic lipid-polymer nanoparticles, also known as erythrocyte membrane-camouflaged polymeric nanoparticles, are created by covering the RBC's membrane into the polymer-based core [27, 28]. The utilization of stem cells, white blood cells, platelets, and other cells in biomimetic LPHN systems could be employed to achieve the site selectivity, evasion of the immune system, extended circulation, and biological barrier interfering, among other things [29].

The cell membrane is initially isolated using techniques such as treatment with hypotonic solutions, sonication/homogenization, differential gradient centrifugation, depending on the presence or absence of the nucleus, in order to create these biomimetic systems. To create monodisperse biomimetic hybrid systems, the cell membrane is compressed only with the polymer across polycarbonate membrane filters after being isolated and purified. This is a reliable, efficient, and cost-effective way for creating biomimetic hybrid systems [30].

Polymer-caged liposomes

Polymer caged liposomes, these particles have a quiet additional coating of polymers on the outside to achieve desired features such increased drug release, improved drug stability, and reduced drug leakage. Additional surface features can be added to polyacrylic acid outer layers, for example. It would be feasible to use carboxylic groups to connect various types of linkers to these, resulting in pH-sensitive activities [31, 12]. Not only can surface characteristics alter, but so can drug release. There are two possible solutions for this, PEGylation and a pH dependent cross-linked Polymeric shell. PEGylation reduces opsonization, and a pH dependent cross-linked polymeric shell will improve liposomal Nanoparticles' stability and reduce drug leakage. Furthermore, at low pH, drug release rate will be enhanced, which will be advantageous in tumor therapy [32].

SYNTHESIS/PREPARATION OF LIPID-POLYMER HYBRID NANOPARTICLES (lipomer)

Single step method

By using nano-precipitation or a solvent evaporation/extraction technology, the single step method which combines the time-consuming dual phases and converted into a single step. In the solvent evaporation approach, the medicine and polymers are should be dissolved in an organic solvent that is immiscible with water, such as dichloromethane, ethyl acetate, or chloroform. After that, sonication or heating which are beneficial to distribute the lipids into the aqueous phase. The organic solution containing the medication and polymer is sonicated before being lipids are added to an aqueous phase. This causes the organic phase to break down into nanospheres, which are then cemented by the lipid covering. A rotary vacuum evaporator is used to evaporate the organic solvent [33]. After the solvent has evaporated, the LPNs are collected by centrifugation. When using lipid–PEG, the lipid tail stretches into the innermost lipid layer, while the PEG head is in contact with the aqueous environment. Acting as a steric stabilizer. Subsequently, after nanoprecipitation of the polymer and lipid components, after the insertion of the lipid PEG vesicles have been conducted, with a greater manufacturing yield reported [13, 26, 34].

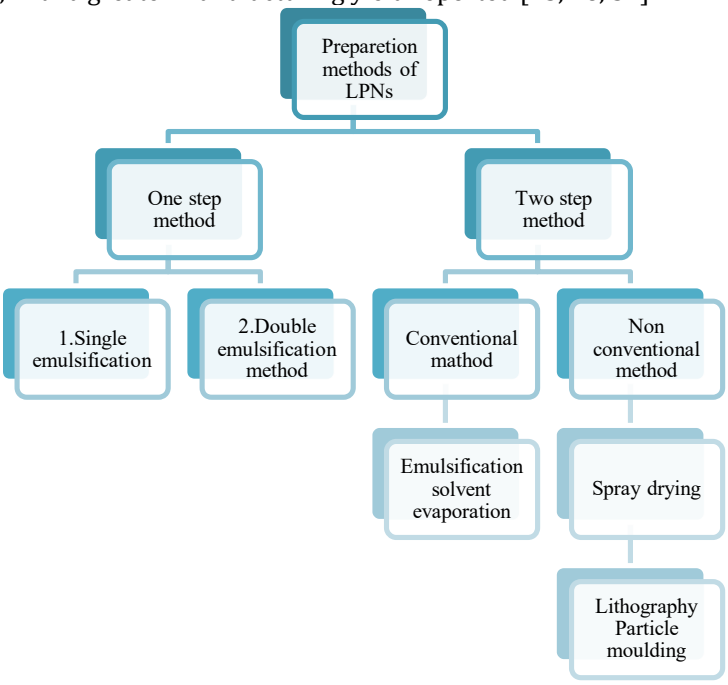

Figure 2: Schematic representation for preparation of Lipid polymers hybrid nanoparticles.

Two step method

Conventional

The earliest methods proposed for the production of LPNs are based on the two-step method, in which polymer-based nanoparticles are combined with produced liposomes, and electrostatic forces stimulate the integration of lipid shell out onto the polymer core's surface [35]. Otherwise, dried lipid film might be applied to the created polymeric nanoparticles. In either case, the introduction of energy via ultra-sonication, as well as heating above the temperature of the lipid layer's phase transition temperature, promotes the assembly of the two components [36]. The polymeric nanoparticles were coated to a dry thin film of the lipid generated by immersing the lipid into the organic solvent and vaporizing it in a rotary evaporator, the solution combined above was treated to ultra-sonication in the conventional method. At temperatures above the lipid transition temperature, which is essential for the formation of LPNs [37].

LPNs are made either with vortexing or ultra-Sonication of the made by mixing the polymeric lipid suspension at the higher temperature than that of the gel to the liquid transition Temperature of the lipid in both methods. LPN's are then kept separate from the non-adsorbing lipid using centrifugation. The LPN suspension is frequently homogenized or extruded after preparation to obtain uniform size LPNs. The LPNs Suspension is managed to pass throughout the porous membrane to generate LPNs are in the size range of the Membranes pores using the extrusion method [38].

Non-conventional

Non-conventional methods such as spray drying are being used in preparation of LPNs in a non-conventional manner. LPNs were prepared for gene delivery using Particle Multiplication in Non-Wetting Templates, a soft lithography Particle moulding technique. This method involves dissolving polymer with

the genetic material in an organic solvent and casting that onto a sheet. The sheet was then heated while being held in contact with the moulding with patterns ranging from 80 to 320 nanometers. When kept at room temperature, the PLGA continues to flow into the mould and solidifies, forming PLGA nanoparticles. The sheets are then collected by rubbing them against a PVA-coated sheet. Because the size and shape of a mould cavity determine the size and shape of a LPNs, the PRINT technique allows for accurate control of their size and shape. It can also produce mono disperse Nanoparticles with various dimensions [13, 26, 39].

Drug release

When contrasting to liposomes and polymer-based nanoparticles, LPN have distinct drug release characteristics. Drugs are released from liposomes through diffusion and partitioning when they pass through the phospholipid bilayer and into the aquatic media. Surface and bulk degradation properties are observed in polymeric nanoparticles by Diffusion of drugs [25, 39]. The drug molecules dispersed out from nanoparticles and then into the release medium on a constant basis. To separate and metric assesses the medications that have been transmitted or persisted within the nanoparticles at various time points, analytical instruments such as mass spectrometry and as well as high-performance liquid chromatography are used [40]. The outer lipid layer protects against drug leakage, inhibits dissolution media entry to the core, and increases long-term drug release. The lipid and polymer used in the hybrid nanoparticles have an impact on their release profile. The drug could be delivered by LPN if it is designed to do so. In reaction to numerous stimuli such as redox, pH, temperature, magnetic field, and others at specified target areas [41].

Drug design

In Lipid polymer hybrid nanoparticles drug delivery systems contain combinations of Lipids and Polymers. Most of these drugs are in solid state. By changing the proportion mass of lipid with the polymer, this innovative delivery system can be optimized for particle size and distribution. It was discovered that increasing the W/W Lipid Polymers ratio by more than 15% resulted in a significant reduction in particle size, while no further reduction in particle size was detected even after increasing the W/W lipid polymer ratio by more than 90% [42]. Lipophilicity and hydrophilicity are two physical features of polymer and lipid coexistence. It differentiates itself from polymeric and lipid-based drug carriers by providing varied potential to LPNs for a variety of payloads [43].

It was also discovered that combining biopolymer with solid lipids resulted in improved drug loading, stability, and the capacity to control release patterns and breakdown characteristics. A bio-degradable polymer, such as poly caprolactone or poly lactic poly glycolic copolymer , was combined with a solid lipid, such as tripalmitin, glycerin stearate,tribehenin, tristearin, cholesterol, tocopherol palmitate, stearic acid, stearyl stearate , tocopheryl succinate,stearyl stearate, tribehenin, cetostearyl alcohol, benzoyl behenate, camauba or cande lilla wax, cocoa butter, and other lipids with a melting point above 20°C Temperature that is in solid state at room temperature [44, 45].

Advantages

LPNs have been designed to encapsulate and deliver a wide range of medicinal substances, whether alone or in combination. LPNs have a wide range of uses in cancer therapy and protein-based therapeutic agent delivery, such as short interfering RNA, nucleic acid, and gene delivery, among others. LPNs can also be used to deliver a variety of drugs orally [32, 43, 46].

Cancer therapy

Nano delivery systems have emerged in the recent two decades as a viable means to improve the therapeutic qualities for anti-cancer drugs by increasing their solubility and stability, as well as to reduce drug toxicity by lowering off-target accumulation. Nano delivery systems have emerged in the recent two decades as a viable means to improve the therapeutic qualities for anti-cancer drugs by increasing its solubility and stability, as well as to reduce drug toxicity by lowering off-target accumulation [36, 47]. To improve treatment efficacy of conventional cancer treatments, a number of efforts are being focused on the development of formulations capable of an extremely precise Engagement with cancer cells [48]. Drugs, genes, peptides, proteins, genes as well as imaging agents are delivered to the tumor site via a variety of NP-based systems, including liposomes, polymers, micelles, inorganic Nanoparticles, and Nano gels [49-51]. Because of their tremendous efficacy in systemic drug delivery, polymeric and lipid-based Nanoparticles are the most efficacious drug delivery systems [52]. LPNs have various benefits over the various nano-systems, including like polymer-based nanoparticles and lipid-based systems, leading in valid alternative cancer treatment options [53]. The ability to incorporate therapeutic drugs with various physicochemical properties, because They have a hybrid structure that is characterized by such a constituent of a polymer and lipids which is able to have distinct properties, is the fundamental advantage of using LPNs throughout the administration of anticancer agents [36,54]. The distribution of therapeutic agents in the control and in a particular way will result in a substantial reduction of undesirable effects on the entire system. LPNs are particularly well-suited in order to combine Ligands targeted, toward tumour cells with overexpressed receptors, hence increasing targeting tumors and trying to maximize

therapeutic impact among the given agents on tumorous cells [55, 56]. Breast cancer is the most commonly found in females, which affecting more than 200,000 women in the United States in 2010.Chemotherapy failure in breast cancer patients is frequently caused by multidrug resistance [57]. Over expression of the membrane drug efflux transporters P-glycoprotein causes' multidrug resistance, which lowers anticancer drug intracellular uptake [58]. There are excellent studies on the causes and strategies for overcoming multidrug resistance [59, 60].

Table 1. Lipomers used in various types of cancer treatment

Types of LPHNPS	Polymer	Lipid	Cancer type	Therapeutic agent	Reference
Lipid polymer Hybrid Nanoparticles	Poly lactic-co-glycolic acid (PLGA)	Carboxylic acid functionalized PEG Lipid and soya bean lecithin	Epithelial human breast cancer cell line.	Doxorubicin and Decitabine	[61]
Polymer Lipid Hybrid Nanoparticles	Epoxidized soya oil hydrolyzed polymer.	Stearic acid	Human Multidrug resistance breast carcinoma Cell line.	Doxorubicin and Elacridar	[62]
Lipid polymer hybrid Nanoparticles (conjugated folic acid)	PLGA	Detergent Lipid Protein Complexes, DSPE-PEG2000 amine polar lipid	Human breast cancer cell lines, Which are the abnormal growth of folate.	Docetaxel	[63]
Lipid-coated PLGA or siRNA Nanoparticles	PLGA	Dioleoyl-3-trimethylammonium propane/1,2-Dioleoyl-sn-glycero-3-phosphoethanolamine	Grade IV adenocarcinoma a cell line from prostate carcinoma.	siRN	[64]
Arg-Gly-Asp modified cyclic lipid polymer hybrid nanoparticles	Plasminogen	1,2-Distearoyl-sn-glycero-3-phosphoethanolamine, Carboxylic acid functionalized PEG Lipid	Hormone-independent breast cancer cell lines	10-hydroxycamptothecin	[65]
Stearic acid Curcumin loaded nanoparticles	2-hydro-xyethyl methacrylate	Stearic acid	Human breast cancer cell line with receptors.	Curcumin	[66]

Biomolecules including such nucleic acids like DNA and RNA, peptides, and proteins have demonstrated significant medicinal Propensity in the cancer treatment when provided in combination with some other drugs for just a therapeutic effect of synergistic effects, resulting in an implement the idea towards chemo resistance [67]. Release of Hydrophobic medicines and coencapsulated, such as the conventional chemotherapeutic medications, with this type of bio-molecules, however, is a key problem that hybrid nanoparticles may be able to overcome [68]. The nanoparticle aided the ingestion of drug conjugation via endocytosis, surpassing the lipid bilayer's transport barrier. Chemotherapeutic drugs have been administered in combined form with radioactive isotopes, nucleotide sequence, diagnostic agents, and proteins using LPNs [69].

Gene delivery

Gene delivery, such as DNA and RNA, has shown to be a difficult task with high chances of success in treating a variety of hereditary diseases, chronic conditions, genetic disorders, and malignancies [70]. Surface chemistry changes are possible thanks to the adaptability of such a lipid-polymer hybrid nanoparticle platform. In order to establish a DNA complex for gene delivery, Li et al. employed cationic lipids in their hybrid nanoparticles. [71, 72]. Although miRNA and siRNA possess different origins and mechanisms, their physical qualities are comparable. MiRNA is an endogenous RNA that targets mRNA by forming improper pairing and hence acts on the mRNA via mRNA degradation, mRNA endonucleolytic cleavage, or translation inhibition [73]. Exogenous siRNA works by cleaving target mRNA through endonucleolytic cleavage [74].

The mRNA target of siRNA is single, but the target of miRNA is numerous. Plasmid DNA contains the recombinant gene or gene of interest which can be used to treat cancer locally or systemically [75].

Table No. 2. Gene Delivery for targeted cell

Gene	Tested Cell	Reference
DNA (pEGFP-N2)	Healthy human embryonic kidney cells line, epithelial cell line isolated from breast tissue breast cancer.	[79]
DNA (pLuc)	Human embryonic kidney cell line.	[80]
siRNA (anti-Luc, KIF11, etc.)	HeLa cervical cancer, cell line of human cells commonly used in the field of oncology, cell line initiated from a bone metastasis of a grade IV prostatic, human prostate cancer cell line. prostate cancer, HepG2 liver cancer	[64]
siRNA (siPlk1)	Ductal carcinoma of the breast.	[81]
siRNA (anti-GFP, anti-Luc, GAPDH.)	HeLa cervical cancer, HepG2 liver cancer	[22]
mRNA	Dendritic	[34]

One such strategy for lipoplexes is to coat the lipoplexes with polymer to protect them against non-specific protein binding [76]. Either one method is to use lipid PEG instead of conventional lipids, with the PEG assisting in the reduction of the lipid or DNA complexes surface charge [77]. Articulation of polyplexes into liposomes have been investigated using a similar principle for the polyplexes. All of these methods have been proven to be efficient in lowering nonspecific protein binding to DNA complexes in vivo, therefore extending their circulation after systemic administration and lowering its uptake in non-targeted tissues [78].

siRNA

iRNA is an evolutionarily conserved cellular monitoring mechanism that has the ability to silence sequence-specific post-transcriptional genes. Studies aimed at evaluating the clinical application of siRNA were described in mouse models, nonhuman primates, and, more recently, humans, since their discovery in mammalian cultured cells as well as mammals [82]. Recently, the FDA approved the first lipid-based iRNA Therapeutic (ONPATTRO™, Alnylam Pharmaceuticals Inc.) in grownups with inherited genetic Transthyretin mediated amyloidosis for something like the diagnosis of polyneuropathy. Nonetheless, a few cellular and preclinical studies on LPHNP-mediated iRNA have been carried out [83, 84]. Yang et al. created LPHNPs using cationic lipid and PLGA polymer in 2012 for systemic RNA delivery of siRNA using a modified nanoprecipitation approach. NPs suppressed tumor growth by efficiently delivering siRNA-mediated polo-like kinase 1 (targeted against the polo kinase 1 onco-Gene) to invasive ductal breast cancer cell in vitro and an invasive ductal breast cancer xenograft mouse model in vivo [82]. In another study, Gao et. al. developed another siRNA delivery technology, using a cationic liposome made comprised of 1, 2-Dioleoyl-3-trimethylammonium propane: The anionic cholesterol grafted poly (amidoamine)/siRNA was combined with DOPE: cholesterol (25:43:25), and the resultant LPHNP has been further transformed with DSPE–PEG/DSPE–PEG-T7 (where T7 is HAIYPRH Peptide). T7-modified, small interfering Epidermal Growth Factor Receptor loaded nanoparticles displayed the best Tumor growth suppression by Transmitting receptor mediated Active targeted delivery in Nude mice having MCF-7 tumor xenografts, according to efficacy research on Mice with no fur bearing breast cancer cell line tumor xenografts [85].
siRNA distribution via cationic complexes like polyplexes and lipoplexes does have a number of drawbacks, including the development of inflammatory reactions, instability, and toxicity. PLGA was used to create nanoparticles containing siRNA that were small (100 nm) and had a lengthy circulation duration. These hybrid nanoparticles have an encapsulation effectiveness of 80% for siRNA and do not degrade significantly after 24 hours. In vitro apoptosis and >90% suppression in no small cell lung cancer were discovered in immuno fluorescence investigations [86].

ANTIMICROBIAL DRUG DELIVERY

Bacterial biofilms are communities of bacteria that are encased in a matrix of extracellular polymer substance that they have self-secreted. These bacterial populations are able to avoid the immune system and are extremely resistant to drugs [87]. Because of its unique physicochemical features, excellent biofilm adhesion, and ability to permeate sputum, LPHNP delivery is intensively researched to combat such Bacterial biofilms. These hybrid nanoparticles are capable of delivering antibiotics to bacterial biofilms in a large amount, hence increasing their antibacterial activity [88, 89]. In recent years there are so many studies are available on antimicrobial drug delivery such as, Using the Emulsification solvent evaporation

process, Dave., et al. synthesized LPHNPs from PLA and Soya lecithin as topical and targeted administration of Norfloxacin. Antimicrobial activity of lipid polymer hybrid nanoparticles against Staphylococcus aureus and Pseudomonas aeruginosa was improved [16]. Seedat., et al. made LPHNPs with vancomycin, glyceryl triplamitate, as well as Eudragit RS100, respectively, as the drug, lipid, and the polymer. Co-excipients included oleic acid, chitosan, and sodium alginate. The results showed that all Nano formulations had better in vitro antibacterial assets against to Staphylococcus aureus & Methicillin tolerance S. aureus, with vancomycin–oleic acid and vancomycin–chitosan having better efficacy against Methicillin tolerance S. aureus [90].

Imagine agent delivery

By encapsulating imaging agents such like iron oxide, fluorescent dyes, and quantum dots into the polymer core, lipid polymer hybrid Nanoparticles it seems to be employed to provide a wide range of options for therapeutic and imaging [91]. Moreover, Mieszawska and colleagues devised a novel approach for appending diagnostic characteristics to LPNs generated by nano-precipitation. They used esterification processes to attach gold nano-crystals and quantum dots into PLGA, which they subsequently combined using soya lecithin and Propylene glycol. In vitro tests in mice macrophages. Further supported the use of gold nano-crystal and quantum dots filled LPHNP's as sensors for image production in biological and medical settings [92]. A strategy that works in tandem was to make the core out of high fluorescence polymers. LPHNP's with a PFBT core and a DMPE–PEG envelope is produced via Nanoprecipitation. Hybrid NPs, in particular, demonstrated a 50% increase in quantum yield. When compared to their non-hybrid counterparts, hybrids have a lot of advantages [93].

LPNs for drug and vaccine therapy

In recent years, LPNs have been considered as a leading vaccine delivery system. LPNs combine the benefits of Polymers with physical stability as well as the biomimetic properties of liposomes [94]. Nanoparticles are excellent adjuvant delivery vehicles for vaccination antigens that can enhance and direct the adaptive immune response [95]. As a result of its ability to regulate the antigen's release. And cod-liver immuno-stimulatory molecules with antigens in the same particle, biopolymer – based microparticles and Nanoparticles made of PLGA have been explored as potential vaccine delivery vehicles [96]. mRNA-based vaccines were produced in a phospholipids shell for delivery [34]. In acidic conditions, Poly (β-amino ester) is a pH dependent polymer that promotes endosomal disruption. Endosomes in Dendritic Cells were disrupted by lipid-enveloped Poly (β-amino ester) particles that were absorbed in the surface with mRNA via electrostatic contact, allowing mRNA to be delivered cytosolically. When compared to naked mRNA, intranasal treatment of these particles significantly induced the activity of reporter protein luciferase in 6 hours, indicating their potential value in mRNA based in-vivo transfection for vaccine applicability [97,98].

Limitations

Being able to accurately supervise and control the impacts of various subjects, such as lipid-polymeric Hybrid nanoparticle, is critical for clinical translation effectiveness. Aside from that, it may be necessary to screen and recognize the highest-quality PLNs for a certain application, which necessitates the continuous process of LPNs with, distinct size, charge, and ligand densities [99].

Conclusion and future perspective

In the last decade nanoparticle drug delivery is one of the most developing and emerging drug deliveries. Nanocarriers have so many advantages like high absorptivity, stability of the therapeutic agent over the GI environment. LPNs are highly applicable in so many drug therapies, because of their complex structure each LPNs shows specific advantages over the other. They are complex in structure but still LPNs can be prepared by simple methods. In hybrid nanoparticles, the lipid polymers hybrid nanoparticle is highly recommended in cancer therapy, gene therapy and single and combinatorial drug delivery.

Pharmacokinetic simply features of nanoparticle drug carriers, including as drug loading capacity, loading efficiency, particle size, surface charge, spatiotemporal drug release and stability, should all be taken into account when creating LPN formulations. For successfully delivering medication into PLNs and precisely managing drug release kinetics, physicochemical compatibility and affinities are required. As a result, for efficient PLN design, a full understanding of material characteristics in respect to the physicochemical process is required [100]. Many Lipid Polymer Hybrid Nanoparticles formulations have been created to encapsulate a single chemotherapeutic drug or a molecule in combination with a chemo sensitizer [62]. Short interfering RNAs in pairing with an anti-cancer drug has sparked a lot of interest in Lipid-Polymer hybrid Nanoparticles for gene therapy and immunotherapy [101]. Polymer Lipid nanoparticles formulations have been seen in cancer cells to rectify efflux transporter Facilitated Multidrug Resistance and strengthen antitumor potency while reducing anticancer drug systemic toxicity [102].

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