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Review Article

Lipid-Based Drug Delivery Systems for Precision Oncology

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ABSTRACT

Lipid-based drug delivery systems (LBDDS) have emerged as a transformative approach in precision oncology, addressing key challenges such as poor drug solubility, stability, and targeted delivery. These systems, including liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), self-emulsifying drug delivery systems (SEDDS), and lipid-drug conjugates (LDCs), offer enhanced bioavailability, controlled drug release, and reduced systemic toxicity. This review explores the advancements in lipid-based formulations, focusing on their applications in cancer therapy, including passive and active targeting strategies. The study also highlights recent developments in stimuli-responsive lipid carriers, multifunctional hybrid nanoparticles, and their integration into personalized medicine. Furthermore, an analysis of past 3-5 years of research data is presented in tabular format table1,2, emphasizing emerging trends and clinical developments in lipid-based nanomedicine. The findings underscore the potential of LBDDS to revolutionize cancer treatment by optimizing drug delivery efficiency, overcoming multidrug resistance, and enhancing therapeutic outcomes. Future perspectives include the incorporation of artificial intelligence in formulation design and the evolution of lipid-based theranostics for real-time monitoring and treatment of cancer. The continued innovation in lipid-based nanocarriers is expected to redefine oncology treatment paradigms and improve patient survival and quality of life.

INTRODUCTION

Overview of precision oncology and its significance:

Precision oncology represents a groundbreaking shift in cancer treatment, emphasizing the customization of therapies to individual patients based on their genetic, molecular, and environmental profiles. Unlike traditional "one-

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size-fits-all" approaches, precision oncology leverages advancements in genomics, proteomics, and other -omics technologies to identify the specific characteristics of a patient's tumor, enabling the selection of targeted therapies that are more effective and less toxic[1].

Key Concepts of Precision Oncology[2,3]

1. Targeted Therapies: These drugs are designed to interact with specific molecular targets, such as oncogenic mutations or signaling pathways, that drive tumor growth and progression.
2. Biomarker-Driven Treatment: Biomarkers, including genetic mutations (e.g., EGFR, KRAS), protein expressions, or epigenetic changes, guide therapy selection and monitor treatment efficacy.
3. Personalized Medicine: By tailoring treatments to individual profiles, precision oncology enhances therapeutic outcomes while reducing side effects.

Significance in Cancer Treatment[1,2,3]

1. Enhanced Efficacy: Precision oncology enables the use of therapies specifically designed to combat molecular aberrations in cancer cells, often achieving better responses than conventional treatments.
2. Reduced Toxicity: By targeting only cancer-specific pathways, these therapies minimize damage to normal cells, leading to fewer adverse effects.
3. Improved Survival Rates: Precision treatments have been shown to extend progression-free and overall survival in various cancers, including lung, breast, and colorectal cancers.
4. Real-Time Monitoring: Technologies such as liquid biopsies allow continuous monitoring of tumor evolution, enabling timely adjustments in therapy.

Challenges Addressed by Precision Oncology[2,3]

1. Heterogeneity of Tumors: Cancer is not a single disease but a collection of diverse conditions. Precision oncology accounts for tumor variability across and within patients.
2. Resistance to Conventional Therapies: By targeting specific molecular mechanisms, precision oncology helps overcome drug resistance that often limits the efficacy of traditional chemotherapy or radiotherapy.

Emergence of Lipid-Based Drug Delivery Systems:

The success of precision oncology relies not only on the identification of molecular targets but also on the efficient delivery of therapeutic agents. This is where lipid-based drug delivery systems play a crucial role. They enhance the solubility, stability, and bioavailability of drugs while enabling targeted delivery to cancer cells, thus complementing the principles of precision oncology[3-5].

Role of lipid-based drug delivery systems in cancer therapy:

Lipid-based drug delivery systems (LBDDS) have revolutionized cancer therapy by addressing several limitations of traditional treatments, such as poor drug solubility, low bioavailability, and systemic toxicity. These systems utilize biocompatible and biodegradable lipid carriers, including liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and self-emulsifying drug delivery systems (SEDDS). By encapsulating therapeutic agents, LBDDS

improve their solubility, stability, and bioavailability, making them highly suitable for delivering anticancer drugs.

One of the key advantages of LBDDS is their ability to achieve targeted drug delivery. Through passive targeting, these systems exploit the enhanced permeability and retention (EPR) effect, which allows nanoparticles to accumulate selectively in tumor tissues due to their leaky vasculature and poor lymphatic drainage. Additionally, LBDDS can be functionalized with ligands, such as antibodies, peptides, or aptamers, for active targeting, enabling the precise delivery of drugs to cancer cells. This targeted approach minimizes damage to healthy tissues, significantly reducing systemic toxicity and improving the therapeutic index of anticancer drugs[6].

Another critical role of LBDDS is their capacity for controlled and sustained drug release. By modulating drug release kinetics, these systems maintain therapeutic drug levels over extended periods, reducing the frequency of dosing and enhancing patient compliance. Furthermore, lipid carriers provide a protective environment for encapsulated drugs, shielding them from enzymatic degradation and harsh physiological conditions. This ensures better stability and prolongs the shelf life of anticancer agents. LBDDS also play a crucial role in overcoming multidrug resistance (MDR), a significant challenge in cancer therapy. Tumor cells often develop resistance to chemotherapy by overexpressing efflux pumps, such as P-glycoprotein (P-gp), which expel drugs from the cells. Lipid-based systems bypass these mechanisms by facilitating the direct delivery of drugs into the cytoplasm, thereby overcoming MDR and enhancing drug efficacy. Moreover, LBDDS enable the co-delivery of multiple therapeutic agents, such as chemotherapeutic drugs and MDR inhibitors, allowing for synergistic effects in combination therapy. The versatility of LBDDS extends to their ability to deliver a wide range of therapeutic agents, including hydrophilic and hydrophobic drugs, as well as genetic materials like siRNA, mRNA, and DNA. This makes them particularly valuable for cancer immunotherapy, where they are used to deliver immune-modulating agents, such as checkpoint inhibitors or cancer vaccines. For instance, lipid nanoparticles have been employed to deliver mRNA-based cancer vaccines, which stimulate the immune system to recognize and attack tumors.[7-10]

Types of Lipid-Based Drug Delivery Systems

Lipid-Based Drug Delivery Systems are classified into different types and they are explained in detail in forthcoming sections.

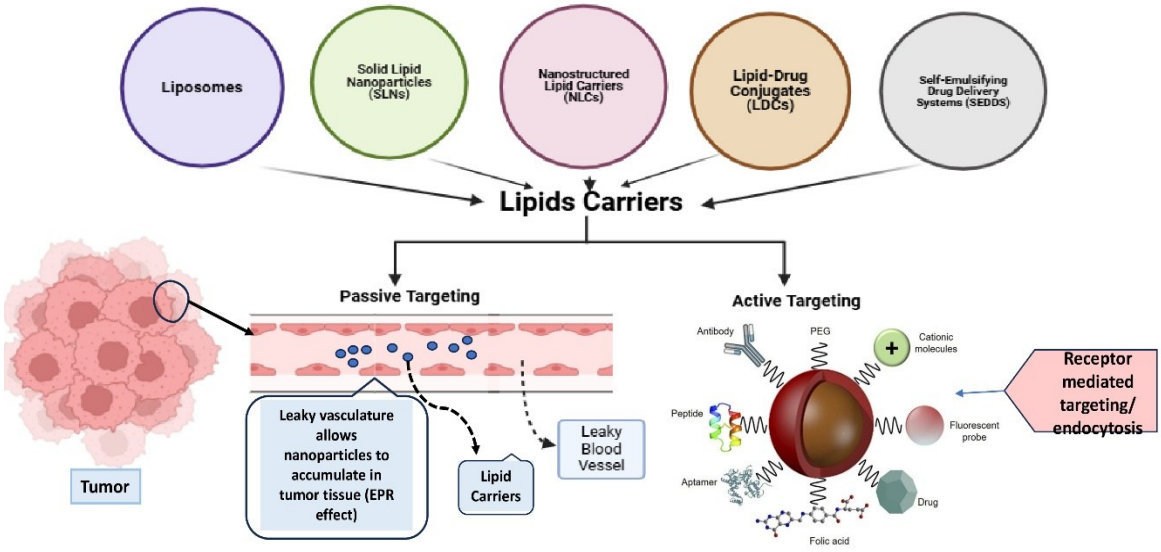

Figure 1: Lipid-Based Drug Delivery Systems: Mechanism of Action in Cancer Therapy

Liposomes:

Liposomes, as lipid-based drug delivery systems, continue to evolve with significant advancements that enhance their application in cancer therapy and beyond. Recent developments in liposome technology focus on overcoming existing limitations, such as stability, drug leakage, and immune clearance, while introducing innovative features for precise and effective drug delivery[11].

One of the most promising innovations in liposome technology is the development of stimuli-responsive liposomes. These advanced carriers are designed to release their drug payload in response to specific tumor microenvironment cues such as pH, temperature, or enzymatic activity. For instance, liposomes sensitive to the acidic pH of the tumor environment ensure the selective release of drugs at the tumor site, minimizing systemic exposure. Another cutting-edge approach is thermoresponsive liposomes, which release drugs upon exposure to hyperthermic conditions, often induced locally through external heat sources. Furthermore, the incorporation of dual-targeting strategies has shown great promise. Liposomes functionalized with ligands that target two different tumor-specific receptors can significantly enhance binding affinity and uptake by cancer cells, improving the therapeutic outcome. For example, combining folic acid and transferrin ligands on liposomes has demonstrated superior efficacy in targeting specific types of cancer cells[12-14].

The advent of gene therapies and RNA-based treatments has expanded liposomal applications, particularly for delivering nucleic acids like siRNA, mRNA, and plasmid DNA in cancer immunotherapy. Lipid nanoparticles (LNPs), a subclass of liposomes, have shown success in mRNA vaccine platforms and are now being adapted for oncology. Multifunctional liposomes capable of co-delivering drugs and gene therapies offer synergistic effects, such as combining cytotoxic drugs with multidrug resistance (MDR) inhibitors, improving efficacy and overcoming drug resistance. Advances in liposome stability, including PEGylation and zwitterionic coatings, have enhanced drug retention and circulation times. Immunoliposomes, conjugated with antibodies, enable precision targeting in oncology, exemplified by HER2-targeted formulations for breast cancer. Beyond cancer, liposomes are

emerging as effective carriers for vaccines, brain-targeted therapies for neurodegenerative diseases, and other therapeutic areas.[14,15]

Solid Lipid Nanoparticles (SLNs):

Solid Lipid Nanoparticles (SLNs) are advanced colloidal carriers composed of biocompatible and biodegradable lipids that remain solid at room and body temperatures, offering a versatile platform for drug delivery. These nanoparticles provide enhanced stability, controlled drug release, and protection for encapsulated drugs against enzymatic degradation. SLNs excel in improving the solubility and bioavailability of poorly water-soluble drugs and can be functionalized with surface modifications like PEGylation or ligand conjugation for targeted delivery. Recent innovations include stimuli-responsive SLNs that release drugs in response to tumor microenvironment triggers like pH or enzymes, making them highly effective in cancer therapy. Additionally, SLNs are being explored for co-delivery of multiple therapeutics, such as anticancer drugs and gene therapies, to achieve synergistic effects. Their potential applications extend to crossing biological barriers, such as the blood-brain barrier, for treating neurological disorders, and they show promise in personalized medicine due to their tunable properties and low systemic toxicity.[16-19]

Nanostructured Lipid Carriers (NLCs):

Nanostructured Lipid Carriers (NLCs) are an advanced drug delivery platform that combines solid and liquid lipids in a unique hybrid structure, creating an amorphous matrix that significantly enhances drug loading, stability, and release efficiency. Unlike traditional carriers, NLCs prevent drug expulsion during storage and allow for fine-tuning of release profiles through the strategic selection of lipid components. Their adaptability enables the co-delivery of diverse therapeutics, including small molecules, peptides, and genetic materials like siRNA or CRISPR-Cas9, paving the way for synergistic treatments. Recent breakthroughs in stimuli-responsive NLCs, which react to tumor-specific triggers such as pH or enzymatic activity, have redefined precision targeting in cancer therapy by minimizing off-target effects. Moreover, NLCs are making strides in crossing biological barriers, such as the blood-brain barrier, offering new possibilities for treating neurological disorders. Their ability to integrate multiple therapeutic strategies while maintaining biocompatibility and low toxicity positions NLCs as a cornerstone of next-generation personalized medicine.[20-24]

Lipid-Drug Conjugates (LDCs):

Lipid-Drug Conjugates (LDCs) represent an emerging and highly versatile approach to drug delivery, leveraging the chemical conjugation of drugs to lipid molecules to overcome solubility, stability, and targeting challenges inherent in conventional therapies. By forming a covalent bond between the drug and lipid, LDCs offer enhanced pharmacokinetic profiles, controlled release, and improved biodistribution. This approach is particularly beneficial for poorly water-soluble drugs, transforming them into amphiphilic conjugates that can self-assemble into nanoparticles, micelles, or liposomes, optimizing their delivery and therapeutic efficacy. LDCs can also enhance membrane permeability, allowing drugs to bypass biological barriers like the gastrointestinal tract or the blood-brain barrier, making them suitable for oral and brain-targeted delivery systems. Recent advancements have introduced stimuli-responsive LDCs, designed to release drugs upon exposure to specific triggers such as pH, temperature, or enzymatic activity, ensuring site-specific drug release and reduced systemic side effects. Additionally, the modular

design of LDCs facilitates the co-conjugation of multiple drugs or the attachment of targeting ligands, enabling personalized combination therapies and precision targeting of disease sites, particularly in cancer and infectious diseases. Emerging research also highlights their potential in gene and RNA delivery, as lipid conjugation improves nucleic acid stability and enhances cellular uptake. With their unique capacity to integrate diverse therapeutic strategies into a single platform, LDCs are poised to address unmet needs in modern medicine, offering transformative solutions for drug delivery challenges across oncology, neurology, and infectious diseases.[25-30]

Self-Emulsifying Drug Delivery Systems (SEDDS):

Self-Emulsifying Drug Delivery Systems (SEDDS) are innovative lipid-based formulations designed to enhance the solubility, stability, and bioavailability of poorly water-soluble drugs, particularly those in Biopharmaceutical Classification System (BCS) Class II and IV. These systems comprise a mixture of oils, surfactants, and co-surfactants that spontaneously form fine oil-in-water emulsions upon mild agitation in aqueous environments, such as the gastrointestinal tract. This self-emulsification mechanism significantly increases the surface area for drug dissolution, bypassing the limitations of conventional formulations. Recent advancements in SEDDS technology include supersaturated SEDDS (S-SEDDS), which create a metastable state with higher drug concentrations, and solid SEDDS, where liquid formulations are adsorbed onto solid carriers for improved handling and stability. SEDDS can be tailored to deliver drugs in a targeted manner by incorporating functional excipients or surface modifications, such as pH-sensitive components or mucoadhesive polymers. Emerging applications include the co-delivery of multiple therapeutic agents, such as small molecules and bioactives like peptides or nucleic acids, for combination therapies. Their ability to bypass hepatic first-pass metabolism and lymphatic transport further positions SEDDS as a transformative platform for oral and systemic delivery, paving the way for more effective and patient-centric drug therapies.[31-34]

Design and Formulation Aspects

Lipid selection

The success of lipid-based drug delivery systems heavily depends on the selection of appropriate lipids, as they form the structural and functional basis of the formulation. Lipids are classified into solid lipids, liquid lipids, and amphiphilic lipids, each offering unique advantages. Solid lipids, such as glyceryl monostearate and stearic acid, provide structural integrity and controlled drug release, making them ideal for Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs). Liquid lipids, such as medium-chain triglycerides (MCTs) and oleic acid, enhance solubility and stability by preventing drug expulsion during storage. Amphiphilic lipids, such as phospholipids (e.g., lecithin), are essential for liposomes and enable the encapsulation of both hydrophilic and lipophilic drugs[35-37].

The selection of lipids is guided by their solubilizing capacity, melting point, and biocompatibility. Lipids with high solubilizing potential ensure efficient drug encapsulation and loading, while those with higher melting points provide thermal stability to the formulation. Biocompatibility and biodegradability are critical to ensuring patient safety, especially for long-term treatments. Advanced formulations often incorporate functional lipids with stimuli-responsive properties, enabling the release of drugs triggered by specific conditions like pH

changes or enzymatic activity, further enhancing the precision of drug delivery[35-37].

Formulation techniques:

Various formulation techniques are used to convert lipid and drug combinations into stable and effective delivery systems. High-pressure homogenization is a widely employed method for producing nanoparticles, where melted lipids and drugs are mixed with emulsifiers and subjected to high pressure to achieve nano-sized particles. This technique is particularly effective for Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs). Another common method is emulsification-solvent evaporation, which involves dissolving drugs and lipids in a volatile organic solvent, emulsifying the mixture in an aqueous phase, and evaporating the solvent to form lipid-based particles[36-38].

Table 1 Common Excipients Used In Lipid Based Formulations

Excipient	Function	Application	Reference
Phospholipids (e.g., Soy Lecithin, Egg Phosphatidylcholine)	Forms lipid bilayer in liposomes, enhances drug encapsulation	Liposomes, solid lipid nanoparticles (SLNs)[11]	Allen & Cullis (2013)
Cholesterol	Stabilizes liposomal membranes, improves drug retention	Liposomes, nanostructured lipid carriers (NLCs)[59]	Torchilin (2005)
Stearic Acid	Solid lipid for nanoparticles, controls drug release	Solid lipid nanoparticles (SLNs)[67]	Mehnert & Mäder (2001)
Glyceryl Monostearate	Surfactant and emulsifier, enhances lipid matrix stability	Nanostructured lipid carriers (NLCs), emulsions[20]	Müller et al. (2011)
Oleic Acid	Permeation enhancer, improves bioavailability	Self-emulsifying drug delivery systems (SEDDS)[68]	Shah et al. (2015)
Tween 80 (Polysorbate 80)	Surfactant, improves solubility and dispersion	Emulsions, micelles, nanoparticles[69]	Date et al. (2012)
PEGylated Lipids (e.g., DSPE-PEG2000)	Prolongs circulation time, reduces immune recognition	Liposomal formulations, PEGylated nanoparticles[70]	Allen et al. (2016)
Sodium Taurocholate	Solubilizer and absorption enhancer	Self-emulsifying drug delivery systems (SEDDS)[73]	Pouton (2000)
Medium Chain Triglycerides (MCTs)	Improves drug solubility, used in lipid emulsions	Lipid-based formulations, parenteral emulsions[72]	Porter et al. (2007)
Ethanol	Co-solvent, improves lipid solubility and formulation stability	Lipid nanoformulations, cosolvent in drug delivery[71]	Pouton & Porter (2006)

Self-Emulsifying Drug Delivery Systems (SEDDS), Self-Microemulsifying Drug Delivery Systems (SMEDDS) and microemulsification uses a mixture of oils, surfactants, and co-surfactants to create thermodynamically stable systems that spontaneously emulsify upon contact with water. Other advanced techniques, such as solvent diffusion and injection, are used to form nanoparticles or liposomes by injecting lipid solutions into aqueous phases, where they self-assemble into nano-sized carriers. Spray drying and lyophilization are often employed to convert liquid formulations into solid forms, improving stability and ease of handling.[36-39]

Encapsulation efficiency and drug loading:

Encapsulation efficiency and drug loading are critical parameters in the design of lipid-based drug delivery systems, directly influencing their therapeutic efficacy and stability. Encapsulation efficiency refers to the percentage of the drug successfully entrapped within the lipid carrier relative to the total drug used, while drug loading indicates the ratio of the drug to the total weight of the formulation, including lipids and other excipients. High encapsulation efficiency ensures minimal drug wastage, while optimal drug loading reduces the carrier burden, enhancing patient compliance. These parameters are influenced by factors such as the solubility of the drug in the lipid matrix, the compatibility of the drug with the lipids, and the formulation process. Hydrophobic drugs generally exhibit higher encapsulation in lipid matrices, whereas hydrophilic drugs may require additional stabilizers or modifications. Techniques like solvent evaporation, high-pressure homogenization, and microemulsification play a crucial role in optimizing these parameters. Advanced strategies, such as selecting lipids with a high affinity for the drug or using amphiphilic surfactants, further enhance drug encapsulation and loading, ensuring a more efficient and effective delivery system.[40-46]

Surface modification for targeted delivery:

Surface modification of lipid-based drug delivery systems is a pivotal strategy for achieving targeted delivery, enhancing therapeutic efficacy while minimizing off-target effects. By functionalizing the surface of carriers with ligands such as antibodies, peptides, aptamers, or small molecules, these systems can selectively bind to overexpressed receptors or antigens on diseased cells, such as tumor cells or inflamed tissues. PEGylation, the attachment of polyethylene glycol chains, is a widely used modification to improve the stealth properties of nanoparticles, reducing immune recognition and extending circulation time, allowing more carriers to reach the target site. Other modifications include pH-sensitive or enzyme-responsive moieties that trigger drug release in specific microenvironments, such as the acidic conditions of tumors or the enzyme-rich extracellular matrix of inflamed tissues. These surface-engineered carriers enable both active and passive targeting, leveraging mechanisms like receptor-mediated endocytosis or the enhanced permeability and retention (EPR) effect. Advances in nanotechnology have enabled multifunctional modifications, allowing simultaneous imaging, therapeutic delivery, and monitoring, further refining precision medicine approaches.[47-53]

Mechanism of Action:

Enhanced permeability and retention (EPR) effect:

The Enhanced Permeability and Retention (EPR) effect is a fundamental mechanism leveraged by lipid-based drug delivery systems to achieve passive targeting of tumors and inflamed tissues. This phenomenon arises from the unique pathophysiological characteristics of tumor

vasculature, which is highly disorganized, leaky, and poorly developed compared to normal tissues. The large fenestrations in tumor blood vessels allow nanoparticles, such as liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), to preferentially accumulate within tumor tissues while minimizing distribution to healthy tissues. Additionally, the impaired lymphatic drainage in tumors prevents the clearance of these nanoparticles, further enhancing their retention at the site. Lipid-based carriers are particularly effective in exploiting the EPR effect due to their customizable size, typically within the optimal range (10–200 nm), and their biocompatible lipid composition, which facilitates prolonged circulation and reduced immune clearance. The EPR effect forms the basis for many FDA-approved lipid-based drugs, such as Doxil® (liposomal doxorubicin), and is a cornerstone of targeted cancer therapy, enabling higher drug concentrations at tumor sites with reduced systemic toxicity.[54-56]

Active and passive targeting strategies:

Active and passive targeting are two key strategies employed in lipid-based drug delivery systems to enhance therapeutic precision and efficacy. Passive targeting relies on the Enhanced Permeability and Retention (EPR) effect, which allows lipid nanoparticles such as liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs) to accumulate in tumors due to their leaky vasculature and poor lymphatic drainage. This mechanism enables selective drug delivery to tumor tissues without the need for specific targeting ligands, making it ideal for treating solid tumors. In contrast, active targeting involves the functionalization of lipid carriers with ligands such as antibodies, peptides, aptamers, or small molecules that bind to specific receptors overexpressed on target cells (e.g., HER2 in breast cancer or folate receptors in ovarian cancer). This receptor-mediated approach enhances cellular uptake via endocytosis, ensuring precise delivery to diseased tissues while sparing healthy cells. Advances in lipid nanotechnology have enabled the combination of active and passive targeting strategies, optimizing both tumor accumulation and intracellular drug delivery. These approaches significantly improve therapeutic outcomes, reduce systemic toxicity, and support the development of personalized medicine.[57,58]

Intracellular drug release mechanisms:

Intracellular drug release mechanisms in lipid-based drug delivery systems are designed to ensure that therapeutic agents reach their target site within cells for maximum efficacy. Once lipid nanoparticles, such as liposomes, solid lipid nanoparticles (SLNs), or nanostructured lipid carriers (NLCs), are internalized by target cells via endocytosis, they are typically trafficked to endosomes. Drug release can be triggered by various intracellular stimuli, such as the acidic pH within endosomes or lysosomes, leading to destabilization of the lipid carrier and release of the drug into the cytoplasm. pH-sensitive lipids, such as those containing ionizable moieties, are often employed to facilitate this process. In some cases, enzymes present within the cell, such as esterases or proteases, can degrade the lipid matrix, enabling controlled drug release. Alternatively, redox-sensitive carriers utilize the high glutathione levels in the cytoplasm to trigger drug release via reduction reactions. Advanced designs also include light- or temperature-sensitive lipids that release drugs upon exposure to external stimuli. These mechanisms ensure precise drug delivery to intracellular targets, enhancing therapeutic outcomes, particularly in cancer and gene therapies.[59,60]

SUMMARY

Applications in Precision Oncology

Delivery of Chemotherapeutics: Lipid-based formulations such as liposomes (e.g., Doxil®) enhance the solubility and stability of chemotherapeutic agents, enabling targeted delivery to tumor tissues via the Enhanced Permeability and Retention (EPR) effect, reducing systemic toxicity.[61]

Gene and RNA-Based Therapies (siRNA, mRNA, DNA): Lipid nanoparticles (LNPs) have revolutionized the delivery of nucleic acids by protecting them from enzymatic degradation and facilitating cellular uptake, exemplified by their use in mRNA vaccines and siRNA-based cancer therapies.[62]

Combination Therapy (Drug-Drug, Drug-Gene): Lipid carriers allow the co-delivery of chemotherapeutics with MDR inhibitors or gene therapies, such as siRNA targeting resistance pathways, achieving synergistic effects in cancer treatment.[63]

Table 2 Marketed Products Of Lipid Based Formulations In Oncology

Marketed Product	Company	Excipients	Drug	Reference
Doxil®	Janssen Pharmaceuticals	Liposomes (Hydrogenated Soy Phosphatidylcholine, Cholesterol, PEGylated Lipids)	Doxorubicin[74]	Barenholz, Y. et al
Abraxane®	Celgene Corporation	Albumin-bound nanoparticles	Paclitaxel[75]	Desai, N. et al
Marqibo®	Talon Therapeutics	Liposomal vincristine formulation	Vincristine[76]	Silverman, J. A.et al
Myocet®	Zeneus Pharma	Liposomes (Cholesterol, Phosphatidylcholine)	Doxorubicin[77]	Batist, G. et al.
DaunoXome®	Gilead Sciences	Liposomes (Cholesterol, Phospholipids)	Daunorubicin[78]	Gill, P. S. et al
Lipusu®	Luye Pharma	Liposomal formulation (Soybean Phospholipid)	Paclitaxel[79]	Tan, Z. et al
Genexol-PM®	Samyang Biopharm	Polymeric micelles (Methoxy-PEG-polylactide)	Paclitaxel[80]	Kim, T. Y. et al
Onivyde®	Ipsen	Liposomal irinotecan formulation	Irinotecan[81]	Wang-Gillam, A. et al
Aroplatin®	Antigenics Inc.	Liposomal cisplatin formulation	Cisplatin[82]	Silverman, J. A. et al

Future Perspectives

Innovations in Lipid-Based Technologies

Lipid-based drug delivery systems are witnessing groundbreaking innovations aimed at addressing challenges like drug stability, targeted delivery, and efficient therapeutic outcomes. Recent

advancements include stimuli-responsive lipids that release drugs in response to specific triggers such as pH, temperature, or enzymatic activity. These systems are particularly useful for targeting tumor microenvironments. Additionally, lipid-based carriers are being combined with novel materials, such as polymers and inorganic nanoparticles, to create hybrid systems with enhanced functionality. For instance, lipid-polymer hybrid nanoparticles offer the structural integrity of polymers and the biocompatibility of lipids, improving drug encapsulation and release profiles. Technologies like 3D printing are also being explored to customize lipid formulations for specific patient needs. Such innovations not only improve efficacy but also expand the applicability of lipid-based systems in diverse therapeutic areas.[64]

Personalized Medicine and Theranostics

Lipid-based technologies are at the forefront of personalized medicine and theranostics, integrating therapy and diagnostics into a single platform. Lipid nanoparticles can be functionalized with imaging agents, such as fluorescent dyes or radioactive isotopes, allowing real-time monitoring of drug distribution and therapeutic outcomes. These systems enable the simultaneous delivery of drugs and diagnostic agents to specific sites, facilitating tailored treatment plans based on an individual's disease profile. For example, HER2-targeted liposomes can deliver chemotherapy while imaging tumor responses in HER2-positive breast cancer patients. Additionally, lipid-based carriers are being developed for gene editing technologies like CRISPR-Cas9, enabling precision treatments for genetic diseases. As the era of precision medicine evolves, lipid-based theranostics provide a powerful tool for tailoring treatments to individual patients, improving outcomes and reducing adverse effects.[65]

Emerging Trends in Nanomedicine for Oncology

Nanomedicine for oncology is rapidly evolving, with lipid-based systems playing a pivotal role in addressing unmet needs in cancer therapy. Emerging trends include the development of multifunctional lipid nanoparticles capable of co-delivering chemotherapeutics, gene therapies, and immune-modulating agents. These carriers are increasingly being designed to overcome multidrug resistance (MDR) through co-delivery strategies or by bypassing efflux pumps. Furthermore, the integration of artificial intelligence (AI) and machine learning is facilitating the design of lipid nanoparticles with optimal properties for specific cancer types. AI-driven algorithms predict particle behavior, drug release profiles, and tumor targeting efficiency, streamlining the development process. Personalized lipid nanomedicines, tailored to a patient's genetic and molecular tumor profile, are becoming a reality, pushing the boundaries of oncology treatment and improving patient survival rates.[66,83]

CONCLUSION

Lipid-based drug delivery systems have emerged as a cornerstone in modern medicine, addressing critical challenges such as poor drug solubility, stability, and off-target effects. Advances in lipid formulations, including liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), have significantly enhanced the precision, efficiency, and safety of therapeutic delivery. These technologies have been instrumental in revolutionizing oncology, enabling both passive and active targeting through mechanisms like the Enhanced Permeability and Retention (EPR) effect and receptor-mediated delivery. The integration of these systems with gene therapies, RNA-based treatments, and

theranostics further underscores their versatility. As precision medicine evolves, lipid-based carriers hold immense potential to tailor treatments to individual patients, reduce systemic toxicity, and improve therapeutic outcomes. Innovations such as stimuli-responsive lipids and hybrid systems with multifunctional capabilities continue to push the boundaries of personalized oncology care. With ongoing research, these systems are poised to play a transformative role in redefining cancer treatment paradigms and improving patient survival and quality of life.

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