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The role of nanotherapeutics in the treatment of Cancer

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Abstract
Using the special qualities of nanoparticles to improve drug delivery and therapeutic efficacy, nanotherapeutics has become a game-changing method of treating cancer. Conventional cancer treatments, such as radiation, chemotherapy, and surgery, frequently have drawbacks such systemic toxicity, non-specific targeting, and drug resistance. These formulations enhance the delivery of immunotherapeutic and nucleic acids while enhancing chemotherapeutics' pharmacokinetics and bioavailability. Prominent FDA-approved nanotherapeutics like Abraxane® and Doxil® serve as examples of this strategy's clinical effectiveness. Biological barriers that prevent efficient drug transport, regulatory obstacles that make clinical translation more difficult, and safety worries about long-term toxicity still pose problems despite these developments. To overcome current obstacles and fully utilize nanotechnology in oncology, more research is necessary.

Keywords: Nanotherapeutics, cancer drug delivery, targeted nanomedicine, polymeric nanoparticles, liposomes in oncology, solid lipid nanoparticles, nanotechnology in cancer treatment

Introduction

Cancer is a major global health issue affecting millions worldwide [1]. In 2022, about 20 million new cases and 9.7 million deaths were reported, and annual cases may rise to nearly 30 million by 2040 [2]. The burden is greater in low- and middle-income countries due to limited access to early diagnosis and effective treatment [3]. This highlights the need for improved therapeutic strategies, including nanotherapeutics [4].

Nanotherapeutics involve the use of nanoscale materials (1–100 nm) to develop advanced drug delivery systems [5]. Due to their small size and modifiable surface properties, nanoparticles can enhance drug solubility, stability, and bioavailability while enabling targeted delivery to tumors [6]. A major benefit is precise drug targeting [7]. Conventional chemotherapy often damages healthy cells along with cancer cells [8], causing severe side effects and limiting treatment success [9]. In contrast, nanotherapeutics can target tumor-specific markers, improving efficacy and reducing toxicity [7]. They may also help overcome drug resistance in cancer therapy [10]. Additionally, nanoparticles can carry chemotherapeutic agents, nucleic acids, and immunotherapeutics [11], demonstrating strong potential to improve survival outcomes [12].

In summary, nanotherapeutics represent a significant advancement in oncology [13]. By integrating nanotechnology with conventional treatments, they enhance effectiveness, lower toxicity, and support personalized medicine approaches [14]. Further discussion will explore their mechanisms, benefits, challenges, and future prospects in cancer treatment [15].

Nanotherapeutics

Nanotherapeutics is a multidisciplinary field integrating nanotechnology with therapeutic applications, particularly in cancer treatment [16]. It focuses on using nanoparticles (1–100 nm) to improve the efficacy and safety of anticancer therapies [17]. This approach addresses limitations of conventional treatments, including non-specific drug distribution, systemic toxicity, and drug resistance [18].

Definition and Types of Nanoparticles

The size and distinct physicochemical characteristics of nanoparticles set them apart from their bulk counterparts. Cancer treatment uses a variety of nanoparticle kinds, each with unique properties and uses [19].

Liposomes in Cancer Therapy

Because they are spherical vesicles made of phospholipid bilayers encasing an aqueous core, liposomes are exceptionally successful drug delivery vehicles in cancer treatment [20]. Because of their special structure, both hydrophilic and hydrophobic medications can be encapsulated, offering a range of therapeutic applications [21]. Liposomes have drawn a lot of attention since Alec Bangham discovered them in the 1960s because of their capacity to boost the therapeutic efficiency of several anticancer medicines, decrease systemic toxicity, and improve the pharmacokinetic characteristics of medications [22].

Composition and Structure

Phospholipids, which can be produced chemically or obtained naturally (such as soy lecithin), make up the majority of liposomes [23, 24]. A liposome's fundamental structure is made up of:

Phospholipid Bilayer

This bilayer, which makes up the liposome's outer shell, can be altered with various lipid compositions to improve stability and usefulness [24]. While the hydrophobic (water-repelling) tails of the phospholipids face inward, away from water, the hydrophilic (water-attracting) heads face outward toward the aquatic environment [23].

Aqueous Core

Hydrophilic medications can be encapsulated in the liposome's core cavity for controlled release and degradation prevention. This characteristic is especially advantageous for chemotherapeutic drugs that are soluble in water [25].

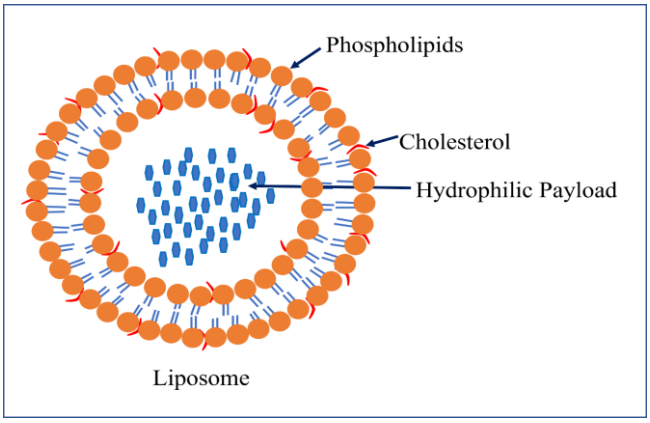

Fig 1: Structure of Liposome

Cholesterol

Cholesterol improves the stability and fluidity of liposomes and is frequently integrated into the lipid bilayer. It can affect medication release profiles and aids in maintaining membrane integrity during bloodstream circulation [26].

Surface Modifications

To increase targeting capabilities and circulation time, liposomes can be functionalized with polyethylene glycol (PEG) or other targeting ligands [27]. PEGylation increases the liposome's half-life in circulation by decreasing immune system recognition [28]. Liposomes are usually between 50 to several micrometers in size [29, 27]. Larger liposomes may collect more efficiently in tumors because of the Enhanced Permeability and Retention (EPR) effect, but smaller liposomes typically have superior tissue penetration and cellular uptake. [30]

2.3 Advantages of Liposomal Formulations

Liposomes provide several advantages over conventional drug delivery systems [31, 27].

Improved pharmacokinetics: Liposomal formulations often exhibit prolonged circulation due to their size and surface modifications that help evade immune clearance, enabling sustained drug exposure at tumor sites [32, 33].

Reduced toxicity: Drug encapsulation in liposomes can significantly lower systemic toxicity, including doxorubicin-associated cardiotoxicity, thereby improving patient tolerability and quality of life [34, 35].

Versatile drug loading: Liposomes can carry diverse therapeutic agents such as small molecules, proteins, nucleic acids, and imaging compounds for theranostic applications, supporting personalized treatment strategies [36].

Enhanced solubility: By improving aqueous solubility of poorly soluble chemotherapeutics, liposomal systems facilitate intravenous administration and better drug absorption [37, 38].

Clinical Applications

Many liposomal formulations have been created and authorized for use in cancer treatment in clinical settings. Among the noteworthy instances are

Table 1: Example of Liposomal Formulations

Liposomal Drug	Active Ingredient	Indication	Approval Year
Doxil® (liposomal doxorubicin)	Doxorubicin	Breast cancer, ovarian cancer	1995
Abraxane® (albumin-bound paclitaxel)	Paclitaxel	Metastatic Breast Cancer	2005
Marqibo® (liposomal vincristine)	Vincristine	Acute Lymphoblastic Leukaemia	2012
Onivyde® (liposomal irinotecan)	Irinotecan	Metastatic pancreatic cancer	2015

Challenges and Limitations

Liposomal formulations offer benefits but also present limitations. Although EPR-based targeting improves tumor drug accumulation, it does not ensure complete specificity, allowing distribution to healthy tissues and possible side effects [39, 40]. Their preparation requires complex and costly techniques, such as thin-film hydration and microfluidics, and variability in manufacturing can hinder batch consistency [41]. While liposomes generally lower systemic toxicity compared with free drugs, hypersensitivity reactions and lipid-related toxicities may still occur [42]. Moreover, clinical translation of new liposomal systems is often delayed due to strict regulatory requirements and extensive safety assessments [43].

Polymeric Nanoparticles in Cancer Therapy

Polymeric nanoparticles (PNPs) have become important in modern cancer therapy due to their versatile drug delivery capabilities [44]. Typically ranging from 10–1000 nm, these carriers can encapsulate or conjugate diverse agents such as chemotherapeutics, proteins, and nucleic acids [45]. Their unique physicochemical properties enable targeted tumor delivery, improved bioavailability, and controlled drug release, helping overcome limitations of conventional treatments [46].

Types of Polymeric Nanoparticles

Based on their composition and structure, polymeric nanoparticles can be divided into different groups. Each variety has unique traits and uses that increase their usefulness in cancer treatment [47]

Polymeric Micelles

Polymeric micelles, which are created when amphiphilic block copolymers self-assemble in aqueous solutions, usually include a hydrophilic shell that improves solubility and stability in circulation and a hydrophobic core that can encapsulate hydrophobic medications (such as doxorubicin and paclitaxel) [48]. Polymeric micelles can be passively targeted via the Enhanced Permeability and Retention (EPR) effect because of their typical size range of 10 to 100 nm [49]. Their capacity to solubilize medications that are poorly soluble in water is especially advantageous for enhancing the bioavailability of specific chemotherapeutics [50]

Nanospheres and Nano capsules

Solid polymeric particles known as nanospheres have the ability to either adsorb pharmaceuticals onto their surface or encapsulate them within their matrix [51]. Because of their porous porosity, they are frequently employed for prolonged drug release [52]. In contrast, a polymeric shell enclosing a drug-containing liquid core makes up nanocapsules [53]. Both kinds can be designed for certain release profiles, enabling regulated distribution over long timeframes [51, 53].

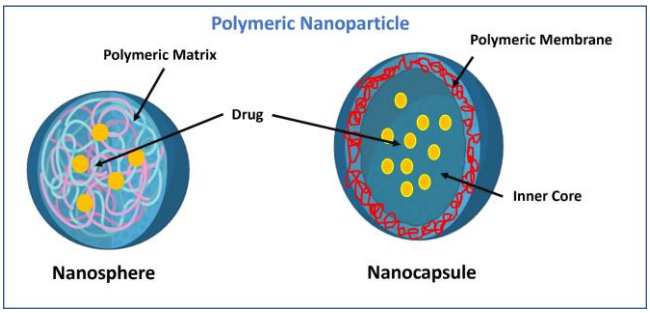

Fig 2 : Polymeric Nanoparticle

Nanogels

In watery settings, these three-dimensional networks of crosslinked polymers swell [54]. Controlled medication release in response to particular conditions within the tumor microenvironment is made possible by nanogels' ability to react to environmental stimuli like pH, temperature, or ionic strength [55]. Because of their reactivity, nanogels are very appealing for site-specific therapeutic delivery [56].

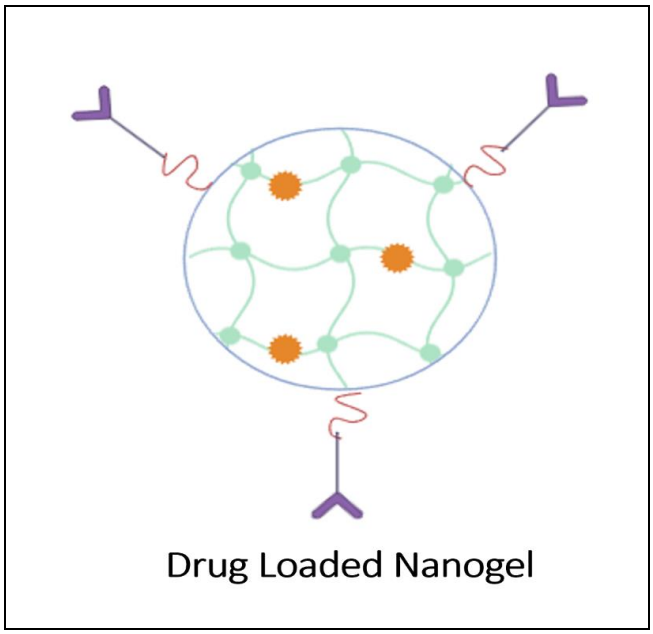

Fig 3 : Structure of Drug Loaded Nanogel

Polymerases

The bilayer structure of polymerases, which are similar to liposomes but composed of block copolymers, enables the encapsulation of both hydrophilic and lipophilic medications [57]. They are good options for combination therapy where several medications must be administered at once due to their stability and capacity to carry heavier payloads [58].

Mechanisms of Action

The two main ways that polymeric nanoparticles improve medication delivery are passive targeting and active targeting [59].

Passive Targeting

This method takes use of the EPR effect, which occurs when nanoparticles preferentially gather in tumor tissues as a result of the tumors' leaky vasculature [60]. Nanoparticles can enter the tumor interstitial because tumor blood arteries are frequently more permeable than those in healthy tissues [61]. Furthermore, tumors have inadequate lymphatic drainage, which makes it easier for nanoparticles to stay in the tumor microenvironment [62]. Higher local concentrations of therapeutic drugs at the tumor site are made possible by this passive accumulation, which also reduces systemic exposure and any adverse consequences [63].

Active Targeting

PNPs can selectively bind to receptors that are overexpressed on cancer cells by functionalizing their surface with certain ligands, such as peptides, antibodies, or small molecules [64, 65]. For example, folate-conjugated nanoparticles are very useful for targeted administration since folate receptors are frequently overexpressed in some malignancies (such as ovarian cancer) [66, 67]. Through receptor-mediated endocytosis, this tailored contact increases cellular absorption in addition to improving drug delivery selectivity [68]. Stimuli-responsive nanoparticles, which release their payload in response to particular environmental triggers (such as pH changes or enzyme activity), may also be used in active targeting tactics [69].

Advantages of Polymeric Nanoparticles

Polymeric nanoparticles (PNPs) offer multiple advantages in cancer therapy.

High drug loading: Their porous or core–shell structure enables encapsulation of substantial amounts of therapeutic agents, allowing effective treatment at lower doses and reducing dose-related side effects [70, 71].

Controlled release: Drug release can be tailored by modifying polymer composition. Hydrophilic polymers may allow faster release, whereas hydrophobic polymers provide sustained delivery, maintaining therapeutic levels and minimizing toxic peak concentrations [72–74].

Biocompatibility and biodegradability: Many PNPs are made from biocompatible, biodegradable polymers that minimize immune reactions and gradually degrade after drug delivery, reducing long-term toxicity [75–77].

Versatility: PNPs can co-deliver multiple drugs for combination therapy, which is beneficial in managing complex cancers requiring multi-targeted approaches [78, 79]

Challenges

Despite their potential, several challenges hinder the clinical translation of polymeric nanoparticles. These include [80]:

Manufacturing Consistency: For clinical applications, batch-to-batch uniformity in nanoparticle synthesis is essential [81].

Regulatory Hurdles: Navigating regulatory pathways for approval can be complex due to the novel nature of nanomedicine [82].

In *Vivo* Stability: Maintaining stability in biological environments while ensuring effective drug release remains a challenge [83].

Current Applications

Polymeric nanoparticles have shown promise across various cancer types. Below is a summary table highlighting some notable applications [84]:

Table 2: Types of Polymeric Nanoparticle

Type of Polymeric Nanoparticle	Size Range (nm)	Therapeutic Agent(s)	Cancer Type(s)	Key Features
Polymeric Micelle	10 - 100	Doxorubicin	Breast cancer	Enhanced solubility; reduced side effects
Nanosphere	100 - 500	Paclitaxel	Colorectal cancer	Sustained release; improved bioavailability
Nanogel	50 - 300	Cisplatin	Lung cancer	Stimuli-responsive; controlled drug release
Dendrimer	5 - 20	RNA therapeutics	Brain cancer	High drug loading efficiency; targeted delivery
Polymersome	100 - 500	Combination therapies	Various cancers	Dual-drug delivery; enhanced targeting apabilities

Dendrimers in Cancer Therapy

Structural Properties of Dendrimers

Multivalency: Dendrimers possess multiple terminal functional groups that can be modified to attach drugs, imaging agents, or targeting ligands, enabling simultaneous delivery and enhanced interaction with biological targets [89].

Nanoscale size: Typically measuring 1–10 nm, dendrimers can cross biological membranes and accumulate in tumors via the EPR effect, while their small size supports improved circulation time [90].

Monodispersity: Their highly branched architecture results in uniform size and shape, ensuring reproducible drug delivery with consistent pharmacokinetic and pharmacodynamic behavior [91].

Surface Functionalization: Researchers can customize dendrimers' characteristics for particular uses by altering their surface chemistry. Terminal groups, for instance, can be changed to increase solubility, boost biocompatibility, or make it easier to target particular cell types.

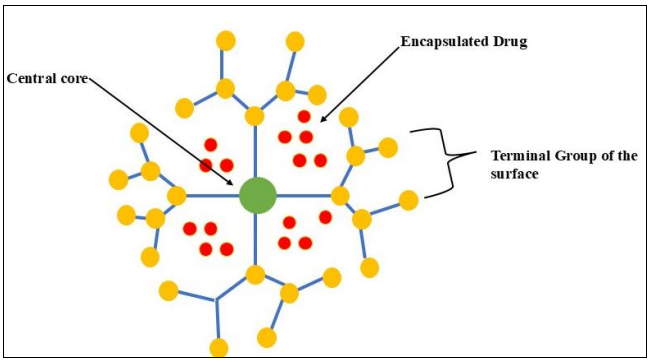

Fig 4 : Structure of Dendrimers

Mechanisms of Action

Dendrimers can deliver anticancer drugs through several mechanisms:

Physical Encapsulation: Non-covalent interactions like hydrogen bonds and van der Waals forces can physically trap drugs inside the dendrimer structure. Drugs can be released to the tumor site gradually over time thanks to this encapsulation, which enables regulated release patterns [92].

Covalent Conjugation: Chemical bonds can be used to covalently attach therapeutic substances to the surface of the dendrimer [93]. This technique gives the medication stability and guarantees that it stays attached until it reaches the intended location. Additionally, precise control over drug loading and release rates is made possible via covalent conjugation [94].

Electrostatic Interactions: Charged drugs can interact with the charged surface of dendrimers through electrostatic forces. This mechanism facilitates drug loading into the dendrimer and can influence the release profile based on changes in environmental conditions (e.g., pH) [195].

Receptor-Mediated Endocytosis: Certain ligand-functionalized dendrimers can attach to receptors that are overexpressed on cancer cells, such as HER2 or folate receptors. Through receptor-mediated endocytosis, this specific connection improves cellular uptake and makes it possible to deliver therapeutic drugs more effectively straight into cancer cells.

Applications in Cancer Therapy

Dendrimers have been explored for various cancer therapy applications.

Targeted drug delivery: Surface modification with ligands such as antibodies or small molecules enables tumor-specific targeting. For example, trastuzumab-conjugated PAMAM dendrimers enhance docetaxel delivery and apoptosis in HER2-positive breast cancer cells compared with non-targeted systems [96, 97].

Combination therapy: Dendrimers can co-deliver multiple agents or integrate modalities like chemotherapy and photothermal therapy, producing synergistic anticancer effects in preclinical models [98].

Diagnostic use: Conjugation with MRI contrast agents or fluorescent dyes allows improved tumor imaging and detection through tunable physicochemical properties [99].

Gene delivery: Their ability to encapsulate nucleic acids supports gene therapy applications, including delivery of plasmid DNA or siRNA targeting oncogenes to suppress tumor growth [100].

Theranostics: Dendrimer platforms can combine therapy and imaging, enabling simultaneous drug delivery and real-time monitoring of treatment response [101].

Advantages of Using Dendrimers in Cancer Treatment

Dendrimers provide a number of strong benefits over traditional drug delivery methods, including:

Table 3: Advantages of Dendrimers in Cancer Treatment

Advantages	Description
Controlled Release	Through a variety of processes, including covalent conjugation and physical encapsulation, dendrimers allow for the prolonged release of medications at the tumor site. This lessens systemic negative effects while increasing treatment efficacy.
Targeted Delivery	By functionalizing with particular ligands, cancer cells can be targeted specifically, reducing harm to healthy tissues and improving the efficacy of treatment.
High Drug Loading Capacity	Because of its high surface area-to-volume ratio and branching structure, dendrimers can encapsulate a sizable number of medicinal drugs
Biocompatibility	Many dendrimer formulations are biocompatible and biodegradable, reducing toxicity concerns associated with traditional chemotherapeutics while enhancing patient safety.
Versatility	The ability to modify surface chemistry allows for customization based on specific therapeutic needs or targeting requirements, enabling tailored treatment strategies.
Multifunctionality	Dendrimers can improve overall treatment efficacy and monitoring capacities by delivering numerous therapeutic agents at once or combining therapeutic and diagnostic functions on a single platform.

Challenges

Despite their potential benefits, several challenges remain in the clinical application of dendrimers:

Toxicity Concerns: While many dendrimer formulations are biocompatible, some may exhibit cytotoxicity depending on their size, charge, and surface modifications. Understanding these interactions is crucial for developing safe formulations [102].

Regulatory Hurdles: The complex nature of dendrimer formulations may pose challenges in regulatory approval processes compared to conventional therapies. Comprehensive studies on safety and efficacy are essential before clinical use.

Scalability of Production: The synthesis of dendrimers can be complex and costly due to multi-step processes required for their preparation and functionalization. Developing scalable manufacturing methods is vital for widespread clinical adoption.

Solid Lipid Nanoparticles (SLNs) in Cancer Therapy

Solid lipid nanoparticles (SLNs), which combine the benefits of conventional drug delivery methods with the special qualities of nanotechnology, have become a very promising platform in cancer therapy. These solid lipid-based nanoparticles offer improved stability and regulated release of therapeutic ingredients because they stay solid at body temperature as well as room temperature. The composition, manufacturing processes, mechanisms of action, benefits, and current uses of SLNs in cancer treatment are all thoroughly examined in this section [103].

Composition and Structure

Biocompatible and biodegradable lipids, which might be synthetic or natural, make up the majority of SLNs. The lipid selection is important since it affects the nanoparticles' stability, release kinetics, and drug loading capacity, among other physicochemical characteristics. Lipids that are frequently utilized in SLN formulations include.

Triglycerides: These are esters derived from glycerol and three fatty acids. Tristearin and tripalmitin are examples that provide a stable matrix for drug incorporation while being well-tolerated by the body [104].

Fatty Acids: It is possible to improve the characteristics of SLNs by using fatty acids like palmitic or stearic acid. These lipids help create the solid-state properties required to keep things stable while being administered and stored [105].

Phospholipids: Compounds like phosphatidylcholine can be included to improve biocompatibility and facilitate interactions with cell membranes. Phospholipids help to stabilize SLNs through their amphiphilic nature, allowing for better dispersion in biological fluids.

Therapeutic chemicals are encapsulated in a solid lipid core that makes up the structure of SLNs., surrounded by surfactants that stabilize the nanoparticle formulation. Surfactants such as polysorbates or cetyl alcohol are often employed to prevent aggregation and maintain a uniform size distribution [106].

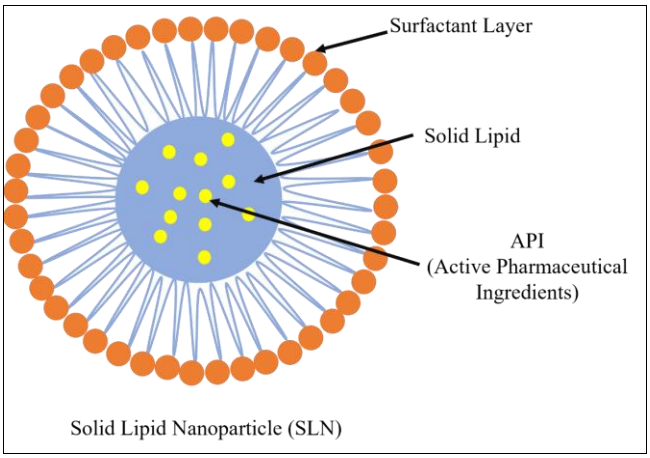

Fig 5 : Structure of Solid Lipid Nanoparticle

Production Methods

There are various methods for formulating SLNs, and each has unique benefits in terms of repeatability, scalability, and control over particle properties:

High-Shear Homogenization This technique uses high-speed mixing to get lipid droplets down to the nanoscale. The lipid phase must normally be heated above its melting point before being emulsified in an aqueous phase that contains surfactants. Solidification is made possible by cooling after homogenization. This method's simplicity and capacity to generate SLNs with tight size distributions make it popular.

Microemulsion-Based SLN: In this technique, microemulsions serve as templates for SLN formation [107]. A microemulsion is formed by mixing oil, water, and surfactants under specific conditions. Upon cooling or upon dilution with water, solid lipid nanoparticles precipitate out from the microemulsion. Compared to other approaches, this technology offers greater control over drug loading and particle size.

Supercritical Fluid Technology: This advanced method utilizes supercritical fluids (such as carbon dioxide) to dissolve lipids and drugs under high pressure. The rapid depressurization leads to nanoparticle formation through precipitation. This technique offers benefits such as solvent-free processing and high purity but may require specialized equipment.

Spray Drying: In spray drying, a liquid formulation containing lipids and drugs is atomized into a hot gas stream, rapidly evaporating the solvent and resulting in dry nanoparticles [147]. This method is advantageous for producing large quantities of SLNs but may require optimization to ensure adequate drug encapsulation [148].

Solvent Emulsification/Evaporation: With this method, pharmaceuticals and lipids are dissolved in organic solvents and subsequently emulsified in an aqueous phase that contains surfactants [149]. Solid nanoparticles are created when the organic solvent is subsequently evaporated at a lower pressure. Although this approach is flexible, it necessitates careful solvent selection to guarantee biocompatibility [150].

Mechanisms of Action

SLNs enhance drug delivery through several key mechanisms:

Passive Targeting via EPR Effect: Because the endothelial cells that line the tumor vasculature are faulty, tumors frequently have aberrant blood vessel architectures that are characterized by increased permeability [151]. Tumors also have inadequate lymphatic drainage networks. Through the Enhanced Permeability and Retention (EPR) effect, these properties enable the passive accumulation of nanoparticles within tumor tissues [152]. SLNs can thereby increase local concentrations at tumor locations while limiting exposure to healthy organs, which is crucial for lowering the systemic toxicity linked to traditional chemotherapy [153].

Active Targeting: Targeting ligands, such as antibodies, peptides, or small compounds that selectively bind to receptors overexpressed on cancer cells (such as HER2 or folate receptors), can be functionalized with SLNs to further improve specificity [154]. By increasing cellular uptake through receptor-mediated endocytosis, this active targeting mechanism makes sure that therapeutic drugs are predominantly supplied to cancer cells rather than healthy cells [155]. These changes not only increase the effectiveness of treatment but also lessen the negative consequences of non-specific drug distribution [156].

Advantages of Solid Lipid Nanoparticles

Solid lipid nanoparticles (SLNs) provide key benefits for cancer drug delivery. Their solid lipid matrix enhances stability, prolonging shelf life and maintaining drug potency [157]. By adjusting lipid and surfactant composition, SLNs enable sustained release, preserving therapeutic levels while reducing peak-related toxicity [158]. Encapsulation improves solubility and bioavailability of hydrophobic drugs such as paclitaxel and curcumin [159]. Targeted delivery decreases systemic exposure to cytotoxic agents, minimizing chemotherapy side effects and improving quality of life [160]. Moreover, SLNs allow multifunctional use, including co-delivery of drugs and integration of imaging agents for combination and diagnostic applications [161]

Current Applications

Numerous studies have explored the potential applications of SLNs for delivering various anticancer agents across different types of cancers [163].

These applications highlight how SLNs can be tailored for specific therapeutic needs across various cancer types while addressing issues related to drug solubility, stability, and targeting efficiency [167].

Advantages of Nanotherapeutics in Cancer Treatment

Nanotherapeutics have revolutionized cancer treatment by providing significant advantages over traditional therapeutic modalities [168]. Among these advantages, improved drug delivery stands out as a critical factor that enhances the efficacy and safety of cancer therapies [169]. This section will explore two primary aspects of improved drug delivery: enhanced bioavailability and pharmacokinetics, as well as focused administration to tumor locations to reduce adverse effects [170].

Improved Drug Delivery

Enhanced bioavailability and pharmacokinetics: Nanotherapeutics improve anticancer drug solubility, circulation time, and distribution, overcoming rapid clearance and non-specific delivery seen with conventional chemotherapy [171]. Their nanoscale size enables passage across biological barriers and prolonged circulation when designed above renal clearance limits, increasing plasma half-life and sustaining therapeutic levels [172–174]. Nanocarriers also enhance tumor accumulation through altered biodistribution, mainly via the EPR effect, which promotes preferential deposition in tumors and reduces systemic toxicity [175–177].

Targeted tumor delivery: Nanoparticles enable precise drug delivery, addressing the poor specificity of traditional therapies [178]. Passive targeting uses the EPR effect for tumor accumulation [179, 180], while active targeting involves ligand attachment—such as antibodies or peptides—to bind tumor-specific receptors and enhance receptor-mediated uptake [181]. This strategy improves cellular internalization and minimizes off-target effects [182]. Examples include nanoparticles targeting folate or HER2 receptors, enabling selective tumor destruction [183, 184]. Additionally, nanotherapeutics support combination therapy by co-delivering multiple drugs within a single carrier, generating synergistic effects with reduced toxicity

Overcoming Drug Resistance

One of the biggest problems in oncology is cancer medication resistance, especially multidrug resistance (MDR), which frequently results in treatment failure and

subpar patient outcomes. Drug efflux pump overexpression, changes in drug targets, modifications in cellular metabolism, and the impact of the tumor microenvironment on treatment efficacy are some of the pathways that can lead to MDR [186]. A possible way to combat these resistance mechanisms and improve the efficacy of cancer treatments is through nanotherapeutics. The different ways that nanotherapeutics can defeat MDR in cancer cells are examined in this section [187].

Mechanisms by Which Nanotherapeutics Counteract Multidrug Resistance (MDR)

Inhibition of Drug Efflux Pumps

The increase of ATP-binding cassette (ABC) transporters, which actively pump chemotherapeutic drugs out of cancer cells, lowering their intracellular concentrations and potency, is one of the main mechanisms causing MDR [188, 189]. Drugs can be encapsulated in nanoparticles to avoid these transporters or to directly inhibit these efflux pumps. For example, it has been demonstrated that specific nanoparticle formulations inhibit P-glycoprotein (P-gp), a well-known drug efflux pump linked to MDR [190]. Researchers can greatly increase the retention of anticancer treatments within resistant cancer cells by employing nanoparticles that either impede P-gp's function or deliver medications in a way that reduces their detection by these transporters [191].

Targeting Tumor Microenvironment:

The presence of stromal cells, hypoxia, and acidity are some of the variables that contribute to the tumor microenvironment's critical involvement in establishing drug resistance [192]. To improve drug delivery and efficacy, nanotherapeutics can be designed to target particular elements of the tumor microenvironment [193]. For instance, nanoparticles can be engineered to react to the acidic pH present in a variety of tumors, facilitating the more efficient release of their therapeutic payloads under these circumstances. Furthermore, by delivering substances that alter the tumor microenvironment itself, including anti-inflammatory medications or substances that restore blood vessel function [194].

on, nanoparticles can enhance the overall effectiveness of chemotherapy.

Enhanced Intracellular Delivery

Many traditional chemotherapeutic agents are unable to penetrate cellular membranes effectively due to their size or hydrophilicity. Nanoparticles can facilitate enhanced intracellular delivery by encapsulating these drugs within lipid-based carriers or polymeric nanoparticles that promote cellular uptake through endocytosis [195]. For instance, studies have shown that liposomal formulations can improve the delivery of doxorubicin directly into the mitochondria of cancer cells, circumventing some of the resistance mechanisms associated with cytoplasmic drug efflux. This targeted delivery not only increases drug accumulation within resistant cells but also allows for localized action at critical cellular sites [196].

Combination Therapy Approaches

Co-delivery of several therapeutic drugs within a single nanoparticle platform is made possible by nanotherapeutics. Combination therapies that target multiple drug resistance mechanisms at once are made possible by this tactic [197]. For instance, nanoparticles can be designed to carry a small molecule inhibitor and a chemotherapeutic drug that targets particular signaling pathways linked to resistance (e.g., PI3K/Akt/mTOR pathways). Combination therapy can be used with nanocarriers to increase therapeutic efficacy and decrease the risk of resistance development [198].

Gene Delivery Systems

Additionally, nanoparticles may be used to deliver genetic treatments that target MDR pathways. For example, nanoparticle-encapsulated messenger RNA (mRNA) or small interfering RNA (siRNA) can be administered to cancer cells to express proteins that make cells more sensitive to chemotherapy or to silence genes that cause treatment resistance [199]. Research has demonstrated that delivering siRNA targeting P-gp using lipid nanoparticles can effectively reduce its expression and restore sensitivity to previously ineffective drugs. This approach represents a novel strategy for overcoming MDR by directly addressing the molecular underpinnings of resistance [200].

Exploiting Tumor Heterogeneity: Tumors are often heterogeneous, consisting of various cell populations with differing sensitivities to treatment. Nanoparticle-based therapies can be designed to target specific subpopulations within tumors more effectively than conventional therapies [201]. By utilizing ligands that bind selectively to markers expressed on resistant cell populations or cancer stem cells (CSCs), nanotherapeutics can improve treatment outcomes by ensuring that these hard-to-target cells are effectively treated. This customized strategy lowers the likelihood of relapse brought on by lingering resistant cell populations and improves overall therapy efficacy [202].

Versatility in Therapeutic Applications

Chemotherapeutics, nucleic acids, and Immunotherapeutics are just a few of the therapeutic agents that can be delivered because to nanotherapeutics' exceptional adaptability in cancer treatment applications. One of the main benefits of nanotechnology in oncology is its adaptability, which enables creative approaches to the intricate problems involved in cancer treatment [203].

Delivery of Various Therapeutic Agents

Chemotherapeutics: Conventional chemotherapy is limited by poor solubility, rapid clearance, and non-specific distribution, leading to reduced efficacy and significant side effects. Encapsulation of chemotherapeutic agents within nanoparticles improves drug stability, solubility, and allows controlled release [204]. For example, liposomal doxorubicin (Doxil®) extends circulation time and promotes tumor accumulation through the EPR effect, enhancing efficacy while lowering systemic toxicity [205]. Nanoparticles can also co-deliver multiple drugs, enabling synergistic effects and reducing drug resistance; combination delivery of gemcitabine and paclitaxel has shown improved anticancer activity in preclinical studies [206].

Nucleic Acids: Nanotherapeutics also enable delivery of nucleic acids such as plasmid DNA, mRNA, and siRNA, offering molecular-level cancer treatment through oncogene silencing or tumor-suppressor expression. Clinical use of these therapies is limited by poor stability, inefficient

transport, and low cellular uptake [207]. Nanoparticles address these issues by protecting nucleic acids and enhancing intracellular delivery. Lipid nanoparticles have demonstrated effectiveness in mRNA-based cancer immunotherapy, while polymeric nanoparticles are being explored for siRNA delivery to target drug-resistance pathways and restore sensitivity to conventional treatments [208].

Immunotherapeutics: Because immunotherapy uses the body's immune system to combat tumors, it has revolutionized the treatment of cancer. When it comes to improving the distribution and effectiveness of immunotherapeutic drugs like cancer vaccines, immune checkpoint inhibitors, and monoclonal antibodies, nanotherapeutics are essential. These medicines can be encapsulated in nanoparticles or coupled with targeted ligands to improve their ability to interact with immune cells [209]. To promote anti-tumor immunity, for instance, nanoparticles coated with antibodies or ligands that target immunological checkpoints (such PD-1 or CTLA-4) can engage T cells more effectively. Furthermore, tumor-associated antigens can be directly delivered to dendritic cells using nanoparticle-based cancer vaccines, enhancing antigen presentation and subsequently T cell activation [210].

Combination Therapies: One of the most intriguing features of nanotherapeutics is the capacity to deploy several therapeutic modalities inside a single nanoparticle platform. Researchers can develop multifunctional platforms that treat several facets of tumor biology at once by mixing Immunotherapeutics, gene therapies, and chemotherapy within a single carrier [211]. In addition to improving therapeutic effectiveness, this integrative approach may lessen adverse effects linked to high dosages of individual medicines. For example, chemotherapeutic and immune-stimulating nanoparticles can be used to directly kill tumor cells and activate the immune system to fight off any disease that may still be present. These combo treatments are presently being assessed in clinical trials after demonstrating promise in preclinical models [212].

Current Advances in Nanotherapeutic Strategies

The field of nanotherapeutics has seen significant advances in recent years, driven by innovations in formulation technologies, clinical applications, and specific case studies that highlight the successful implementation of these strategies in cancer treatment. This section will explore innovative nanoparticle platforms, an overview of FDA-approved nanotherapeutics and ongoing clinical trials, and specific examples of successful applications in various malignancies [213].

Innovative Formulations and Technologies

Recent advances in nanotherapeutics have produced innovative platforms that enhance drug delivery and anticancer efficacy, including albumin-bound nanoparticles and exosome-based systems. Albumin-bound formulations, such as Abraxane® (albumin-paclitaxel), improve drug solubility and tumor targeting by exploiting albumin receptors (gp60) overexpressed on cancer cells, promoting receptor-mediated uptake and better pharmacokinetics. This strategy has shown success in cancers like breast and pancreatic tumors where conventional formulations face toxicity and solubility limitations [214, 215].

Exosome-based therapies use naturally secreted extracellular vesicles as biocompatible carriers capable of transporting proteins, nucleic acids, and small molecules. Their stability and ability to cross biological barriers allow targeted delivery to specific cells, making them particularly promising for hard-to-reach tumors such as those in the brain [216].

Clinical Applications and Trials

Clinical progress in nanotherapeutics is expanding, with multiple approved formulations and others in trials [217]. Doxil® (liposomal doxorubicin) improves pharmacokinetics and lowers cardiotoxicity in breast, ovarian, and Kaposi's sarcoma [218]. Abraxane® (albumin-bound paclitaxel) enhances solubility and reduces hypersensitivity, with approval for metastatic breast and non-small cell lung cancers [219]. Oncaspar® (pegaspargase) provides better pharmacokinetics for acute lymphoblastic leukemia treatment [220].

Among investigational agents, Aurimune is being tested for targeted immunotherapeutic delivery across cancers [221], while CRLX101, a camptothecin-loaded polymeric nanoparticle, is evaluated for resistant solid tumors [222]. These studies focus on safety, efficacy, and reducing drug resistance and non-specific toxicity.

Case Studies

Table 5: Case Study

Category	Details
A. Innovative Formulations and Technologies	
Albumin-Bound Drugs	- Example: Abraxane® (paclitaxel bound to albumin) - Enhances drug solubility and targets tumor tissues via albumin receptors [227].
Exosome-Based Therapies	- Utilize naturally occurring extracellular vesicles for drug delivery. - Can encapsulate proteins, nucleic acids, and small molecules with inherent biocompatibility [228].
B. Clinical Applications and Trials	
FDA-Approved Nanotherapeutics	- Doxil®: For Kaposi's sarcoma, ovarian cancer, and breast cancer, liposomal doxorubicin - Abraxane®: Albumin-bound paclitaxel for non-small cell lung cancer and metastatic breast cancer - Oncaspar®: For acute lymphoblastic leukemia (ALL), pegylated L-asparaginase is used.
Ongoing Clinical Trials	- Aurimune: Evaluating nanoparticle delivery of immunotherapeutic agents in various cancers. - CRLX101: Investigating polymeric nanoparticle delivering camptothecin for solid tumors resistant to conventional therapies.
C. Case Studies	
Breast Cancer	When compared to conventional regimens, Abraxane® has improved overall survival rates for metastatic breast cancer.

Prostate Cancer	- Nanoparticles loaded with docetaxel target prostate tumors using ligands that bind to prostate-specific membrane antigen (PSMA) [229].
Ovarian Cancer	- Doxil® improves progression-free survival in ovarian cancer compared to free doxorubicin formulations [230].
Pancreatic Cancer	- Nanoparticles designed for selective release in the acidic tumor microenvironment show enhanced efficacy in preclinical models [231].

Challenges and Limitations

Although nanotherapeutics show great promise in the treatment of cancer, several obstacles and restrictions limit their efficacy. The main difficulties about biological barriers, legal restrictions, and safety and toxicity issues are described in this section.

Biological Barriers

Biological barriers significantly limit efficient delivery of nanotherapeutics to tumors [232].

Circulatory barriers: After administration, nanoparticles must avoid rapid clearance by renal filtration and the reticuloendothelial system. Size and surface properties influence circulation; smaller particles may be quickly excreted, while larger ones show longer retention but reduced tumor penetration [233].

Tumor microenvironment: Tumor heterogeneity, abnormal vasculature, and dense extracellular matrix create physical obstacles that hinder nanoparticle diffusion and uniform drug distribution [234].

Cellular barriers: Effective therapy requires nanoparticle internalization, typically via endocytosis, but many particles become trapped in endosomes or lysosomes, limiting cytoplasmic drug release [235, 236].

Tumor heterogeneity: Diverse cancer cell populations with variable receptor expression reduce the effectiveness of uniformly targeted nanotherapeutics [237].

Interpatient variability: Differences in tumor biology, immune response, and patient health affect treatment outcomes and complicate standardized approaches [238].

EPR limitations: Although the EPR effect promotes tumor accumulation, factors such as poor vascularization, high interstitial pressure, and lymphatic drainage can restrict nanoparticle deposition [239].

Regulatory Hurdles

Regulatory challenges can hinder the clinical translation of nanotherapeutics in cancer treatment, as approval requires extensive preclinical and clinical evidence of safety and efficacy [240].

Formulation complexity: The diversity of nanoparticle systems and their interactions with biological environments demand detailed characterization, including size distribution, composition, surface properties, and physiological stability [241].

Safety evaluation: Assessment must address toxicity from both the nanoparticle carrier and the drug, examining biodistribution, accumulation in non-target organs, immunogenicity, and long-term effects [242].

Standardization issues: The absence of uniform evaluation protocols creates variability in data interpretation and approval processes, highlighting the need for standardized manufacturing, quality control, and testing guidelines [243].

Long Approval Timelines: The rigorous requirements for preclinical studies and clinical trials often result in lengthy approval timelines for new nanotherapeutic agents. This delay can hinder timely access to potentially life-saving treatments for patients with cancer [244].

Safety and Toxicity Concerns

Although nanotherapeutics enable targeted delivery, they present important safety concerns.

Adverse effects: Due to their size and surface properties, nanoparticles may trigger toxicity or unintended immune responses, including inflammation or hypersensitivity in susceptible individuals [245].

Long-term safety: The consequences of prolonged nanoparticle accumulation remain unclear, requiring studies on chronic exposure and potential bioaccumulation [246].

Biological interactions: Nanoparticles can interact with proteins, lipids, and nucleic acids, possibly altering cellular functions or producing unexpected effects [247].

Regulatory oversight: Owing to these risks, nanotherapeutics face stricter regulatory evaluation, and thorough risk assessment is essential to ensure safety and approval [248].

Future Perspectives

The prospects for nanotherapeutics in cancer treatment is promising, with further research and innovation aimed at overcoming existing challenges and enhancing therapeutic efficacy. This section explores emerging research directions, integrative approaches that combine nanotherapeutics with other treatment modalities, and the potential for personalized medicine tailored to individual patient profiles.

Research Directions

Emerging technologies and novel nanoparticle designs are at the forefront of advancing nanotherapeutics for cancer treatment. Recent developments include:

Smart Nanoparticles: These nanoparticles can react to environmental stimuli or biological cues, such changes in temperature, pH, or certain enzymes present in the tumor microenvironment. Smart nanoparticles can release their medication payloads selectively at the tumor site by integrating sensitive components, increasing therapeutic efficacy and reducing off-target effects. For instance, to improve the penetration and release of the encapsulated medications, nanoparticles may be engineered to contract or alter their charge in response to the acidic environment characteristic of many cancers [249].

Hierarchical Targeting Technologies: Targeting strategy advancements are meant to enhance the accumulation of nanotherapeutics inside malignancies. This involves focusing on particular cell types or subcellular organelles within tumor tissues in addition to the tumor tissues themselves [250]. Researchers can increase cellular absorption and improve treatment outcomes by functionalizing nanoparticles with ligands that bind to antigens or receptors unique to tumors [251].

Artificial Intelligence (AI) Integration: The integration of AI in the design and optimization of nanoparticles is an exciting frontier. AI can assist in predicting the behaviour of nanoparticles in biological systems, optimizing formulations for better efficacy, and identifying novel targets for drug delivery. This approach could lead to more sophisticated nanoparticle designs that minimize adverse effects while optimizing therapeutic advantages [252].

Integrative Approaches

Combining nanotherapeutics with other treatment modalities can significantly improve cancer therapy [253].

Radiotherapy: Nanoparticles can deliver radiosensitizers directly to tumors, enhancing radiation effectiveness while limiting damage to surrounding healthy tissues [254].

Gene therapy: Nanocarriers facilitate delivery of genetic materials such as plasmid DNA and siRNA targeting oncogenic pathways. Co-delivery with chemotherapeutics on a single platform provides synergistic therapeutic effects [255].

Immunotherapy: Nanotherapeutics can strengthen immune responses by transporting immune checkpoint inhibitors or co-delivering tumor antigens with adjuvants to tumor sites [256].

Personalized medicine: Nanotherapeutics support individualized oncology approaches. Tailored nanoparticle formulations can be designed using patient-specific genetic and tumor profiles to target relevant molecular markers [257]. Nanoparticles incorporating imaging agents enable real-time monitoring of treatment response and therapy adjustment [258]. Additionally, multifunctional personalized nanocarriers can address tumor heterogeneity by adapting targeting strategies to diverse cancer cell populations [259].

Conclusion

Nanotherapeutics offer transformative potential in cancer treatment by overcoming limitations of conventional therapies. By enhancing pharmacokinetics, improving drug uptake, and enabling targeted tumor delivery, nanoparticles increase therapeutic efficacy while reducing adverse effects. Their ability to bypass biological barriers such as drug resistance and tumor heterogeneity makes them a strong alternative to traditional approaches.

Advances in nanotechnology have led to innovative systems, including albumin-bound drugs and exosome-based therapies, many of which are in clinical trials. FDA-approved formulations like Doxil® and Abraxane® demonstrate improved patient outcomes, while ongoing research explores combination strategies with immunotherapy and radiotherapy to further enhance effectiveness.

Despite progress, challenges remain, including biological barriers, safety concerns, and regulatory requirements. Continued research is needed to optimize nanoparticle design, improve targeting precision, and ensure safety through comprehensive evaluation.

Overall, nanotherapeutics hold significant promise for reshaping cancer care, particularly through personalized treatment strategies tailored to individual patient profiles, ultimately improving survival and quality of life.

References

1. Cheng Z, Wang T, Jiao Y, Qi J, Zhang X, Zhou S, *et al*. Burden of digestive system diseases in China and its provinces during 1990–2019: Results of the 2019 Global Disease Burden Study. Chin Med J (Engl), 2024, 14.
2. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, *et al*. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin,2024:74(3):229–263.
3. Tfayli AH, El-Halabi LN, Khuri FR. Global disparities in cancer care: Bridging the gap in affordability and access to medications between high and low-income countries. Cancer,2025:131(1).
4. Osarogiagbon RU, Sineshaw HM, Unger JM, Acuña-Villaorduña A, Goel S. Immune-Based Cancer Treatment: Addressing Disparities in Access and Outcomes. American Society of Clinical Oncology Educational Book,2021;(41):66–78.
5. Cheng Z, Li M, Dey R, Chen Y. Nanomaterials for cancer therapy: current progress and perspectives. J Hematol Oncol,2021:14(1):85.
6. Zhuo Y, Zhao YG, Zhang Y. Enhancing Drug Solubility, Bioavailability, and Targeted Therapeutic Applications through Magnetic Nanoparticles. Molecules,2024:29(20):4854.
7. Ali ES, Sharker SMd, Islam MT, Khan IN, Shaw S, Rahman MdA, *et al*. Targeting cancer cells with nanotherapeutics and nanodiagnostics: Current status and future perspectives. Semin Cancer Biol,2021:69:52–68.
8. van den Boogaard WMC, Komninos DSJ, Vermeij WP. Chemotherapy Side-Effects: Not All DNA Damage Is Equal. Cancers (Basel),2022:14(3):627.
9. Anand U, Dey A, Chandel AKS, Sanyal R, Mishra A, Pandey DK, *et al*. Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. Genes Dis,2023:10(4):1367–1401.
10. Garg P, Malhotra J, Kulkarni P, Horne D, Salgia R, Singhal SS. Emerging Therapeutic Strategies to Overcome Drug Resistance in Cancer Cells. Cancers (Basel),2024:16(13):2478.
11. Akkın S, Varan G, Bilensoy E. A Review on Cancer Immunotherapy and Applications of Nanotechnology to Chemoimmunotherapy of Different Cancers. Molecules,2021:26(11):3382.
12. Nirmala MJ, Kizhuveetil U, Johnson A, G B, Nagarajan R, Muthuvijayan V. Cancer nanomedicine: a review of nano-therapeutics and challenges ahead. RSC Adv,2023:13(13):8606–8629.
13. Rodríguez F, Caruana P, De la Fuente N, Español P, Gámez M, Balart J, *et al*. Nano-Based Approved

Pharmaceuticals for Cancer Treatment: Present and Future Challenges. Biomolecules,2022:12(6):784.
14. Song Y, Hou W. State of the Art in Nanomedicine. In: Nanomedicine. Wiley, 2024, 1–48.
15. Domingues C, Santos A, Alvarez-Lorenzo C, Concheiro A, Jarak I, Veiga F, *et al*. Where Is Nano Today and Where Is It Headed? A Review of Nanomedicine and the Dilemma of Nanotoxicology. ACS Nano,2022:16(7):9994–10041.
16. Zhao CY, Cheng R, Yang Z, Tian ZM. Nanotechnology for Cancer Therapy Based on Chemotherapy. Molecules,2018:23(4):826.
17. Abdellatif AAH, Mohammed HA, Khan RA, Singh V, Bouazzaoui A, Yusuf M, *et al*. Nano-scale delivery: A comprehensive review of nano-structured devices, preparative techniques, site-specificity designs, biomedical applications, commercial products, and references to safety, cellular uptake, and organ toxicity. Nanotechnol Rev,2021:10(1):1493–1559.
18. Teixeira P V., Fernandes E, Soares TB, Adega F, Lopes CM, Lúcio M. Natural Compounds: Co-Delivery Strategies with Chemotherapeutic Agents or Nucleic Acids Using Lipid-Based Nanocarriers. Pharmaceutics,2023:15(4):1317.
19. Aghebati-Maleki A, Dolati S, Ahmadi M, Baghbanzhadeh A, Asadi M, Fotouhi A, *et al*. Nanoparticles and cancer therapy: Perspectives for application of nanoparticles in the treatment of cancers. J Cell Physiol,2020:235(3):1962–1972.
20. Allahou LW, Madani SY, Seifalian A. Investigating the Application of Liposomes as Drug Delivery Systems for the Diagnosis and Treatment of Cancer. Int J Biomater,2021:2021:1–16.
21. Khan MI, Hossain MI, Hossain MK, Rubel MHK, Hossain KM, Mahfuz AMUB, *et al*. Recent Progress in Nanostructured Smart Drug Delivery Systems for Cancer Therapy: A Review. ACS Appl Bio Mater,2022:5(3):971–1012.
22. Rommasi F, Esfandiari N. Liposomal Nanomedicine: Applications for Drug Delivery in Cancer Therapy. Nanoscale Res Lett,2021:16(1):95.
23. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. Heliyon,2022:8(5):e09394.
24. Lombardo D, Kiselev MA. Methods of Liposomes Preparation: Formation and Control Factors of Versatile Nanocarriers for Biomedical and Nanomedicine Application. Pharmaceutics,2022:14(3):543.
25. Zhang M, Xiang C, Niu R, He X, Luo W, Liu W, *et al*. Liposomes as versatile agents for the management of traumatic and nontraumatic central nervous system disorders: drug stability, targeting efficiency, and safety. Neural Regen Res,2025:20(7):1883–1899.
26. Ismail Y, Harish M, Vijaya Kumar Voleti, Haja Nazeer Ahamed, Thameemul Ansari LH. Descriptive Review on Liposomal Drug Delivery System. Journal of Pharma Insights and Research,2024:2(4):045–58.
27. Wang S, Chen Y, Guo J, Huang Q. Liposomes for Tumor Targeted Therapy: A Review. Int J Mol Sci,2023:24(3):2643.
28. Guo C, Yuan H, Wang Y, Feng Y, Zhang Y, Yin T, *et al*. The interplay between PEGylated nanoparticles and blood immune system. Adv Drug Deliv Rev,2023:200:115044.
29. Liu P, Chen G, Zhang J. A Review of Liposomes as a Drug Delivery System: Current Status of Approved Products, Regulatory Environments, and Future Perspectives. Molecules,2022:27(4):1372.
30. Ejigah V, Owoseni O, Bataille-Backer P, Ogundipe OD, Fisusi FA, Adesina SK. Approaches to Improve Macromolecule and Nanoparticle Accumulation in the Tumor Microenvironment by the Enhanced Permeability and Retention Effect. Polymers (Basel),2022:14(13):2601.
31. Cardoso RV, Pereira PR, Freitas CS, Paschoalin VMF. Trends in Drug Delivery Systems for Natural Bioactive Molecules to Treat Health Disorders: The Importance of Nano-Liposomes. Pharmaceutics,2022:14(12):2808.
32. van der Koog L, Gandek TB, Nagelkerke A. Liposomes and Extracellular Vesicles as Drug Delivery Systems: A Comparison of Composition, Pharmacokinetics, and Functionalization. Adv Healthc Mater,2022:11(5).
33. Ghazal H, Waqar A, Yaseen F, Shahid M, Sultana M, Tariq M, *et al*. Role of nanoparticles in enhancing chemotherapy efficacy for cancer treatment. Next Materials,2024:2:100128.
34. Dorostkar H, Haghiralsadat BF, Hemati M, Safari F, Hassanpour A, Naghib SM, *et al*. Reduction of Doxorubicin-Induced Cardiotoxicity by Co-Administration of Smart Liposomal Doxorubicin and Free Quercetin: *In vitro* and In *Vivo* Studies. Pharmaceutics,2023:15(7):1920.
35. Jones IC, Dass CR. Doxorubicin-induced cardiotoxicity: causative factors and possible interventions. Journal of Pharmacy and Pharmacology,2022:74(12):1677–1688.
36. Wang Z, Li J, Lin G, He Z, Wang Y. Metal complex-based liposomes: Applications and prospects in cancer diagnostics and therapeutics. Journal of Controlled Release,2022:348:1066–1088.
37. Manzari-Tavakoli A, Babajani A, Tavakoli MM, Safaeinejad F, Jafari A. Integrating natural compounds and nanoparticle-based drug delivery systems: A novel strategy for enhanced efficacy and selectivity in cancer therapy. Cancer Med,2024:13(5).
38. Moholkar DN, Kandimalla R, Gupta RC, Aqil F. Advances in lipid-based carriers for cancer therapeutics: Liposomes, exosomes and hybrid exosomes. Cancer Lett,2023:565:216220.
39. Nikolova MP, Kumar EM, Chavali MS. Updates on Responsive Drug Delivery Based on Liposome Vehicles for Cancer Treatment. Pharmaceutics,2022:14(10):2195.
40. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, Heller DA. Targeted drug delivery strategies for precision medicines. Nat Rev Mater,2021:6(4):351–370.
41. Tomsen-Melero J, Merlo-Mas J, Carreño A, Sala S, Córdoba A, Veciana J, *et al*. Liposomal formulations for treating lysosomal storage disorders. Adv Drug Deliv Rev,2022:190:114531.
42. Thomazini VC, da Cunha GM, Guimarães NM, Saleme SD, de Melo RCG, de Paula GA, *et al*. Impact of concerning excipients on animal safety: insights for veterinary pharmacotherapy and regulatory considerations. DARU Journal of Pharmaceutical Sciences,2023:32(1):289–305.

43. Biscaia-Caleiras M, Fonseca NA, Lourenço AS, Moreira JN, Simões S. Rational formulation and industrial manufacturing of lipid-based complex injectables: Landmarks and trends. Journal of Controlled Release,2024:373:617–639.
44. Dristant U, Mukherjee K, Saha S, Maity D. RETRACTED: An Overview of Polymeric Nanoparticles-Based Drug Delivery System in Cancer Treatment. Technol Cancer Res Treat,2023:22.
45. Zhang W, Taheri-Ledari R, Ganjali F, Afruzi FH, Hajizadeh Z, Saeidirad M, *et al*. Nanoscale bioconjugates: A review of the structural attributes of drug-loaded nanocarrier conjugates for selective cancer therapy. Heliyon,2022:8(6):e09577.
46. Chandrakala V, Aruna V, Angajala G. Review on metal nanoparticles as nanocarriers: current challenges and perspectives in drug delivery systems. Emergent Mater,2022:5(6):1593–1615.
47. Bhatia S. Nanoparticles Types, Classification, Characterization, Fabrication Methods and Drug Delivery Applications. In: Natural Polymer Drug Delivery Systems. Cham: Springer International Publishing; 2016. p. 33–93.
48. Tyrrell ZL, Shen Y, Radosz M. Fabrication of micellar nanoparticles for drug delivery through the self-assembly of block copolymers. Prog Polym Sci,2010:35(9):1128–1143.
49. Shinde VR, Revi N, Murugappan S, Singh SP, Rengan AK. Enhanced permeability and retention effect: A key facilitator for solid tumor targeting by nanoparticles. Photodiagnosis Photodyn Ther,2022:39:102915.
50. Kumari L, Choudhari Y, Patel P, Gupta G Das, Singh D, Rosenholm JM, *et al*. Advancement in Solubilization Approaches: A Step towards Bioavailability Enhancement of Poorly Soluble Drugs. Life,2023:13(5):1099.
51. Mehandole A, Walke N, Mahajan S, Aalhate M, Maji I, Gupta U, *et al*. Core–Shell Type Lipidic and Polymeric Nanocapsules: the Transformative Multifaceted Delivery Systems. AAPS PharmSciTech,2023:24(1):50.
52. Guo W, Ding P, Valentine Okoro O, Sun Y, Jiang G, Shavandi A, *et al*. Drug Delivery System and Technologies. In 2025. p. 73–97.
53. Mudzingwa KR, Patel A, Patel S, Panjwani D, Ahlawat P. Polymeric Nanoparticles: Targeted Delivery in Breast Cancer - A Review. Current Materials Science,2024:18.
54. Zhang C, Qi Y, Zhang Z. Swelling Behaviour of Polystyrene Microsphere Enhanced PEG-Based Hydrogels in Seawater and Evolution Mechanism of Their Three-Dimensional Network Microstructure. Materials,2022:15(14):4959.
55. Du X, Gao Y, Kang Q, Xing J. Design and Applications of Tumor Microenvironment-Responsive Nanogels as Drug Carriers. Front Bioeng Biotechnol,2021:9.
56. Narayanan K, Bhaskar R, Han S. Recent Advances in the Biomedical Applications of Functionalized Nanogels. Pharmaceutics,2022:14(12):2832.
57. Agiba AM, Arreola-Ramírez JL, Carbajal V, Segura-Medina P. Light-Responsive and Dual-Targeting Liposomes: From Mechanisms to Targeting Strategies. Molecules,2024:29(3):636.
58. Liu B, Zhou H, Tan L, Siu KTH, Guan XY. Exploring treatment options in cancer: tumor treatment strategies. Signal Transduct Target Ther,2024:9(1):175.
59. Rahim MA, Jan N, Khan S, Shah H, Madni A, Khan A, *et al*. Recent Advancements in Stimuli Responsive Drug Delivery Platforms for Active and Passive Cancer Targeting. Cancers (Basel),2021:13(4):670.
60. Subhan MA, Yalamarty SSK, Filipczak N, Parveen F, Torchilin VP. Recent Advances in Tumor Targeting via EPR Effect for Cancer Treatment. J Pers Med,2021:11(6):571.
61. Huang D, Sun L, Huang L, Chen Y. Nanodrug Delivery Systems Modulate Tumor Vessels to Increase the Enhanced Permeability and Retention Effect. J Pers Med,2021:11(2):124.
62. Li Z, Zhong N, Cao L, Cai Z, Xiao Y, Wang G, *et al*. Nanoparticles Targeting Lymph Nodes for Cancer Immunotherapy: Strategies and Influencing Factors. Small,2024:20(19).
63. Zang R, Barth A, Wong H, Marik J, Shen J, Lade J, *et al*. Design and Measurement of Drug Tissue Concentration Asymmetry and Tissue Exposure-Effect (Tissue PK-PD) Evaluation. J Med Chem,2022:65(13):8713–8734.
64. Sabir F, Qindeel M, Zeeshan M, Ul Ain Q, Rahdar A, Barani M, *et al*. Onco-Receptors Targeting in Lung Cancer via Application of Surface-Modified and Hybrid Nanoparticles: A Cross-Disciplinary Review. Processes,2021:9(4):621.
65. Kunjiappan S, Pavadai P, Vellaichamy S, Ram Kumar Pandian S, Ravishankar V, Palanisamy P, *et al*. Surface receptor-mediated targeted drug delivery systems for enhanced cancer treatment: A state-of-the-art review. Drug Dev Res,2021:82(3):309–340.
66. Shakeri-Zadeh A, Rezaeyan A, Sarikhani A, Ghaffari H, Samadian H, Khademi S, *et al*. Folate receptor-targeted nanoprobes for molecular imaging of cancer: Friend or foe? Nano Today,2021:39:101173.
67. Martín-Sabroso C, Torres-Suárez AI, Alonso-González M, Fernández-Carballido A, Fraguas-Sánchez AI. Active Targeted Nanoformulations via Folate Receptors: State of the Art and Future Perspectives. Pharmaceutics,2021:14(1):14.
68. Rizwanullah Md, Ahmad MZ, Ghoneim MM, Alshehri S, Imam SS, Md S, *et al*. Receptor-Mediated Targeted Delivery of Surface-Modified Nanomedicine in Breast Cancer: Recent Update and Challenges. Pharmaceutics,2021:13(12):2039.
69. Sun Y, Davis E. Nanoplatforms for Targeted Stimuli-Responsive Drug Delivery: A Review of Platform Materials and Stimuli-Responsive Release and Targeting Mechanisms. Nanomaterials,2021:11(3):746.
70. van der Kooij RS, Steendam R, Frijlink HW, Hinrichs WLJ. An overview of the production methods for core–shell microspheres for parenteral controlled drug delivery. European Journal of Pharmaceutics and Biopharmaceutics,2022:170:24–42.
71. Gao Q, Feng J, Liu W, Wen C, Wu Y, Liao Q, *et al*. Opportunities and challenges for co-delivery nanomedicines based on combination of phytochemicals with chemotherapeutic drugs in cancer treatment. Adv Drug Deliv Rev,2022:188:114445.
72. Sivadasan D, Sultan MH, Madkhali O, Almoshari Y, Thangavel N. Polymeric Lipid Hybrid Nanoparticles

(PLNs) as Emerging Drug Delivery Platform—A Comprehensive Review of Their Properties, Preparation Methods, and Therapeutic Applications. Pharmaceutics,2021:13(8):1291.
73. CeCe R, Jining L, Islam M, Korvink JG, Sharma B. An Overview of the Electrospinning of Polymeric Nanofibers for Biomedical Applications Related to Drug Delivery. Adv Eng Mater,2024:26(1).
74. Kang JH, Yang JK, Cho KH, Lee OH, Kwon H, Kim SY, *et al*. Intracalvariosseous administration of donepezil microspheres protects against cognitive impairment by virtue of long-lasting brain exposure in mice. Theranostics,2024:14(17):6708–6725.
75. Karnwal A, Jassim AY, Mohammed AA, Sharma V, Al-Tawaha ARMS, Sivanesan I. Nanotechnology for Healthcare: Plant-Derived Nanoparticles in Disease Treatment and Regenerative Medicine. Pharmaceuticals,2024:17(12):1711.
76. Han X, Alu A, Liu H, Shi Y, Wei X, Cai L, *et al*. Biomaterial-assisted biotherapy: A brief review of biomaterials used in drug delivery, vaccine development, gene therapy, and stem cell therapy. Bioact Mater,2022:17:29–48.
77. Pei J, Yan Y, Palanisamy CP, Jayaraman S, Natarajan PM, Umapathy VR, *et al*. Materials-based drug delivery approaches: Recent advances and future perspectives. Green Processing and Synthesis,2024:13(1).
78. Dodero A, Alberti S, Gaggero G, Ferretti M, Botter R, Vicini S, *et al*. An Up-to-Date Review on Alginate Nanoparticles and Nanofibers for Biomedical and Pharmaceutical Applications. Adv Mater Interfaces,2021:8(22).
79. Mao JJ, Pillai GG, Andrade CJ, Ligibel JA, Basu P, Cohen L, *et al*. Integrative oncology: Addressing the global challenges of cancer prevention and treatment. CA Cancer J Clin,2022:72(2):144–164.
80. Tewari AK, Upadhyay SC, Kumar M, Pathak K, Kaushik D, Verma R, *et al*. Insights on Development Aspects of Polymeric Nanocarriers: The Translation from Bench to Clinic. Polymers (Basel),2022:14(17):3545.
81. Shen Y, Gwak H, Han B. Advanced manufacturing of nanoparticle formulations of drugs and biologics using microfluidics. Analyst,2024:149(3):614–637.
82. Kumar R, Dutt S, Tripathi AD, Singh AK, Chaturvedi VK, Singh SK. Navigating Safety and Toxicity Challenges in Nanomedicine: Strategies, Assessment, and Mitigation. In 2024. p. 15–37.
83. Nsairat H, Lafi Z, Al-Najjar B, Al-Samydai A, Saqallah F, El-Tanani M, *et al*. How Advanced are Self-Assembled Nanomaterials for Targeted Drug Delivery? A Comprehensive Review of the Literature. Int J Nanomedicine,2025;Volume 20:2133–2161.
84. Beach MA, Nayanathara U, Gao Y, Zhang C, Xiong Y, Wang Y, *et al*. Polymeric Nanoparticles for Drug Delivery. Chem Rev,2024:124(9):5505–5616.
85. Gawande V, Choudhury H, Kesharwani P. Dendrimer nomenclature and synthesis methods. In: Dendrimer-Based Nanotherapeutics. Elsevier; 2021. p. 75–94.
86. Mazidi Z, Javanmardi S, Naghib SM, Mohammadpour Z. Smart stimuli-responsive implantable drug delivery systems for programmed and on-demand cancer treatment: An overview on the emerging materials. Chemical Engineering Journal,2022:433:134569.
87. Kaurav M, Ruhi S, Al-Goshae HA, Jeppu AK, Ramachandran D, Sahu RK, *et al*. Dendrimer: An update on recent developments and future opportunities for the brain tumors diagnosis and treatment. Front Pharmacol, 2023, 14.
88. De R, Mahata MK, Kim K. Structure-Based Varieties of Polymeric Nanocarriers and Influences of Their Physicochemical Properties on Drug Delivery Profiles. Advanced Science,2022:9(10).
89. Rawding PA, Bu J, Wang J, Kim DW, Drelich AJ, Kim Y, *et al*. Dendrimers for cancer immunotherapy: Avidity-based drug delivery vehicles for effective anti-tumor immune response. WIREs Nanomedicine and Nanobiotechnology,2022:14(2).
90. Muley S, Dhila H, Gote M. Calixarene-Guest Complexes: The Next Innovation in Delivery of Drugs and Biologics. Adv Ther (Weinh),2024:7(10).
91. Camacho C, Tomás H, Rodrigues J. Use of Half-Generation PAMAM Dendrimers (G0.5–G3.5) with Carboxylate End-Groups to Improve the DACHPtCl2 and 5-FU Efficacy as Anticancer Drugs. Molecules,2021:26(10):2924.
92. Zhang S qi, Fu Q, Zhang Y jie, Pan J xing, Zhang L, Zhang Z rong, *et al*. Surface loading of nanoparticles on engineered or natural erythrocytes for prolonged circulation time: strategies and applications. Acta Pharmacol Sin,2021:42(7):1040–1054.
93. Mittal P, Saharan A, Verma R, Altalbawy FMA, Alfaidi MA, Batiha GES, *et al*. Dendrimers: A New Race of Pharmaceutical Nanocarriers. Biomed Res Int,2021:2021(1).
94. Buschmann D, Mussack V, Byrd JB. Separation, characterization, and standardization of extracellular vesicles for drug delivery applications. Adv Drug Deliv Rev,2021:174:348–368.
95. Manoj GM, Shalini M, Thenmozhi K, Ponnusamy VK, Hari S. Recent advancements in the surface modification and functionalization of magnetic nanomaterials. Applied Surface Science Advances,2024:21:100608.
96. Rai DB, Medicherla K, Pooja D, Kulhari H. Dendrimer-Mediated Delivery of Anticancer Drugs for Colon Cancer Treatment. Pharmaceutics,2023:15(3):801.
97. Jogdeo CM, Siddhanta K, Das A, Ding L, Panja S, Kumari N, *et al*. Beyond Lipids: Exploring Advances in Polymeric Gene Delivery in the Lipid Nanoparticles Era. Advanced Materials,2024:36(31).
98. Yang Y, Zeng W, Huang P, Zeng X, Mei L. Smart materials for drug delivery and cancer therapy. VIEW,2021:2(2).
99. Shetty A, Chikhaliwala P, Suryawanshi J, Chandra S. Understanding Physico-chemical Interactions of Dendrimers with Guest Molecules for Efficient Drug and Gene Delivery. Curr Pathobiol Rep,2021:9(2):57–70.
100. Pandey VK, Tripathi A, Taufeeq A, Dar AH, Samrot A V, Rustagi S, *et al*. Significance and applications of carbon dots in anti cancerous nanodrug conjugate development: A review. Applied Surface Science Advances,2024:19:100550.

101. Dubey N, Dhiman S, Koner AL. Review of Carbon Dot-Based Drug Conjugates for Cancer Therapy. ACS Appl Nano Mater,2023:6(6):4078–4096.
102. Qamhieh K, Nylander T. Electrostatic interactions between cationic dendrimers and anionic model biomembrane. Chem Phys Lipids,2022:246:105214.
103. Sultana A, Zare M, Thomas V, Kumar TSS, Ramakrishna S. Nano-based drug delivery systems: Conventional drug delivery routes, recent developments and future prospects. Med Drug Discov,2022:15:100134.
104. Prajapati A, Rangra S, Patil R, Desai N, Jyothi VGSS, Salave S, *et al*. Receptor-Targeted Nanomedicine for Cancer Therapy. Receptors,2024:3(3):323–361.
105. Banushi B, Joseph SR, Lum B, Lee JJ, Simpson F. Endocytosis in cancer and cancer therapy. Nat Rev Cancer,2023:23(7):450–473.
106. Sanjanwala D, Patravale V. Aptamers and nanobodies as alternatives to antibodies for ligand-targeted drug delivery in cancer. Drug Discov Today,2023:28(5):103550.
107. Sitia L, Sevieri M, Signati L, Bonizzi A, Chesi A, Mainini F, *et al*. HER-2-Targeted Nanoparticles for Breast Cancer Diagnosis and Treatment. Cancers (Basel),2022:14(10):2424.
108. Chakraborty S, Chakraborty A, Mukherjee B, Besra SE, Dewanjee S, Mukherjee A, *et al*. Assessment of superiority of HSP70-targeting aptamer-functionalized drug-nanocarrier over non-targeted commercially available counterpart in HCC therapy: *in vitro* and in *vivo* investigations and molecular modeling. Life Sci,2023:317:121467.
109. Sun L, Li Z, Lan J, Wu Y, Zhang T, Ding Y. Better together: nanoscale co-delivery systems of therapeutic agents for high-performance cancer therapy. Front Pharmacol,2024:15.
110. Ouyang Z, Gao Y, Shen M, Shi X. Dendrimer-based nanohybrids in cancer photomedicine. Mater Today Bio,2021:10:100111.
111. Bober Z, Bartusik-Aebisher D, Aebisher D. Application of Dendrimers in Anticancer Diagnostics and Therapy. Molecules,2022:27(10):3237.
112. Parvin N, Kumar V, Mandal TK, Joo SW. Advancements in Nanoporous Materials for Biomedical Imaging and Diagnostics. J Funct Biomater,2024:15(8):226.
113. Kheiriabad S, Dolatabadi JEN, Hamblin MR. Dendrimers for gene therapy. In: Dendrimer-Based Nanotherapeutics. Elsevier; 2021. p. 285–309.
114. Cring MR, Sheffield VC. Gene therapy and gene correction: targets, progress, and challenges for treating human diseases. Gene Ther,2022:29(1–2):3–12.
115. Chis AA, Dobrea CM, Rus LL, Frum A, Morgovan C, Butuca A, *et al*. Dendrimers as Non-Viral Vectors in Gene-Directed Enzyme Prodrug Therapy. Molecules,2021:26(19):5976.
116. Kedar P, Saraf A, Maheshwari R, Sharma M. Advances in Dendritic Systems and Dendronized Nanoparticles: Paradigm Shifts in Cancer Targeted Therapy and Diagnostics. Mol Pharm,2025:22(1):28–57.
117. Marques L, Costa B, Pereira M, Silva A, Santos J, Saldanha L, *et al*. Advancing Precision Medicine: A Review of Innovative In Silico Approaches for Drug Development, Clinical Pharmacology and Personalized Healthcare. Pharmaceutics,2024:16(3):332.
118. Sharma R, Singh D, Gaur P, Joshi D. Intelligent automated drug administration and therapy: future of healthcare. Drug Deliv Transl Res,2021:11(5):1878–1902.
119. Rastogi V, Yadav P, Porwal M, Sur S, Verma A. Dendrimer as nanocarrier for drug delivery and drug targeting therapeutics: a fundamental to advanced systematic review. International Journal of Polymeric Materials and Polymeric Biomaterials,2024:73(4):310–332.
120. Dash BS, Jose G, Lu YJ, Chen JP. Functionalized Reduced Graphene Oxide as a Versatile Tool for Cancer Therapy. Int J Mol Sci,2021:22(6):2989.