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NANOMEDICINE IN CANCER THERAPY: ADVANCES IN TARGETED DRUG DELIVERY, NANO IMMUNOTHERAPY AND EMERGING THERAPEUTIC STRATEGIES

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ABSTRACT

Limited drug solubility, insufficient tumor accumulation, systemic toxicity, multidrug resistance, and the biological heterogeneity of tumors are some of the key obstacles that cancer therapy still faces. In order to enhance the localization and regulated release of anticancer medicines, the review also looks into passive, active, tumor-microenvironment-responsive, and biomimetic targeting techniques. Additionally highlighted is the potential of nanocarriers to transport nucleic acids, immune-modulating drugs, and combination treatments, especially for boosting anticancer immune responses and overcoming therapeutic resistance. Lastly, new strategies such multifunctional nanocarriers, nucleic acid delivery, biomimetic and exosome-based systems, precision nanomedicine, and theragnostic platforms are explored as possible avenues for cancer treatment in the future.

KEYWORDS: Cancer; Nanomedicine; Nanoparticles; Targeted Drug Delivery; Nano-Immunotherapy; Stimuli-Responsive Nanocarriers; Multidrug Resistance; Tumor Heterogeneity; Precision Nanomedicine; Cancer Therapy.

INTRODUCTION

One of the biggest global health issues is cancer, which continues to place a heavy burden on healthcare systems all around the world. Uncontrolled cell proliferation, aberrant tissue invasion, genetic and epigenetic changes, and, in more advanced stages, metastatic dispersion to distant organs are the hallmarks of this diverse group of disorders. The most common cancer detected worldwide was lung cancer, which was followed by stomach, colorectal, breast, and prostate cancers in women. The ongoing need for novel therapeutic techniques that can enhance therapy is highlighted by the

rising incidence of cancer, persistent mortality, and discrepancies in access to good diagnosis and treatment. (Bray et al., 2024).

In particular, cytotoxic chemicals are often distributed non-specifically during conventional chemotherapy, exposing both healthy and malignant tissues. Furthermore, a lot of anticancer medications have poor pharmacokinetic characteristics, quick systemic clearance, poor water solubility, and insufficient accumulation at the targeted tumour location. These constraints can contribute while adding to therae-limiting therapeutic efficacy. Consequently, increasing the delivery of anticancer therapies while retaining enough drug exposure at the tumour site has become a key target in current cancer research (Shi et al., 2017; Hare et al., 2017).

The capacity of nanomedicine to alter the pharmacological and biological properties of traditional therapeutic drugs is one of its main benefits. When a medication is incorporated into a nanoscale carrier, it can prevent early breakdown and allow for regulated or prolonged release after delivery. (Mitchell et al., 2021).

Another crucial area in the advancement of cancer nanomedicine is tumour targeting. Crucially, preclinical research analysis has shown that just a tiny percentage of given nanoparticles usually reach solid tumors, underscoring the limits of presuming that tumour accumulation happens consistently across various malignancies. (Wilhelm et al., 2016; Shi et al., 2017).

For the purpose of guiding nanoparticles toward certain biological targets, ligands such as peptides, aptamers, polysaccharides, and antibodies have been studied. The density and accessibility of the target receptor, ligand properties, nanoparticle size and surface characteristics, tumor heterogeneity, and the biological milieu surrounding the tumor are some of the variables that affect how effective active targeting is. (Shi et al., 2017; Mitchell et al., 2021).

The development of these responsive systems has consequently expanded the potential applications of nanomedicine from simple drug encapsulation toward more sophisticated therapeutic delivery platforms (Mitchell et al., 2021; Anchordoquy et al., 2017).

Such systems have been investigated for combining chemotherapeutic agents with molecularly targeted drugs, nucleic acids, or other therapeutic modulators. (Shi et al., 2017; Mitchell et al., 2021).

In this manner, nanomedicine may support immune activation while simultaneously providing controlled delivery of therapeutic components. The integration of nanotechnology with immunotherapy represents an expanding area of cancer research because it provides opportunities to manipulate both drug delivery and the tumor–immune microenvironment (Mitchell et al., 2017; Shi et al., 2017).

Such heterogeneity can influence nanoparticle penetration, cellular uptake, biodistribution, and therapeutic response. Consequently, a nanocarrier that demonstrates favourable performance in a particular experimental model may not necessarily exhibit the same behavior in different tumor types or patient populations. (Wilhelm et al., 2016; Hare et al., 2017).

Despite considerable progress, several challenges continue to influence the development of cancer nanomedicine. In

addition, physicochemical characteristics such as particle size, surface chemistry, morphology, and composition can strongly influence biological behavior. (Shi et al., 2017; Anchordoquy et al., 2017).

The continuous evolution of nanotechnology has consequently shifted cancer nanomedicine from relatively simple drug-carrier systems toward multifunctional and biologically responsive platforms. Current research increasingly focuses on smart nanocarriers, stimuli-responsive systems, biomimetic nanoparticles, multifunctional nanostructures, targeted delivery, nano immune therapy, combination therapy, and approaches designed. (Mitchell et al., 2021; Shi et al., 2017).

LITERATURE SEARCH STRATEGY

The search was designed to cover the major themes addressed in this review, including nanomedicine platforms, targeted drug delivery, tumor targeting, smart and stimuli-responsive nanocarriers, nano immunotherapy, combination cancer therapy, multidrug resistance, tumor heterogeneity, safety and biocompatibility, and emerging nanomedicine technologies.

The search strategy employed combinations of controlled vocabulary and free-text keywords related to the major concepts of the review. The principal search terms included “cancer,” “cancer therapy,” “oncology,” “nanomedicine,” “nanoparticles,” “nanocarriers,” “nanotechnology,” “targeted drug delivery,” “tumor targeting,” “smart nanocarriers,” “stimuli-responsive nanoparticles,” “nano immunotherapy,” “cancer immunotherapy,” “multidrug resistance,” “tumor heterogeneity,” “combination therapy,” “nanotoxicity,” “biocompatibility,” and “emerging nanomedicine technologies.” Synonyms and related terms were combined using the Boolean operators AND OR to broaden or refine the search as appropriate.

(Cancer OR oncology OR “cancer therapy” OR “cancer treatment”) AND (nanomedicine OR nanotechnology OR nanoparticle OR nanocarrier*)* AND (“drug delivery” OR “targeted drug delivery” OR “tumor targeting” OR “stimuli-responsive” OR nano immunotherapy OR immunotherapy OR “combination therapy” OR “multidrug resistance” OR “tumor heterogeneity” OR safety OR toxicity OR biocompatibility).

The literature search covered publications from database inception to 2010-2026.

The final selection of literature was based on its relevance to the objectives and thematic scope of the present review.

Nanomedicine Platforms for Cancer Therapy

Liposomes can improve drug stability, modify pharmacokinetics, prolong circulation, and reduce exposure of healthy tissues to free cytotoxic drugs. **(**Wang et al., 2023; Zaragoza-Jiménez et al., 2026).

Liposomal systems can also be engineered as long-circulating, ligand-functionalized, or stimuli-responsive formulations. These modifications can influence drug release, biodistribution, and interactions with tumor cells. (Cheng et al., 2025; Fidan et al., 2024).

Their hydrophobic core can solubilize poorly water-soluble anticancer drugs, whereas the hydrophilic outer layer can improve aqueous stability and circulation characteristics. (Shi et al., 2017; Mitchell et al., 2021).

Their internal cavities and numerous surface functional groups provide opportunities for drug encapsulation, chemical

conjugation, and attachment of targeting molecules. Their structural precision has made dendrimers attractive for the development of multifunctional cancer nanomedicines; however, surface charge, toxicity, biodegradability, and interactions with biological components must be carefully considered during formulation development (Shi et al., 2017; Mitchell et al., 2021).

In cancer research, lipid-based systems have been investigated for chemotherapy, nucleic-acid delivery, cancer vaccines, and combination therapeutic approaches. These platforms illustrate the increasing diversification of nanomedicine beyond conventional polymeric and liposomal systems (Cheng et al., 2025; Shi et al., 2017).

For example, gold-based nanostructures can be engineered for drug loading and photothermal applications, while magnetic nanoparticles can provide opportunities for magnetically influenced delivery and therapeutic manipulation. Silica-based systems offer tunable pore structures that can facilitate drug loading and controlled release. (Kunjachan et al., 2012; Shi et al., 2017).

Overall, cancer nanomedicine encompasses a broad spectrum of platforms, each offering distinct advantages and limitations. Liposomes provide versatile lipid-based encapsulation, polymeric nanoparticles and micelles offer controlled delivery and improved solubilization, dendrimers provide highly functionalizable architectures, while lipid, protein, metallic, inorganic, and hybrid systems provide additional opportunities for specialized therapeutic applications. Current research is increasingly focused on optimizing these platforms through surface engineering, biomimetic design, stimuli-responsive release, combination delivery, and tumor-specific targeting. (Shi et al., 2017; Mitchell et al., 2021).

Nano medicine Platform	Main Application	Key Advantage	References
Liposomes	Anticancer drug delivery	Improved drug stability and circulation	Barenholz, 2012; Fidan et al., 2024
Polymeric nanoparticles	Controlled drug delivery	Sustained and tunable drug release	Mitchell et al., 2021
Polymeric micelles	Delivery of poorly soluble drugs	Improved drug solubilization	Gaucher et al., 2005
Dendrimers	Drug encapsulation and targeting	High surface functionality	Mitchell et al., 2021
Lipid-based nanoparticles	Drug and nucleic-acid delivery	Flexible loading and intracellular delivery	Hou et al., 2021
Metallic nanoparticles	Drug delivery and photothermal therapy	Unique physical properties	Kunjachan et al., 2012
Hybrid nanocarriers	Combination and targeted therapy	Multiple therapeutic functions	Mitchell et al., 2021

Tumor Targeting and Smart Nanocarrier Design

Effective delivery of nanomedicines to tumor tissue is one of the major objectives in cancer nanotechnology. Characteristics of anticancer agents, their therapeutic performance depends strongly on their ability to reach the tumor, penetrate the tumor microenvironment, and release their therapeutic cargo at the desired site. (Bi et al., 2016).

Which results from the abnormal vascular characteristics and impaired lymphatic drainage frequently observed in solid tumors. Tumor type, interstitial fluid pressure, extracellular matrix composition, and disease stage. Therefore, passive accumulation alone may not provide sufficient or homogeneous nanoparticle delivery in all tumors. (Bi et al., 2016; Fernandes et al., 2018).

After reaching the tumor region, ligand–receptor interactions can enhance the association of nanoparticles with target

cells and may facilitate receptor-mediated internalization. Active targeting can therefore improve intracellular delivery of therapeutic cargo; however, its effectiveness depends on the expression level and accessibility of the selected target, ligand density, nanoparticle characteristics, and tumor heterogeneity. (Mukherjee et al., 2013).

Antibodies and antibody fragments can provide high molecular recognition, whereas smaller ligands such as peptides, folate, and aptamers may offer advantages related to size, stability, or ease of chemical modification. This heterogeneity can influence the overall effectiveness of ligand-mediated targeting and highlights the importance of selecting molecular targets that are sufficiently accessible and relevant to the intended cancer type (Bi et al., 2016).

Compared with many normal tissues, solid tumors can exhibit characteristics such as mildly acidic extracellular pH, hypoxia, elevated reactive oxygen species, altered redox conditions, increased levels of certain enzymes, and abnormal extracellular matrix organization. Such changes may include nanoparticle destabilization, surface-charge alteration, degradation of a protective coating, exposure of a targeting ligand, or release of the therapeutic payload. TME-responsive systems therefore aim to achieve spatially controlled drug delivery while limiting premature release under normal physiological conditions (Uthaman et al., 2018).

In these systems, naturally derived cell membranes or cell-derived components can be incorporated onto synthetic nanoparticles to reproduce selected biological properties of the source cells. Red blood cell, platelet, leukocyte, cancer-cell, and stem-cell membranes have all been investigated as components of biomimetic nanocarriers. Such membrane coatings can provide prolonged circulation, improved biocompatibility, immune evasion, and in some cases enhanced interaction with specific tumor-associated environments. Biomimetic approaches therefore attempt to combine the controllable properties of synthetic nanoparticles with selected biological functions of natural cells (Guido et al., 2020).

Recent biomimetic designs have also explored the use of natural cell–cell and cell–tumor interactions to improve tumor localization. In addition, biomimetic coatings may provide protection from rapid clearance while maintaining the functional properties required for therapeutic delivery. However, the complexity of membrane isolation, characterization, formulation reproducibility, storage stability, and large-scale manufacturing remains important when developing these systems for practical applications (Li et al., 2021; Mengyuan et al., 2024).

The therapeutic performance of a smart nanocarrier depends on the coordinated optimization of several physicochemical and biological parameters. Ligand density, drug-loading capacity, colloidal stability, circulation behavior, and stimulus sensitivity can all influence biodistribution and cellular uptake. An effective nanocarrier should remain sufficiently stable during circulation, reach the intended tumor region, interact appropriately with the target or tumor microenvironment, and release its payload at the desired location and time. Therefore, the design process requires balancing stability with responsiveness and tumor accumulation with efficient tissue penetration (Fathi et al., 2020).

Despite these advances, challenges associated with tumor heterogeneity, variable target expression, incomplete penetration, biological clearance, and reproducibility remain important considerations. (Tian et al., 2022).

Nanomedicine-Based Drug Delivery in Cancer

Nanocarriers can also protect drug molecules from premature degradation and provide sustained or controlled drug release, thereby modifying the pharmacokinetic behavior of conventional therapeutic agents (Mitchell et al., 2021).

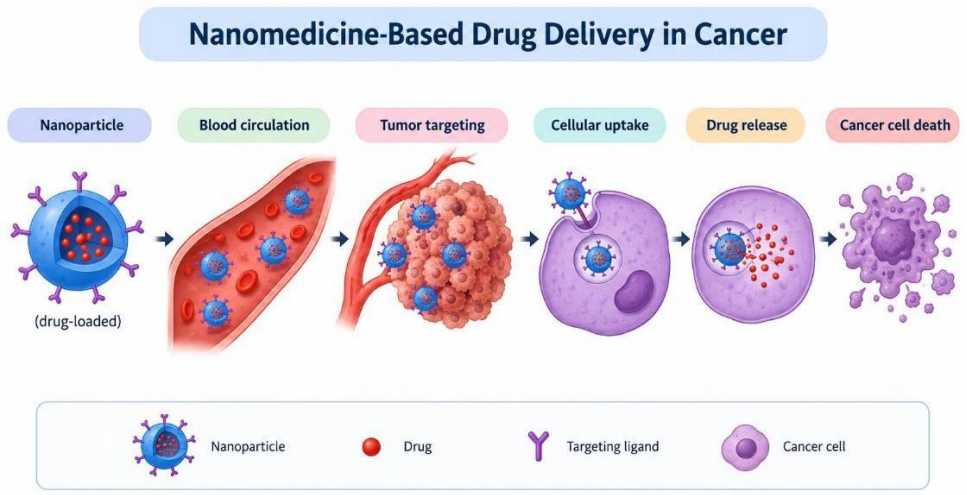

Figure 1.

The hydrophobic core can accommodate poorly soluble drugs, whereas the hydrophilic shell helps maintain dispersion in aqueous biological environments. Their relatively small size and tunable structure make them promising systems for improving drug solubilization and tumor delivery (Gaucher et al., 2005).

Antibodies, peptides, aptamers, carbohydrates, and small molecules can be employed as targeting ligands. Following interaction with the corresponding receptor, the nanocarrier may undergo receptor-mediated cellular uptake and facilitate intracellular delivery of the therapeutic payload. Nevertheless, factors such as tumor heterogeneity, receptor expression, ligand density, and interactions with biological proteins can influence the overall effectiveness of active targeting (Bae and Park, 2011).

Nanomedicine can also provide stimuli-responsive drug delivery, in which drug release is triggered by specific conditions present within the tumor or by externally applied stimuli. Such systems can be designed to remain relatively stable during circulation and release their therapeutic payload under selected conditions. (Mura et al., 2013).

These include variability in nanoparticle preparation, difficulties in large-scale manufacturing, stability problems, biological barriers, heterogeneous tumor accumulation, potential toxicity, and challenges in predicting clinical performance from preclinical models. (Blanco et al., 2015).

Future research should focus on improving tumor penetration, understanding nanoparticle–biological interactions, reducing toxicity, and establishing reproducible manufacturing and characterization strategies to facilitate successful clinical translation (Shi et al., 2017).

Nano immunotherapy and Combination Cancer Therapy

However, free antigens may undergo rapid degradation and may not efficiently reach antigen-presenting cells. Nanoparticles can encapsulate or display antigens and deliver them to dendritic cells, where antigen processing and presentation can occur. Incorporation of immune adjuvants into the same nanoplatform may further enhance dendritic-cell activation and T-cell responses. Thus, nanocarriers can function not only as drug-delivery vehicles but also as

immunological platforms for coordinated antigen presentation and immune stimulation (Miao et al., 2019).

Antibodies targeting these pathways have demonstrated significant therapeutic activity in several cancers. However, systemic administration can lead to broad immune activation and immune-related adverse effects. (Fang et al., 2018).

An important advantage of nano immunotherapy is its ability to facilitate combination cancer therapy. Cancer is a heterogeneous disease involving multiple molecular and cellular mechanisms, and treatment with a single therapeutic modality may not always provide adequate tumor control. This may include combinations of chemotherapeutic drugs with immune stimulators, checkpoint inhibitors with targeted therapies, or nucleic-acid therapeutics with conventional anticancer agents. Co-delivery can provide synchronized exposure to different therapeutic components and may improve treatment efficacy while reducing the need for multiple separate formulations (Shi et al., 2017).

Chemotherapeutic agents can directly destroy tumor cells, but certain treatments can also promote immunogenic cell death. During immunogenic cell death, tumor cells may release tumor-associated antigens and danger-associated molecular patterns that stimulate immune recognition. Potentially linking tumor-cell destruction with immune activation. (Galluzzi et al., 2017).

However, nucleic acids are vulnerable to enzymatic degradation and generally have limited ability to cross cellular membranes. For example, nanoparticles can deliver siRNA against immunosuppressive targets or mRNA encoding tumor antigens and immunomodulatory proteins. This provides opportunities for developing highly specific therapeutic strategies based on molecular characteristics of individual tumors (Hou et al., 2021).

Another important area is the development of personalized nano immunotherapy. Tumors differ substantially in their antigenic profile, immune-cell composition, molecular characteristics, and response to treatment. Personalized cancer vaccines, neoantigen delivery, and tumor-specific immune modulation are being explored to improve treatment specificity. (Sahin et al., 2017).

These include variability in nanoparticle distribution, tumor heterogeneity, immune-system complexity, potential toxicity, manufacturing difficulties, and limited. Furthermore, excessive immune stimulation may produce unwanted inflammatory or immune-related effects. (Corbo et al., 2016).

Their ability to support combination therapy and modulate the tumor microenvironment provides opportunities for achieving more effective and durable antitumor responses.

Nanomedicine for Overcoming Multidrug Resistance and Tumor Heterogeneity

These subpopulations may differ in their growth rate, drug sensitivity, metastatic potential, and response to treatment. (Majidinia et al., 2020).

Conventional administration of higher drug doses may not adequately overcome this mechanism and can increase systemic toxicity. Modifying cellular uptake pathways, and reducing the influence of drug efflux mechanisms. (Mohammad et al., 2020).

A nanocarrier can simultaneously transport a cytotoxic drug and a molecule designed to suppress a resistance

mechanism. (Liu et al., 2021).

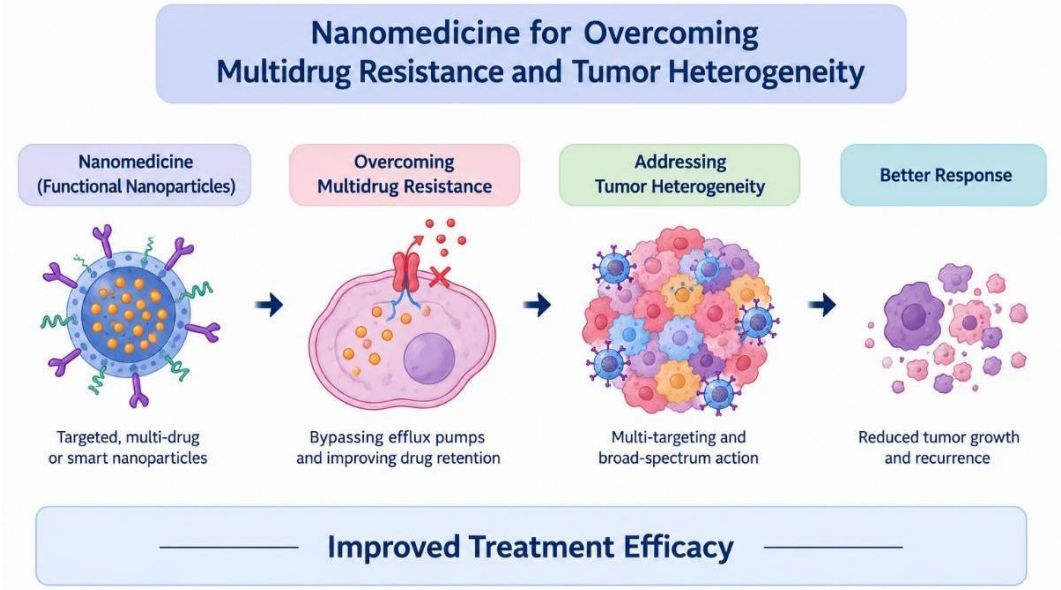

Figure 2.

Multifunctional nanoparticles can incorporate several components within a single platform, allowing different mechanisms of action to be activated simultaneously or sequentially. (Zhu et al., 2021).

As a result, a drug that effectively eliminates one cancer-cell population may have limited activity against another population within the same tumor. This can lead to incomplete tumor eradication and the subsequent expansion of resistant cell populations. (Lepeltier et al., 2020).

Targeted nanocarriers can further improve drug delivery to heterogeneous tumor tissues. However, because receptor expression may vary between different tumor-cell populations, a single targeting ligand may not be sufficient to address the complete tumor. Consequently, researchers have explored multifunctional nanoparticles containing multiple Such approaches may improve the probability of reaching different tumor-cell populations and may reduce the limitations associated with single-target therapy (Su et al., 2021).

Nanocarriers may also facilitate the co-delivery of cytotoxic drugs and molecular agents directed against specific signaling pathways involved in CSC maintenance. Targeting both bulk tumor cells and resistant stem-like populations may provide a more comprehensive therapeutic strategy than targeting only the rapidly proliferating tumor-cell population (Zhu et al., 2021).

Nanomedicine also provides opportunities for gene-based approaches to MDR reversal. RNA involved in drug efflux, anti-apoptotic signaling, DNA repair, or other resistance-associated pathways. (Mohammad et al., 2020).

Nanoparticles can be coated with cell membranes or combined with biological components to obtain properties that facilitate interaction with tumors or reduce rapid clearance. Exosome-based systems are another emerging platform that can exploit naturally occurring intercellular communication mechanisms for therapeutic delivery. Nevertheless, their complexity presents additional challenges related to manufacturing, characterization, reproducibility, and regulatory

development (Lepeltier et al., 2020).

Such systems, commonly described as theragnostic nanomedicines, may combine imaging components with therapeutic agents. Imaging can potentially provide information regarding nanoparticle distribution, tumor localization, and treatment response, while the same platform delivers therapeutic payloads. However, clinical translation requires reliable imaging methods and a clear relationship between nanoparticle characteristics, biodistribution, and therapeutic outcomes (Su et al., 2021).

Despite the promising potential of nanomedicine, several challenges remain. Tumor heterogeneity can affect nanoparticle accumulation and target-receptor expression, while biological barriers may restrict penetration into solid tumors. Nanoparticle properties can also change after interaction with biological fluids, potentially affecting biodistribution and cellular uptake. Manufacturing complexity, batch-to-batch reproducibility, long-term toxicity, and regulatory requirements are additional factors that influence successful translation of advanced nanomedicines (Liu et al., 2021).

Through targeted drug delivery, co-delivery of therapeutic combinations, gene silencing, stimuli-responsive release, tumor-microenvironment modulation, and multifunctional nanocarriers, nanotechnology may target resistant cancer-cell populations, and establishing clinically reproducible strategies for translating multifunctional nanocarriers from laboratory research into effective cancer therapies.

Safety, Toxicity and Biocompatibility of Cancer Nanomedicines

Nanocarriers can enhance drug solubility, prolong circulation, facilitate controlled release, and potentially reduce exposure of healthy tissues to cytotoxic agents. Therefore, the evaluation of safety, toxicity, and biocompatibility is an essential component of cancer nanomedicine development. (Liu et al., 2020).

Nanoparticles interact with biological systems immediately after administration. Consequently, the biological behavior of a nanoparticle cannot always be predicted solely from its original physicochemical characteristics. (Monopoli et al., 2012).

Changes in particle size can influence circulation time, cellular uptake, renal clearance, and accumulation in different organs. Very small nanoparticles may exhibit different biological behavior from larger particles, while aggregation can substantially alter the effective size of the formulation. Therefore, controlling particle-size distribution and maintaining formulation stability are important during both development and storage. (Blanco et al., 2015).

However, excessive surface charge may also increase nonspecific interactions with proteins and cell membranes and may contribute to cytotoxicity or inflammatory responses. Neutral or mildly charged nanoparticles may demonstrate improved stability and reduced nonspecific interactions in some applications. Therefore, optimization of surface charge is necessary to achieve an appropriate balance between cellular uptake, circulation, and safety (Foroozandeh and Aziz, 2018).

Some inorganic nanoparticles may also interact directly with cellular organelles and alter mitochondrial function. Depending on the material and dose, nanoparticles may therefore produce apoptosis, inflammation, membrane damage, or other cellular responses. These effects emphasize the importance of evaluating oxidative stress and mitochondrial

function during preclinical safety assessment (Nel et al., 2006).

Certain formulations may stimulate complement activation or cytokine release, whereas others may be rapidly removed from circulation by macrophages. Although immune interactions can sometimes be beneficial for immunotherapeutic applications, uncontrolled immune activation may lead to undesirable inflammatory effects. (Dobrovolskaia and McNeil, 2007).

Long-term accumulation is of particular concern for certain inorganic nanoparticles because some materials may degrade slowly or persist within the body. (Liu et al., 2020).

Biodegradability and biocompatibility are important characteristics for the development of safer nanomedicines. However, the degradation products themselves must also be evaluated for toxicity. A nanocarrier may demonstrate good biocompatibility under one experimental condition but show different behavior at higher concentrations, prolonged exposure, or after repeated administration. Therefore, biocompatibility should be assessed under clinically relevant conditions rather than through a single toxicity test (Fadeel, 2019).

The route of administration can substantially influence nanoparticle safety. Intravenous administration exposes nanoparticles directly to blood components and systemic immune mechanisms, whereas oral, pulmonary, transdermal, or local administration introduces different biological barriers and potential toxicity pathways. For intravenous nanomedicines, hemocompatibility is particularly important because nanoparticles may interact with erythrocytes, platelets, plasma proteins, and complement proteins. Evaluation of hemolysis, coagulation, platelet activation, and complement activation may therefore be required depending on the formulation and intended clinical application (Dobrovolskaia et al., 2008).

Another important aspect is the possibility of organ-specific toxicity. Nanoparticles that accumulate in the liver may influence hepatocellular function, while accumulation in the kidneys may affect renal clearance or cause tissue injury. The toxicity profile is strongly dependent on the chemical composition, dose, particle characteristics, exposure duration, and route of administration. Consequently, comprehensive preclinical evaluation should include appropriate biochemical, histopathological, hematological, and functional assessments of relevant organs (Kermanizadeh et al., 2016).

Safety assessment should also consider the manufacturing process and formulation reproducibility. Variations in particle size, drug loading, surface properties, residual solvents, impurities, aggregation, or degradation products can alter the biological performance of a nanomedicine. Large-scale manufacturing may introduce additional challenges compared with laboratory-scale preparation. Therefore, appropriate characterization and quality-control procedures are required to ensure that different production batches demonstrate consistent physicochemical and biological properties. Manufacturing-related risks should be considered early during formulation development rather than only during late-stage clinical development (Zhang et al., 2023).

Such an approach may reduce development failures and facilitate the transition of promising nanomedicines from laboratory research to clinical studies (Zhang et al., 2023).

Differences between in vitro, animal, and human biological systems can make it difficult to predict clinical safety

accurately. Furthermore, the complexity of multifunctional nanoparticles may require more extensive characterization than conventional small-molecule drugs. Standardized methods for evaluating nanoparticle toxicity, biodistribution, immunological responses, and long-term effects are therefore important for improving regulatory assessment and clinical development (Liu et al., 2020).

Overall, safety, toxicity, and biocompatibility are fundamental considerations in the development of cancer nanomedicines. Comprehensive assessment of particle characteristics, protein corona formation, oxidative stress, immune responses, biodistribution, organ toxicity, biodegradability, and long-term effects is therefore necessary. Future cancer nanomedicine development should increasingly adopt safe-by-design principles, standardized toxicity assessment, and clinically relevant models to improve the reliability, safety, and successful translation of nanoparticle-based cancer therapies.

Current Trends, Emerging Technologies and Future Perspectives

Cancer nanomedicine is rapidly evolving from conventional nanoparticle-based drug delivery toward multifunctional and highly specialized therapeutic platforms. Early nanomedicines primarily focused on improving the solubility, stability, pharmacokinetics, and tolerability of established anticancer drugs. Current research is increasingly directed toward precise tumor targeting, controlled drug release, modulation of the tumor microenvironment, combination therapy, nucleic-acid delivery, and personalized treatment. (Bobo et al., 2016).

A single nanocarrier may be designed to incorporate a chemotherapeutic drug, an immune-modulating molecule, a targeting ligand, and an imaging component. Such systems can potentially combine diagnosis, targeted delivery, controlled release, and treatment within one platform. This concept is particularly relevant to cancer because tumor diagnosis, drug delivery, and monitoring of therapeutic response can be integrated into a single strategy. (Estelrich et al., 2015).

Conventional nanomedicines are generally designed for broad patient populations, whereas precision approaches attempt to account for differences in tumor genetics, receptor expression, immune status, and tumor microenvironment. Targeting ligands may be selected according to receptor expression, while drug combinations may be designed according to specific resistance mechanisms. This approach may contribute to more individualized cancer treatment, although reliable biomarkers and clinically validated patient-selection strategies remain necessary (Shi et al., 2022).

Internal stimuli include acidic pH, enzymes, reactive oxygen species, glutathione concentration, and other characteristics of the tumor microenvironment. External stimuli may include light, ultrasound, magnetic fields, and temperature. Stimuli-responsive systems can potentially reduce premature drug release and provide greater control over the location and timing of drug delivery. (Li et al., 2020).

Their successful application in other therapeutic areas has encouraged researchers to investigate their use for cancer vaccines, immune modulation, gene silencing, and protein replacement. LNP composition can be optimized using ionizable lipids, phospholipids, cholesterol, and surface-associated components to control stability and delivery. In oncology, LNPs may provide a platform for delivering tumor antigens or therapeutic RNA molecules and could become increasingly relevant to individualized cancer immunotherapy (Hou et al., 2021).

Another emerging area is biomimetic nanotechnology, in which nanoparticles are designed to imitate or utilize

biological structures. Cell-membrane-coated nanoparticles, exosome-inspired systems, protein-based nanocarriers, and other biomimetic platforms are being explored to improve circulation, immune compatibility, tumor targeting, and cellular uptake. Because biological membranes naturally possess specific recognition and communication functions, their incorporation into nanocarriers may provide advantages over completely synthetic systems. However, reproducible preparation, characterization, stability, and large-scale manufacturing remain important challenges for the clinical translation of biomimetic nanomedicines (Fang et al., 2018).

Their biological origin and ability to interact with recipient cells have stimulated interest in using them as delivery vehicles for cancer therapeutics. However, challenges associated with isolation, purification, loading efficiency, heterogeneity, scalability, and quality control must be addressed before their widespread clinical application (Kalluri and LeBleu, 2020).

Computational methods can assist researchers in analyzing relationships between nanoparticle characteristics and biological outcomes, optimizing formulation parameters, and identifying potential drug combinations. Data-driven approaches may support the prediction of nanoparticle behavior and help reduce the number of experimental formulations that need to be evaluated. (Mitchell et al., 2021).

Another important future direction is the development of nanomedicine-assisted combination therapy. Nanocarriers can potentially co-deliver different therapeutic agents and control their release at specific sites. This approach may improve treatment synchronization and reduce some limitations associated with administering multiple drugs independently. Future multifunctional platforms may therefore combine cytotoxic, immune-modulating, and molecularly targeted agents within a single nanoscale system (Riley et al., 2019).

Tumors can evolve during therapy, leading to changes in molecular targets, immune characteristics, and drug sensitivity. A future nanomedicine strategy could potentially incorporate information from tumor profiling and treatment response to modify therapeutic payloads or targeting approaches. Such adaptive systems remain largely experimental, but they illustrate a broader movement toward dynamic and individualized cancer treatment rather than fixed therapeutic regimens (Shi et al., 2022).

These include biological variability between patients, heterogeneous tumor accumulation, limited tumor penetration, nanoparticle stability, manufacturing complexity, long-term safety, regulatory requirements, and difficulties in reproducing laboratory findings in clinical settings. Many sophisticated nanoplatforms demonstrate promising results in experimental models but require extensive validation to establish their clinical benefit. Therefore, future research should not focus solely on increasing nanoparticle complexity but should also emphasize reproducibility, safety, scalability, and clinically meaningful therapeutic outcomes (Bobo et al., 2016).

Greater understanding of tumor biology advances in biomaterials, improvements in nucleic-acid delivery, and integration of nanotechnology with immunotherapy may create new therapeutic opportunities.

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