Nanotechnology Approaches for Cancer Therapy: Key Tools and Drug-Delivery Mechanisms

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Abstract. Amidst the global health crisis of cancer, the introduction of nanotechnology has begun to revolutionise cancer therapeutic approaches. By addressing inherent limitations of conventional treatments such as non-specificity, drug toxicity, resistance and inadequate tumour penetration. This review focuses on the current major nanoparticle-based platforms (1-100 nanometres) and their clinical potential and current advancements. The key nanocarriers featured in this review include liposomes and lipid nanoparticles (LNPs) for co-encapsulation and nucleic acid delivery, mesoporous silica nanoparticles (MSNs) enabling stimuli-responsive release, polymeric nanoparticles (PNPs) with emphasis on biocompatibility and hybrid nanoparticles for synergistic therapies (such as photothermal therapy). Mechanisms of these nanotechnologies are also outlined via denoting various delivery strategies, including passive targeting through the enhanced permeability and retention (EPR) effect, active targeting through ligand mediation, stimuli-responsive release and ratio-optimised co-delivery. Clinically approved formulations are explored whilst preclinical breakthroughs (Triplet LNPs in immunotherapy and bacteria-targeted MSNs) validate improved efficacy, reduced systemic toxicity and further clinical potentials. At the same time, critical limitations and future perspectives are also assessed in order to provide a general systematic outlook of this newly emerging option in the field of cancer therapy.

Keywords: Nanotechnology; cancer therapy; nanocarriers; tumor targeting.

1. Introduction

To this day, cancer remains among the most formidable global challenges, resulting in millions of deaths annually, whilst placing a significant burden and strain on public health systems worldwide. Despite commendable progress in surgical methods, radiotherapy and systemic chemotherapy, conventional treatment strategies continue to face various profound limitations. This includes non-specific distribution of cytotoxic drugs, severe dose-limiting toxicities, poor solubility of drugs, rapid clearance (for instance, clearance through the body's immune defences and barriers) and limited ability to discriminate between healthy and malignant tissues [1]. Moreover, tumours often develop multiple mechanisms of resistance towards conventional treatments, including upregulation of drug efflux pumps, channelling adaptive survival signalling pathways and tumour microenvironment-driven hypoxia and genomic instabilities, which undermine long-term treatment efficacy. At the same time, the highly heterogeneous and dynamic tumour microenvironment, composed of abnormal vasculature, elevated interstitial pressure and a dense extracellular matrix, which hinders the diffusion and penetration of drugs and reduces the likelihood of therapeutic success.

However, given these challenges, nanomedicine emerged as a promising avenue. This offers scientists a chance to reengineer and redefine the field of drug delivery, enabling enhanced tumour targeting, highly controlled release, improved pharmacokinetics and potentially, reduced systemic toxicity. By integrating drug release with nanoscale properties, nanocarriers can bypass many biological barriers, to provide multifaceted platforms merging therapeutic treatments, diagnostics and monitored payload release [2].

As of 2025, several nanomedicines have been approved for clinical use, and multiple nanocarrier platforms have entered phase II clinical trials, but issues such as targeted delivery efficiency and long-term biosafety remain key research focuses. This paper aims to present and discuss major recent nanoparticle-based platforms and technologies for cancer therapy, with emphasis on their clinical

applications, current drug delivery mechanisms and research-based findings, whilst also denoting the current obstacles and future directions in the field.

2. Nanotechnology in Medicine

Under the context of biomedical sciences, nanotechnology (or nanomedicines) encompasses the design, synthesis and medical applications using materials with typical sizes of 1-100 nanometres (a nanometre is one-billionth of a metre). These are ultrasmall substances known as nanoparticles. Fascinatingly, the nature and properties of these molecules allow them to harness physicochemical properties that are unavailable to bulk materials. At this nanoscale, particles display extremely high surface area to volume ratios, tunable surface chemistries and size-dependent biodistribution, which can influence cellular uptake and the ability to penetrate and demolish malignant tissues [3]. These distinct characteristics enable nanoparticles to encapsulate or conjugate a diverse spectrum of cancer therapeutic agents, including molecular chemotherapeutics, photosensitizers, nucleic acids and immunomodulators. Simultaneously, nanoparticles can also deliver these agents with enhanced stability whilst reducing off-target effects.

Primarily, nanotechnology platforms harness both passive targeting (via enhanced permeability and retention (EPR) effect in aberrant tumour vasculature) and active targeting (through exploiting surface functionalisation with ligands such as antibodies, peptides or aptamers which bind to tumour-associated receptors). The major classes of current clinically associated and experimentally advanced nanocarriers include liposomes or lipid nanoparticles (LNPs), polymeric nanoparticles, mesoporous silica nanoparticles (MSNs), metallic or inorganic nanoparticles (such as gold, magnetic iron oxide, silicon dioxide), hybrid or multifunctional nano-systems and carrier-free nanomedicines [1]. Overall, these platforms work to expand the possibilities and choices in terms of therapeutic applications, which effectively bridge various methods of cancer therapy including drug delivery, imaging, immunotherapy and controlled-release strategies.

3. Key Nanotechnology Tools for Cancer Treatment

3.1. Liposomes and LNPs

Liposomes are spherical vesicles composed of hydrophilic cores and hydrophobic phospholipid bilayers. These properties are ideal in that individual vesicles can be engineered and excel at encapsulating both hydrophilic and hydrophobic therapeutic agents. This prevents the cargo from degradation whilst reducing systemic side effects. To date, clinically approved liposomal formulations such as Doxil® (PEGylated doxorubicin, approved for the treatment of metastatic breast cancer and ovarian cancer) and Onivyde® (irinotecan liposomes, approved for pancreatic cancer) have validated the utility of lipid-based nanoparticles in treating metastatic breast, pancreatic and ovarian cancers, through enhancing drug accumulation in tumours via enhanced permeability and retention effect [3].

LNPs are advanced lipid-based nanocarriers that are optimised for nucleic acid delivery, with powerful contributions to cancer immunotherapy platforms. Unlike traditional liposomes, LNPs incorporate ionisable lipids that facilitate endosomal escape and intracellular delivery of mRNA, siRNA and other immunomodulatory molecules. A study done in 2024 demonstrates that the intratumoral delivery of LNPs co-encapsulating mRNAs that encode three immunomodulators (‘Triplet LNP’) 4-1BBL, IL-21, IL-7 resulted in profound anti-tumoral immunity in preclinical models of cancer cells, including MC38 colon carcinoma and E0771 triple-negative breast cancer models. The ‘Triplet LNP’ formulation designed by the team of researchers enhanced tumour-infiltrating CD8+ T cell frequency and function, which led to the eradication of established tumours and conferred long-term immunologic al memory (for instance, mice that survived initial tumour exposure remained protected when the cancer cells were reintroduced weeks later). Critically, the ‘Triplet LNP’ outperformed immune checkpoint inhibitors (such as anti-PD1) in resistant models,

and when the two are combined, complete tumour regression was achieved in all the mice involved. Therefore, highlighting how LNPs can potentially address unmet needs in patients who are unresponsive to standard cancer immunotherapies [4].

Furthermore, a meta-analysis featuring 273 preclinical studies further confirmed the efficacy of multi-drug lipid-based nanoparticles. With co-encapsulation in a single nano formulation, it reduces tumour growth by an additional 19% in comparison to co-administration of individual nanomedicines. This synergy arises due to the ability of LNPs to maintain optimal drug ratios, synchronise delivery to target cells and augment circulation half-life, providing resolutions to uncoordinated pharmacokinetics which used to limit free drug combinations [5]. Notably, LNPs exhibit a generally favourable safety profile. Under a research trial setting, no significant weight loss, acute toxicity or long-term hepatotoxicity is reported in treated mice [4].

3.2. Mesoporous Silica Nanoparticles

Mesoporous silica nanoparticles are inorganic nanomaterials comprising ordered, hexagonally arranged mesopores (2-10 nanometres in width) and a silica-based framework, which are features that derive from surfactant-templated sol-gel synthesis. Their porous structure is highly mendable and can be designed to act as ‘nanoscale containers’ to hold cancer therapeutic drugs. Moreover, their surface can be easily modified to target cancerous regions or respond to stimuli such as pH fluctuations or near-infrared (NIR) light, whilst leaving healthy tissues unharmed [6].

In preclinical research, MSNs have displayed promising results. For example, in a study from 2024, thiol-modified MSNs paired with gold nanorods and the drug doxorubicin (AuNR@S-MCM-41-DOX) cleared lung cancer cells more effectively than chemotherapy or photothermal therapy under pH and NIR-monitored conditions [6].

Furthermore, a recent study in 2025 for breast cancer harnesses MSNs loaded with a natural anticancer agent known as astragaloside IV (PP@M-TD/AS). This drug was delivered to the cancerous regions via tumour-targeting bacteria, which then released the drug when stimulated by focused ultrasound ablation (FUAS). Results exhibit high antitumour efficacy and minimal systemic toxicity in comparison to single therapies, which display limited efficacy when targeting residual tumours [7].

3.3. Polymeric Nanoparticles

Polymeric nanoparticles (PNPs) are highly versatile and biocompatible nanocarriers built from synthetic or natural polymers (such as albumin, PLGA, chitosan). Their modular design makes room for interaction and functionalisation with various ligands (like peptides or aptamers) to target tumour cells, cancer-associated fibroblasts (CAFs) and cancer stem cells (CSCs). This aids the PNPs to overcome complex biological barriers such as the dense stroma of pancreatic ductal adenocarcinoma (PDAC), illustrated in a recent pre-clinical study in 2025, involving multifunctional PNPs (‘smart’ PNPs) [8]. On the other hand, under a clinical setting, the impacts of PNPs can already be arrayed through the application of Abraxane® (albumin-bound paclitaxel) in breast, pancreatic and lung cancer treatments [3].

3.4. Hybrid and Inorganic Nanoparticles

Hybrid nanoparticles are nanocarriers engineered through the combination of two or more distinct types of nanomaterial (such as polymers, lipids, metals). A prominent example of which is the lipid-polymer hybrid nanoparticles (LPNPs), which comprises a biodegradable polymeric core (such as PLGA) acting as a stable vessel for drug encapsulation, whilst the lipid shell (such as TPGS, lecithin) enhances the biocompatibility and controlled drug releases of hybrid nanoparticles. These systems leverage the stability of the carrier whilst protecting the payloads (such as doxorubicin) during drug circulation within the body. For instance, a preclinical study from 2022 denotes how pH-sensitive PLGA-TPGS LPNPs loaded with doxorubicin and α-tocopherol succinate (TS) form ion pairs that dissociate in the acidic tumour microenvironment (TME), which enables targeted drug release.

Furthermore, these LPNPs achieved an overall 86% of tumour growth inhibition in breast cancer models, outperforming liposomes and free drugs whilst minimising systemic toxicity [9].

Inorganic nanoparticles are composed of non-carbon-based materials (such as metals, metal oxides and layered minerals), meaning that they embody inherent physicochemical properties which are tailored for cancer therapeutics, imaging and synergistic effects. Moreover, metallic nanoparticles (such as gold, platinum, bismuth) have been proven to excel in photothermal therapy (PTT) and radio sensitisation. This can be portrayed in a 2023 study where Fe3O4 (magnetite) nanoparticles enable targeted hyperthermia via heat generation within a series of alternating magnetic fields. This in turn induces cancer cell necrosis (uncontrolled cell death due to metabolic stress) without affecting the surrounding tissues [10].

3.5. Summary of Key Nanotechnology Tools

Different nanocarriers have unique advantages tailored to diverse therapeutic needs: liposomes and LNPs excel in co-encapsulating hydrophilic and hydrophobic drugs (especially LNPs for nucleic acid delivery); MSNs are superior in stimuli-responsive drug release due to their adjustable porous structure; polymeric nanoparticles have outstanding biocompatibility and are suitable for functional modification to overcome stromal barriers; hybrid and inorganic nanoparticles integrate multiple properties, such as the stability of polymers and the photothermal effect of metals, enabling synergistic therapy.

4. Mechanism of drug delivery involving nanotechnology

The core mechanisms that drive the effective delivery of nanoparticles rely on leveraging nanoparticle properties, such as size, surface functionalisation and responsiveness towards tumour microenvironment cues, to enhance drug bioavailability, target specificity and therapeutic outcomes [3]. Overall, the two primary targeting strategies involve either passive or active targeting. These methods form the basis of nanomedicine delivery, whilst stimuli-responsive release and co-delivery further optimise associated therapeutic outcomes.

Passive targeting is a type of mechanism that relies on the enhanced permeability and retention (EPR) effect, which is a hallmark of tumour biology characterised by leaky vasculature (leaky blood vessels, fenestrations of 200-2000 nanometres) and impaired lymphatic drainage [3]. Therefore, nanoparticles can extravasate (slip) through these gaps and accumulate in the TME without needing targeted coatings. A typical carrier for passive targeting is PEGylated liposomes (e.g., Doxil®)—their surface is modified with hydrophilic polyethylene glycol (PEG), which prevents rapid clearance by the mononuclear phagocyte system, prolonging circulation and enabling sustained drug release at tumour sites, thus reducing off-target toxicity [5].

Active targeting is an approach where nanoparticles are functionalised with ligands (such as antibodies, peptides or folate) that bind to receptors overexpressed on the surface of cancer cells (such as EGFR or folate receptors) [3]. A representative example is GE11 peptide-conjugated liposomes (2025 study), which target EGFR to significantly improve docetaxel and siRNA delivery to laryngeal cancer cells and overcome multidrug resistance [2].

Contrastingly, stimuli-responsive nanoparticles only release their drug cargo when they detect the TME, triggered by endogenous cues (such as acidic pH, reactive oxygen species) or the introduction of exogenous stimuli (ultrasound, near-infrared light). For instance, a study outlines how pH-sensitive liposomes destabilise and break open to release their payload in the acidic TME (ph6.0-6.5), and thermosensitive liposomes respond to ultrasound-induced hyperthermia, making them release drugs exactly at the tumour site. This means that fewer drugs accumulate in healthy tissues, minimising systemic toxicity whilst maximising intratumoral drug concentration, creating an effective drug delivery pathway [2].

Moreover, the co-delivery of multiple drugs encapsulated within a single nanocarrier addresses issues such as drug resistance (cancer often resists single drug targeting) whilst promoting synergistic

effects. Co-delivery is achieved through ratio metric drug dosing (via identifying an optimal drug ratio using combination analysis models). For instance, the clinically approved liposomal formulation Vyxeos® co-delivers cytarabine and daunorubicin at a 5:1 synergistic ratio. This improved the overall survival rate in acute myeloid leukemia (AML) patients by 4 months in comparison to the free drug combination [5]. Currently, co-delivery is used alongside targeting strategies such as passive and active targeting (exploiting the EPR effect or via modification involving ligands) to accumulate preferentially in the targeted tumour tissue. As a result, side effects are minimised as targeted delivery minimises the exposure of healthy tissues to cytotoxic drugs.

5. Current Success and Progress

Since its advancements in the 2000s, the application of nanotechnology in cancer therapeutics has proven to be advantageous in comparison to conventional therapies such as chemotherapy and radiation therapy. These therapeutic approaches pose several concerns, such as the efficacy of delivery and occurrence of long-term side effects due to uneven distribution within the body and cytotoxicity, damaging healthy tissues whilst putting strain on the overall health and well-being of the patient. On the other hand, nanoparticles are highly specific, bringing about a new approach to targeted therapy in cancer treatment. Their passive and active targeting mechanisms support and increase the intratumoral concentration of drugs whilst also being designed to react to different stimuli (being sensitive to pH, temperature), making them highly versatile and adaptable for various types of cancer. Furthermore, studies have demonstrated that nanoparticles show potential to penetrate areas in the body that are otherwise therapeutically inaccessible to chemotherapy agents. For example, in the case of brain cancer, chemotherapy drugs are often limited to intraventricular or intracerebral infusions. This is because of the presence of the blood-brain barrier (BBB), which is a specialised structure that shields the central nervous system from cytotoxic agents. Fortunately, nanoparticles can cross the BBB via employing various modifications and stimuli, such as EPR effect, ultrasound systems, peptide-modified endocytosis and transcytosis [3].

6. Challenges and Limitations

Despite significant developments, nanotechnology-based cancer therapies still face certain challenges that hinder their overall clinical translation and efficacy. Firstly, modification is the key to the highly specific tumour targeting ability and drug release control. Hence, without modifications, nanoparticles lack these abilities and may start to display off-target biodistribution, requiring integration with targeting agents such as Bifidobacterium bifidum (BF). Yet, these modification approaches may rely on microorganism-nanoparticle interactions (such as bacterial-nanoparticle interaction), which may be disrupted under complex biological environments (such as the TME). Secondly, although the application of stimuli-responsive systems (pH-sensitive, temperature-sensitive) enables controlled payload release in nanocarriers, ensuring precise activation only at tumour sites remains difficult. This is due to associating risks such as premature leakage or inadequate releases under variable physiological conditions within the body [7]. Thirdly, ineffectiveness displayed through cell line-specificity is another critical challenge. The results shown from a 2022 study outline how pH-sensitive PLGA-TPGS hybrid nanoparticles (LPNP-TS-DOX) illustrated no significant cytotoxicity or cellular uptake advantages over the free drug doxorubicin in MDA-MB-231 breast cancer cells, despite displaying strong efficacy in 4T1 and MCF-7 cell lines. This variability underscores the sheer difficulty in developing nanotechnologies that can universally target a diverse range of cancer cell phenotypes (which may differ in receptor expression and endocytic pathways) [9]. Moreover, long-term biosafety is also a pressing concern. Wide clinical application of nanotechnology is currently limited due to the need for more systematic assessment and research on their biodegradation, systemic immune responses and potential long-term toxicity. Various studies

have shown that the nature of these nanotechnologies is highly varied and often unpredictable, making many doubt their current applicability [7].

7. Future Perspectives and Applications

Overall, nanotechnology holds transformative potential within the field of cancer therapy. Research findings have already outlined its emerging directions, focusing on enhancing targeting precision, overcoming resistance and expanding theragnostic capabilities. Moving on, research should focus on the refinement of treatment methods whilst assessing long-term toxicity and side effects of the nanocarriers in clinical models. Additionally, research should also aim to augment the accessibility and applicability of nanotechnology in a clinical setting, to support advancements such as personalised and multifunctional nanomedicine and related enhancements regarding cancer immunotherapy.

8. Conclusion

In conclusion, nanotechnology has firmly established itself as a prevailing element within the fields of cancer research, clinical advancements and treatments, supporting more potential anti-cancer applications in the foreseeable future. Its synthesis propounds the longstanding limitations of conventional treatment methods (non-specific drug distribution, systemic toxicity, drug resistance, poor tumour penetration) which have plagued and hindered elevation in clinical oncology for decades. From clinically validated liposomes and lipid nanoparticles to highly versatile research-based models such as the mesoporous silica nanoparticles and synergistic hybrid and inorganic nano systems, each of which leverages unique physicochemical properties such as high surface area to volume ratios, stimuli responsiveness and tuneable surface chemistries, which are highly efficient in aiding treatment through enhanced specificity and targeted delivery. This can be achieved with delivery mechanisms ranging from passive targeting (harnessing the EPR effect) to active ligand-mediated binding, stimuli-triggered release and ratio-optimised co-delivery. Together, these progressions have translated into tangible clinical success. Evidently demonstrated through the approval of formulations such as Doxil®, Abraxane® and Vyxeos®, which are currently in use to treat various forms of cancer such as metastatic ovarian cancer, myeloma, AIDS-related sarcoma, acute myeloid leukemia and breast cancer. Moreover, nanotechnology also underscores promising breakthroughs in preclinical trials, such as the newly formulated Triplet LNPs for refractory immunotherapy and bacteria-targeted MSNs to support residual tumour eradication, manifesting the potential of nanomedicine in augmenting drug efficacy whilst reducing systemic harm. On the other hand, significant barriers to full clinical translation have been identified as a persisting limitation. Despite the commendable, highly specific characteristics of the nanocarriers, targeted delivery efficiency remains inconsistent. Cell line-specific variability limits universal applicability, meaning that more time and economic effort must be invested to support fully personalised treatment. Furthermore, the chances of premature drug leakage threaten therapeutic precision, whilst long-term biosafety (particularly regarding biodegradation and immune responses) raises concerns for many patients, therefore requiring more systematic assessments and investigations. Overcoming these challenges demands continued refinement in the design and manufacture of the nanocarriers. While placing the focal point on enhancing targeting specificity and developing personalised formulations tailored to the tumour phenotypes of each individual. Simultaneously, future research should also be prioritised via integrating nanotechnology with emerging therapeutic modalities, such as immunotherapy and theragnostic, to create multifunctional systems which combine drug delivery, medical imaging and immune modulations, moving towards a more effective, multifaceted and safer treatment option. Ultimately, transforming patient outcomes and reducing the public health burden of cancer.

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