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Impact of Nanoparticles on Cancer Therapy: A Comprehensive Review

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ABSTRACT: Background: Cancer remains a leading cause of global mortality, accounting for approximately 10 million deaths in 2020 alone. Conventional therapies, including chemotherapy, radiotherapy, and surgery, are often plagued by systemic toxicity, poor pharmacokinetics, inadequate tumor selectivity, and multidrug resistance. Objective: This review comprehensively evaluates the mechanistic basis, therapeutic applications, and future prospects of nanoparticle (NP)-mediated drug delivery in oncology, with special emphasis on the integration of natural bioactive compounds within nanotechnology platforms. Methods: A synthesis of peer-reviewed literature was performed, drawing from two key review articles and their cited evidence base. Results: NPs confer a range of advantages including enhanced bioavailability, controlled drug release, passive and active tumor targeting via the enhanced permeability and retention (EPR) effect and receptor-mediated endocytosis, and the capacity for combination and gene therapy. Natural compounds—including anthocyanins, ellagic acid, resveratrol, and quercetin—demonstrate potent anticancer properties but are severely limited by poor aqueous solubility and rapid in vivo clearance; nano-encapsulation resolves many of these limitations.

Conclusion: Nanomedicine represents a transformative paradigm in cancer care. Continued innovation in NP design, safety profiling, and clinical translation is essential to fully realize the potential of this field.

Keywords: Nanoparticles; Cancer therapy; Drug delivery; EPR effect; Natural compounds; Nanomedicine; Targeted therapy; Bioavailability; Combination therapy.

INTRODUCTION

Cancer is one of the most pressing health challenges of the 21st century. According to the GLOBOCAN 2020 database, approximately 19.3 million new cancer cases and 10 million cancer-related deaths were recorded in 2020 alone [1]. Despite decades of research, conventional treatment modalities surgery, chemotherapy, radiation therapy, and immunotherapy continue to face fundamental limitations. Chemotherapeutic agents frequently damage rapidly dividing healthy cells, including those of the gastrointestinal epithelium, bone marrow, and hair follicles, resulting in severe acute and long-term toxicities [2]. Some drugs are additionally impeded by physiological barriers such as the blood–brain barrier (BBB), limiting their access to intracranial tumors [3]. Low tumor drug concentrations inevitably promote cellular drug resistance, further reducing therapeutic efficacy [4]. Nanomedicine has emerged as a transformative approach to overcome these challenges. Nanoparticles (NPs), typically ranging from 1 to 250 nm in diameter, possess unique physicochemical properties—including high surface area-to-volume ratios, tunable surface chemistry, and the capacity to encapsulate diverse therapeutic payloads—that can be engineered to optimize biological interactions [5]. Nanocarrier platforms such as liposomes, polymeric micelles, solid lipid nanoparticles, dendrimers, mesoporous silica nanoparticles (MSNs), quantum dots, carbon nanotubes, and metallic nanoparticles have been extensively

evaluated in both preclinical and clinical settings [6]. Concurrently, naturally occurring bioactive compounds derived from plants, fungi, and marine organisms have attracted significant interest as anti-cancer agents. Phytochemicals such as anthocyanins, ellagic acid, resveratrol, and quercetin possess antioxidant, anti-inflammatory, pro-apoptotic, and antitumor activities. However, their therapeutic utility is frequently limited by poor aqueous solubility, rapid metabolic degradation, and inadequate bioavailability [7]. The integration of such natural compounds within nanoparticle-based delivery platforms represents a synergistic strategy capable of enhancing efficacy, improving pharmacokinetics, and achieving selective cancer cell targeting [8]. This review comprehensively examines the mechanisms of NP-mediated drug delivery, the application of nanomedicine across major oncological treatment modalities, the role of nanotechnology in enhancing natural compound delivery, and the current challenges and future directions within the field.

Mechanisms Of Nanoparticle-Mediated Drug Delivery

2.1 Passive Targeting: The EPR Effect

The cornerstone of passive NP tumor accumulation is the enhanced permeability and retention (EPR) effect. Solid tumors undergo rapid and disorganized angiogenesis, producing vasculature characterized by irregular architecture, wide inter-endothelial gaps (100–800 nm), and defective pericyte coverage. These structural abnormalities allow NPs of appropriate size (typically 5–250 nm) to extravasate from tumor capillaries and accumulate within the interstitial space. Simultaneously, impaired tumor lymphatic drainage retards clearance of extravasated macromolecules, resulting in sustained local accumulation [6].

Particle size is a critical determinant of passive targeting efficiency. NPs smaller than 5 nm are rapidly eliminated by renal filtration, whereas those exceeding 200 nm are rapidly sequestered by splenic filtration or phagocytosed by mononuclear phagocytes. Surface properties also govern biological fate: hydrophilic, neutrally or negatively charged particles exhibit reduced non-specific protein opsonization and prolonged circulation half-lives compared to hydrophobic or cationic counterparts [6].

A principal challenge to prolonged circulation is rapid clearance by the reticuloendothelial system (RES). Steric stabilization using polyethylene glycol (PEG) coating—known as PEGylation—generates "stealth" nanocarriers that resist opsonization and extend plasma half-life. PEGylated lipid nanoparticles represent the delivery platform underpinning both approved mRNA-based COVID-19 vaccines [6]. However, emerging evidence demonstrates that repeated systemic administration of PEGylated formulations can elicit anti-PEG antibody responses, potentially triggering hypersensitivity and accelerated blood clearance. Intergenerational inheritance of anti-PEG IgG antibodies has also been documented, raising longer-term safety concerns [6]. Novel strategies such as incorporating gangliosides into PEGylated liposomes may attenuate this immunogenicity.

2.2 Active Targeting

Active targeting involves the surface functionalization of NPs with ligands—including antibodies, peptides, aptamers, or small molecules—that bind with high affinity to receptors overexpressed on tumor cells or tumor vasculature [6]. Upon ligand-receptor interaction, receptor-mediated endocytosis is triggered, internalizing the nanocarrier and its therapeutic cargo into the target cell. This strategy substantially increases intratumoral drug concentrations while minimizing off-target exposure.

Anti-HER2 monoclonal antibody-modified magnetic NPs have demonstrated 10 to 30-fold higher tumor tissue accumulation compared to non-targeted counterparts [6]. Folate receptor-targeted nano systems exploit the overexpression of folate receptors on numerous tumor types; folate-conjugated polymeric micelles loaded with curcumin exhibit enhanced aqueous stability, sustained drug release, and potent reactive oxygen species (ROS) generation in folate receptor-overexpressing cancer cells [6].

A related active targeting mechanism, transcytosis-based nanomedicine, enables NP transport across cellular barriers—including the BBB and dense tumor stroma—by exploiting cellular endocytic and exocytic machinery. This is particularly valuable for treating glioblastoma and other CNS malignancies, where conventional drug penetration is severely restricted [6].

A significant challenge to active targeting is the formation of a protein corona—an adsorptive layer of serum proteins that rapidly coats NPs upon systemic administration. This corona can sterically occlude targeting ligands, alter pharmacokinetics,

and provoke unintended immune interactions, fundamentally modifying the in vivo behavior of engineered nanocarriers [6].

2.3 Stimuli-Responsive Drug Release

Following cellular internalization, therapeutic efficacy depends critically on timely and efficient drug release. Stimuli-responsive nanocarriers are engineered to release their payload in response to specific physicochemical cues within the tumor microenvironment (TME) or upon external stimulation. Endogenous stimuli exploited include acidic intratumoral pH (typically 6.5–6.8 versus physiological 7.4), elevated intracellular glutathione (redox stimuli), overexpressed proteases such as matrix metalloproteinases (MMPs), and reactive oxygen species (ROS) [6].

External stimuli including heat, near-infrared (NIR) light, ultrasound, and alternating magnetic fields have also been applied to trigger spatiotemporally controlled drug release. For example, cisplatin-loaded thermoresponsive liposomes have demonstrated markedly enhanced cytotoxicity at temperatures corresponding to mild tumor hyperthermia [6]. Temozolomide-loaded magnetic nanoparticles combined with an alternating magnetic field have significantly suppressed glioma growth and improved survival in animal models [6]. ROS-responsive nanocarriers exploit the elevated hydrogen peroxide characteristic of tumors to trigger drug release, achieving an approximately 16-fold increase in calprotectin release within excised tumor tissues compared to conventional micelles [6].

3. Benefits Of Nanoparticle-Mediated Drug Delivery

Relative to conventional small-molecule chemotherapy, NP-based drug delivery confers four principal advantages that collectively position nanomedicine as a superior therapeutic platform [5,6].

Enhanced Specificity: The ability to functionalize NP surfaces with tumor-selective ligands or antibodies ensures preferential accumulation at the tumor site, increasing local drug concentration while reducing systemic exposure. This targeting specificity attenuates off-target toxicity and preserves therapeutic indices that conventional agents cannot achieve [6].

Improved Efficiency: NPs can encapsulate both hydrophilic and hydrophobic drugs, protect them from enzymatic degradation, and transport them across physiological barriers including the blood-brain barrier. Their small size permits navigation through the vascular network, infiltration of solid tumors, and delivery of cargo to target cells. Extended plasma half-life through surface engineering further enhances tumor exposure [6].

Multifunctionality: A single NP platform can simultaneously carry multiple therapeutic agents, enabling co-delivery and synergistic combination therapy. NPs can also incorporate diagnostic imaging agents such as quantum dots (QDs) or iron oxide, enabling theragnostic applications that integrate therapy with real-time monitoring [6]. For example, nanoliposomes co-loaded with gemcitabine and paclitaxel demonstrated superior anti-cancer activity relative to free drug combinations in metastatic breast cancer models [6].

Personalized Therapy: NPs can be customized to incorporate patient-derived tumor biomarkers or patient-specific cells, enabling precision medicine approaches. This individualization offers the prospect of dramatically improved therapeutic outcomes through tailored drug selection, dosing, and targeting strategies [6].

4. Applications of Nanomedicine in Cancer Treatment

4.1 Surgery

NPs have enhanced surgical oncology in several ways. Intraoperative guidance is greatly improved by NP-based fluorescence and imaging agents, which illuminate tumor margins, map sentinel lymph nodes, and label residual micro metastatic deposits invisible to the naked eye. Lanthanide-doped NaGdF4-based NIR-II-emitting NPs have notably improved image-guided surgery (IGS) in metastatic ovarian cancer models [6]. Dual-function NPs such as CLIO-Cy5.5 serve simultaneously as MRI contrast agents and near-infrared fluorescent optical probes, enabling precise intraoperative tumor delineation in orthotopic animal models [6]. NPs also improve cryosurgery by enhancing freezing temperature distribution and controlling the ice-ball formation zone, reducing collateral injury to surrounding healthy tissue [6].

4.2 Chemotherapy

Chemotherapy remains the most widely deployed systemic cancer treatment, yet is fundamentally constrained by non-selective toxicity, rapid systemic clearance, and drug resistance. NP-based chemotherapy overcomes these limitations by enabling tumor-selective drug delivery, protecting drug cargo from degradation, and enabling multi-drug co-delivery. Lactic acid-modified mesoporous silica NPs

have demonstrated specific binding to desalinated glycoprotein receptors on hepatocellular carcinoma cells, providing a tumor-targeted chemotherapeutic platform [6].

Among the most clinically advanced NP chemotherapeutic platforms is NC-6004, a cisplatin-encapsulating polymeric micelle that has successfully completed Phase I/II clinical trials and demonstrated efficacy in a Phase III trial in Japan. It is under further evaluation in combination with immune checkpoint blockade in head and neck squamous cell carcinoma [6]. Genexol PM, a paclitaxel-loaded polymeric micelle that exploits the EPR effect for passive tumor accumulation, is approved in South Korea for metastatic breast cancer and is under Phase II investigation for pancreatic cancer in the United States [6]. DaunoXome, a liposomal daunorubicin formulation, has received FDA approval, underscoring the clinical viability of passive targeting strategies [6].

4.3 Immunotherapy

Cancer immunotherapy harnesses the body's immune system to recognize and destroy tumor cells, yet overall response rates remain modest at approximately 10% with conventional approaches [6]. Nanomedicine offers multiple strategies to enhance immunotherapeutic efficacy. Nanoparticle-based cancer vaccines (nano-vaccines) enable simultaneous co-delivery of tumor antigens and immunological adjuvants to antigen-presenting cells (APCs), augmenting APC activation and antigen-specific immune responses [6].

Metal-containing NPs have demonstrated intrinsic immunostimulatory properties: iron NPs induce tumor cell apoptosis through Fenton reactions and promote adaptive immunity; zinc NPs trigger immunogenic cell death; and copper NPs serve as adjuvants that enhance dendritic cell maturation and antigen presentation [6]. NP platforms also enable co-delivery of PD-1/PD-L1 checkpoint inhibitors with immune stimulants or chemotherapy, providing synergistic disruption of tumor immune evasion mechanisms [6].

4.4 Radiotherapy

Radiotherapy destroys cancer cells through ionizing radiation-induced DNA damage, but solid tumors are frequently hypoxic—rendering them two to three times more radioresistant than normal oxygenated tissues [6]. NP-based strategies address radio resistance through two complementary mechanisms. First, oxygen delivery nanocarriers using fluorocarbon materials with high oxygen affinity can continuously release molecular oxygen within the hypoxic TME, enhancing radiosensitivity. Second, metallic NPs serve as radiosensitizers; tantalum oxide NPs modified with perfluorocarbon concentrate radiation energy at the tumor while simultaneously releasing oxygen. Silver NPs have demonstrated significant cytotoxic and radiodensities effects in triple-negative breast cancer, inducing increased DNA damage, enhanced Bax/caspase-3-mediated apoptosis, and suppression of antioxidant defenses [6].

4.5 Photodynamic and Photothermal Therapy

Photodynamic therapy (PDT) employs light-activated photosensitizers (PSs) to generate cytotoxic ROS within tumor tissue, while photothermal therapy (PTT) converts light energy—typically from near-infrared sources—into localized heat sufficient to ablate tumor cells [6]. Both modalities face practical challenges: PDT is constrained by tumor hypoxia and limited tissue penetration of short-wavelength light; PTT is limited by heat shock protein-mediated thermal tolerance. Nanophotosensitisers address PDT limitations by improving PS photophysical properties and enabling targeted PS delivery, while gold nanorods and carbon nanotube-based PTT agents provide superior NIR absorption. The TME-responsive AuNC@MnO2 nanoplatform has demonstrated effective tumor growth suppression and metastasis inhibition in breast cancer models by boosting oxygen levels during PDT [6].

4.6 Gene Therapy

Gene therapy offers the prospect of correcting oncogenic genetic alterations through overexpression of tumor suppressor genes or silencing of oncogenes via RNA interference (RNAi) [6]. Non-viral nanocarriers—including gold nanoparticles, polymeric NPs, and lipid NPs—have emerged as safer alternatives to viral vectors, which carry significant immunogenicity and toxicity concerns. Systemic delivery of PTEN mRNA via polymer-lipid hybrid NPs restored tumor growth suppression in prostate cancer models [6]. Dual receptor-mediated siRNA delivery systems have achieved sequence-specific gene silencing with low cytotoxicity, successfully halting tumor growth in preclinical models [6].

4.7 Tumor Diagnosis and Imaging

NPs have transformed cancer diagnostics by enabling multimodal imaging with substantially improved sensitivity

and specificity compared to conventional contrast agents. Quantum dots serve as exceptional fluorescent nanoprobes for cancer detection. Liposome accumulation within tumor tissues guides the selection of targeted therapies. Gold nanoparticles (AuNPs), due to their biocompatibility and unique plasmonic properties, function as superior X-ray contrast agents enabling early-stage tumor detection. Nanoparticle-encapsulated iodinated CT contrast agents yield superior imaging while minimizing iodine cytotoxicity. Novel radiopharmaceuticals combining NPs with radiolabels have demonstrated promising results for SPECT/CT imaging of melanoma and breast cancer [6].

5. Natural Compounds in Nanoparticle-Based Cancer Therapy

A rapidly expanding area of oncological nanomedicine involves the encapsulation of naturally occurring bioactive phytochemicals within NP delivery platforms. Natural compounds derived from plants, herbs, fungi, and marine organisms—including anthocyanins, ellagic acid, resveratrol, and quercetin—display diverse and potent anticancer mechanisms. However, each is significantly constrained by poor aqueous solubility, limited gastrointestinal bioavailability, rapid first-pass metabolism, and inadequate tumor accumulation when administered in free form [7,8].

5.1 Anthocyanins

Anthocyanins are water-soluble flavonoid pigments widely distributed in red, blue, and purple fruits and vegetables. They exhibit anti-proliferative and pro-apoptotic activities across multiple cancer types including colon, breast, liver, prostate, lung, and skin cancer. Their clinical utility is hampered by sensitivity to intestinal degradation, limited oral bioavailability, and poor membrane permeability [8].

Liposomal micellar encapsulation of bilberry anthocyanins (Nutra Nanospheres) achieved bioavailability exceeding 90% in the gastrointestinal tract and demonstrated markedly superior direct cytotoxic effects on K562 human erythroleukemic cancer cells compared to non-encapsulated bilberry extract [8]. Iron-chelated poly (L-glutamic acid)-based anthocyanin nanoparticles achieved complete tumor ablation in MCF-7 breast cancer xenografts within 26 days under photoacoustic and MRI guidance [8]. Black carrot anthocyanins encapsulated within pH-responsive halloysite nanotubes exploited the acidic TME to achieve controlled release, reducing cancer cell viability by approximately two-fold compared to free anthocyanins in HT-29 colon and MCF-7 breast cancer cell lines [8]. Furthermore, anthocyanin-doxorubicin nano-complexes loaded into hyaluronic acid exhibited improved CD44-targeted apoptosis and tumor growth inhibition in HT-29 colon cancer cells, with reduced doxorubicin accumulation in the lungs and kidneys, demonstrating an improved toxicity profile [8].

5.2 Ellagic Acid

Ellagic acid, a polyphenolic compound found in pomegranate, walnuts, strawberries, and raspberries, exerts antiproliferative effects across colon, bladder, lung, liver, breast, prostate, and endometrial cancers by modulating signaling pathways, inhibiting the cell cycle, and inducing apoptosis [8]. Its clinical application is severely limited by its classification as a Biopharmaceutical Classification System (BCS) Class IV drug, characterized by poor aqueous solubility and low intestinal permeability [8].

Chitosan nanoparticles loaded with ellagic acid demonstrated significant cytotoxicity against oral cancer KB cell lines, with genomic DNA fragmentation confirming apoptotic cell death, and an IC50 value lower than that of free ellagic acid [8]. Oral bioavailability studies using biodegradable polymeric nanoparticles loaded with ellagic acid showed a 3.6-fold increase in the area under the pharmacokinetic curve compared to the free compound, with absorption facilitated via intestinal Peyer's patches [8]. A dual-agent MSN platform co-delivering pemetrexed and ellagic acid demonstrated enhanced cytotoxicity against MCF-7 breast cancer cells, with lactoferrin surface functionalization enabling active cancer cell targeting and EPR-mediated passive accumulation [8].

5.3 Resveratrol

Resveratrol, a natural stilbene polyphenol abundant in grapes and red wine, demonstrates anti-carcinogenic activity at all three stages of cancer development—initiation, promotion, and progression—through MAPK and protein kinase C (PKC) signaling pathways. It effectively inhibits breast, skin, liver, colon, prostate, pancreas, and lung cancer cell growth and can reverse multidrug resistance [8]. Despite these properties, resveratrol undergoes rapid intestinal and hepatic first-pass metabolism, yielding poor systemic bioavailability.

Resveratrol-loaded solid lipid nanoparticles (RES-SLNs) demonstrated potent anti-proliferative activity and inhibited invasion and migration of MDA-MB-231 triple-negative breast cancer cells, accelerating the Bax/Bcl-2 pro-apoptotic ratio while reducing cyclin D1 and c-Myc expression [8]. Resveratrol encapsulated within IL-13Rα2-targeting nanoparticles (Pep-PP@) showed strong cytotoxicity against rat C6 glioblastoma cells with prolonged intracellular resveratrol residence exceeding 24 hours—compared to less than 4 hours for free resveratrol—through JNK pathway activation [8]. Polymeric nanoparticles co-loading paclitaxel and resveratrol improved BBB penetration and demonstrated superior anti-glioma efficacy compared to individual or combined free drug components, with enhanced brain distribution and bioavailability in murine models [8].

5.4 Quercetin

Quercetin is a ubiquitous dietary polyphenolic bioflavonoid found in broccoli, onions, apples, tea, and many other plant-based foods. It exhibits broad-spectrum anticancer activity against breast, colorectal, liver, lung, prostate, and skin cancers through caspase activation, Bcl-2 family modulation, mitochondrial membrane disruption, and inhibition of key signaling pathways including PI3K/AKT and NF-κB [8]. Its major limitations include extreme hydrophobicity, partial aqueous solubility, gastrointestinal instability, and dose-dependent toxicity at high concentrations [8].

PLGA-quercetin nanoparticles significantly reduced cervical and breast cancer cell viability via PI3K/AKT downregulation and upregulation of FoxO1 and caspases 3 and 7 [8]. Quercetin-encapsulated chitosan-copper oxide nanoparticles reduced breast tumor progression in rat models through p53 upregulation, caspase-3 and cytochrome c activation, and cell cycle arrest [8]. Quercetin-conjugated titanium dioxide nanotubes demonstrated in vivo antitumor activity against the B16F10 melanoma model, reducing hyperplasia and inhibiting tumor angiogenesis [8]. A mixed micellar formulation of quercetin demonstrated sustained and consistent release over 24 hours, with an IC50 substantially lower than that of free quercetin in breast cancer cells [8].

A Phase 2 clinical trial (NCT05456022) has been initiated to investigate the anticancer effect of quercetin—both free and encapsulated within PEG-PLGA nanoparticles—against tongue squamous cell carcinoma, reflecting the growing translational momentum in this field [8].

6. Challenges And Future Perspectives

Despite compelling preclinical evidence, the translation of nanomedicine from bench to bedside remains challenged by multiple interrelated biological, technical, regulatory, and economic barriers [6,7,8].

Biological Barriers: At the vascular level, poor tumor perfusion associated with inflammation and abnormal vasculature restricts drug delivery. At the tissue level, elevated interstitial fluid pressure and tumor heterogeneity in vascularization, cellular composition, and genetic profiles impede uniform drug distribution. At the cellular level, reliance on passive diffusion gradients limits the intracellular drug concentration achievable without active transport mechanisms [6].

Toxicology and Safety: Certain nanomaterials—including carbon nanotubes and dendrimers—have not yet received FDA approval due to unresolved toxicity concerns. Long-term effects of NP accumulation in non-target organs, reproductive toxicity, and genotoxicity require comprehensive characterization prior to clinical deployment [6]. Anti-PEG immunogenicity represents an emerging concern as PEGylated formulations become increasingly prevalent in clinical medicine [6].

Drug Loading and Release Control: Achieving high drug loading efficiency, preventing premature drug leakage during circulation, and ensuring adequate release at the tumor site in vivo remain significant engineering challenges. The disparity between in vitro release profiles—conducted under idealized conditions—and complex in vivo environments frequently results in suboptimal therapeutic outcomes [6].

Natural Compound-Specific Challenges: Selecting natural compounds compatible with nanoparticle formulation is non-trivial, as not all phytochemicals can be efficiently encapsulated or exhibit sufficient stability within nanocarrier matrices. Optimizing physicochemical attributes of nanocarriers—morphology, size, surface charge, and hydrophobicity—to accommodate the diverse chemical structures of natural compounds requires compound-specific engineering [8].

Regulatory and Manufacturing Challenges: The complex synthesis routes, high production costs, batch-to-batch

variability, and limited scalability of many nanomedicines constrain their broader clinical adoption. Innovative manufacturing technologies such as microfluidics and non-infiltrating template microprinting offer promising avenues for large-scale, reproducible NP production [6].

Future Directions: Several key priorities will drive the next generation of oncological nanomedicine. Establishing rigorous safety evaluation standards for nanomaterials, developing precision nano-drug delivery strategies tailored to specific tumor types and molecular subtypes, and ensuring carrier stability and controlled drug release will be paramount. Simplifying NP design to facilitate regulatory approval and clinical translation, exploiting advanced 3D tumor organoid models for predictive preclinical evaluation, and expanding clinical trials of natural compound-NP combinations represent pivotal future directions. The integration of NP platforms with artificial intelligence-driven drug design and patient-specific tumor profiling may further accelerate the development of truly personalized nanomedicine [6,7,8].

7. Conclusion

Nanoparticle-based drug delivery systems have fundamentally redefined the therapeutic landscape of oncology. By overcoming the pharmacokinetic limitations of conventional chemotherapy—including poor tumor selectivity, rapid systemic clearance, multidrug resistance, and inadequate bioavailability—NPs enable targeted, controlled, and combination cancer therapy with substantially improved efficacy and safety profiles. The incorporation of natural bioactive compounds within nanoparticle platforms represents a particularly promising strategy, merging the inherent anticancer properties of phytochemicals with the precision delivery capabilities of nanotechnology.

Clinical translation has already yielded approved nanomedicines including liposomal doxorubicin, paclitaxel-albumin nanoparticles, and NC-6004 cisplatin micelles, validating the fundamental concept. However, significant challenges remain in toxicology, drug release control, manufacturing scalability, and regulatory harmonization. Addressing these hurdles through innovation in NP design, rigorous preclinical characterization, and expansion of clinical trial programmed will be essential to fully realize the transformative potential of nanomedicine. As our understanding of tumor biology, NP-immune interactions, and nano-manufacturing deepens, personalized and effective nanoparticle-based cancer treatments are expected to become a standard pillar of oncological care.

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