

Review Article

Polymer Nanoparticles and Gold Nanoparticles in Cancer Therapy: A Comprehensive Review

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Abstract

Cancer remains a leading cause of mortality worldwide, driving the urgent need for more effective and less toxic therapeutic strategies. Nanoparticle-based platforms have emerged as transformative tools in oncology, offering solutions to the limitations of conventional therapies such as systemic toxicity, poor bioavailability, and drug resistance. This review provides a comprehensive overview of two prominent classes of nanocarriers—polymer-based nanoparticles (PNPs) and gold nanoparticles (AuNPs)—in cancer therapy, with a strong focus on their applied uses and clinical translation. PNPs offer versatile drug delivery platforms with tunable physicochemical properties, high drug-loading efficiency, and controlled release capabilities; several polymer-based formulations are already in clinical use. AuNPs contribute unique plasmonic properties, biocompatibility, and multifunctional theranostic potential; they are being evaluated in numerous clinical trials for photothermal therapy, radiosensitization, and imaging. Furthermore, the convergence of these technologies into hybrid polymer-gold nanosystems enables synergistic therapeutic effects, combining the targeting and delivery advantages of polymers with the diagnostic and phototherapeutic functionalities of gold. This review synthesizes recent advances in synthesis strategies, targeting mechanisms, applied clinical applications, and translational challenges, providing a framework for future research directions in precision nano-oncology.

Keywords: Polymer nanoparticles, gold nanoparticles, cancer therapy, targeted drug delivery, theranostics, photothermal therapy, clinical translation, hybrid nanosystems

Introduction

Cancer continues to impose a staggering global health burden, accounting for nearly 10 million deaths annually despite advances in early detection and treatment (Sung et al., 2021). Conventional therapeutic modalities—surgery, chemotherapy, and radiotherapy—face fundamental limitations: chemotherapeutic agents often suffer from poor solubility, non-specific biodistribution, and dose-limiting toxicities, while radiotherapy is constrained by radiation resistance and damage to surrounding healthy tissues (Peer et al., 2007).

Nanomedicine has emerged as a paradigm-shifting approach to address these challenges. Nanoparticles, typically ranging from 10 to 200 nm, exploit the unique biological characteristics of tumors, particularly the enhanced permeability and retention (EPR) effect, to achieve passive accumulation at disease sites (Maeda et al., 2000). Among the diverse array of nanocarriers developed, polymer-based nanoparticles (PNPs) and gold nanoparticles (AuNPs) have garnered particular attention for their distinct yet complementary properties.

PNPs, including polymeric micelles, nanospheres, dendrimers, and nanocapsules, offer exceptional versatility as drug delivery vehicles. Their biocompatible and biodegradable nature, coupled with the ability to encapsulate both hydrophobic and hydrophilic therapeutics, has led to clinical successes such as Abraxane® (albumin-bound paclitaxel) and Doxil® (liposomal doxorubicin) (Bobo et al., 2016). AuNPs, in contrast,

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contribute unique physicochemical attributes derived from their nanoscale gold cores—surface plasmon resonance (SPR) enabling photothermal conversion, facile surface functionalization, and high atomic number for radiosensitization (Jain et al., 2008).

This review aims to consolidate recent advances in both PNPs and AuNPs for cancer therapy, with particular emphasis on their applied clinical uses and the integration of these platforms. We examine synthesis methodologies, targeting strategies, therapeutic mechanisms, and the translational barriers that must be overcome to realize the full clinical potential of these technologies.

1. Polymer-Based Nanoparticles in Cancer Therapy

1.1 Overview and Classification

Polymer-based nanoparticles constitute a diverse family of colloidal carriers derived from natural or synthetic polymers. Their classification encompasses several architectural forms:

Polymeric micelles self-assemble from amphiphilic block copolymers, forming core-shell structures ideal for solubilizing hydrophobic drugs. **Nanospheres** comprise solid polymer matrices where drugs are dispersed throughout, while **nanocapsules** feature a liquid core surrounded by a polymer shell (Elsabagy & Wooley, 2012). **Dendrimers**, highly branched macromolecules with precisely defined structures, offer multivalent surface functionality for targeted delivery (Kesharwani et al., 2014).

The choice of polymer significantly influences nanoparticle behavior. Biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA), polylactic acid (PLA), and chitosan are widely employed for their favorable safety profiles (Kumari et al., 2010). Polyethylene glycol (PEG) is frequently incorporated to impart “stealth” properties, reducing opsonization and prolonging circulation half-life (Suk et al., 2016).

1.2 Synthesis Strategies

The fabrication of PNPs requires precise control over physicochemical parameters that govern in vivo performance. Key synthesis methods include:

Solvent evaporation, a traditional technique where polymer and drug are dissolved in organic solvent, emulsified, and evaporated to yield nanoparticles typically ranging 100–400 nm (Soppimath et al., 2001). This method effectively encapsulates hydrophobic compounds but raises concerns about residual organic solvents.

Nanoprecipitation (solvent displacement) achieves precise size control (50–200 nm) through controlled precipitation upon mixing polymer solution with a non-solvent. This technique produces monodisperse formulations but shows lower efficiency for hydrophilic drugs (Fessi et al., 1989).

Emulsion-diffusion methods improve size uniformity through controlled solvent diffusion, while **emulsion polymerization** generates nanoparticles with high drug loading and narrow size distributions, particularly suitable for hydrophilic therapeutics (Rao & Geckeler, 2011).

1.3 Drug Loading and Delivery Performance

The therapeutic efficacy of PNPs stems from their ability to optimize pharmacokinetic profiles and achieve targeted delivery. Recent studies demonstrate drug loading efficiencies of 80–90%, circulation half-life extensions of 2–5 fold, and tumor accumulation improvements of 3–10 times compared to free drugs (Bertrand & Leroux, 2012).

The EPR effect serves as the primary mechanism for passive tumor targeting. Nanoparticles within the 10–200 nm range preferentially extravasate through the fenestrated vasculature characteristic of solid tumors and accumulate due to impaired lymphatic drainage (Maeda et al., 2000). Active targeting strategies further enhance specificity through surface conjugation of ligands—antibodies, peptides, aptamers, or small molecules—that recognize tumor-associated biomarkers (Byrne et al., 2008).

Stimuli-responsive PNPs represent an advanced design paradigm. These systems exploit tumor microenvironment characteristics—acidic pH, elevated enzyme concentrations, or redox gradients—to trigger drug release specifically at the target site. pH-responsive polymers, such as those containing ionizable groups, release payloads upon encountering the acidic tumor extracellular environment or upon endosomal internalization (Gao et al., 2010).

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1.4 Applied Uses and Clinical Translation of Polymer Nanoparticles

Several polymer-based nanoparticle formulations have successfully reached clinical application, establishing the translational feasibility of this platform.

Abraxane® (albumin-bound paclitaxel nanoparticles) was approved by the FDA in 2005 for metastatic breast cancer and later for non-small cell lung cancer and pancreatic adenocarcinoma. The 130 nm particles leverage the natural transport properties of albumin to enhance tumor accumulation and improve paclitaxel's therapeutic index compared to Cremophor-based formulations (Green et al., 2006).

Doxil® (PEGylated liposomal doxorubicin), while liposomal rather than purely polymeric, paved the way for polymer–lipid hybrid concepts. Its long circulation and reduced cardiotoxicity established the value of PEGylated nanocarriers (Barenholz, 2012).

Genexol-PM® (polymeric micelle formulation of paclitaxel) received approval in South Korea for breast cancer and non-small cell lung cancer. The monomethoxy poly(ethylene glycol)-block-poly(D,L-lactide) (mPEG-PDLLA) micelles solubilize paclitaxel without Cremophor EL, allowing higher doses with reduced hypersensitivity reactions (Kim et al., 2004).

NK105 (paclitaxel-loaded polymeric micelles) and **NK012** (SN-38-loaded micelles) have been evaluated in clinical trials, demonstrating favorable pharmacokinetics and antitumor activity in advanced solid tumors (Hamaguchi et al., 2005; Matsumura et al., 2010).

Beyond oncology, polymer nanoparticles are being explored for oral delivery of chemotherapeutics, overcoming gastrointestinal barriers. PLGA-based formulations of docetaxel and curcumin have shown enhanced bioavailability in preclinical models (Jain et al., 2011). Additionally, polymer-coated nanoparticles for **intraperitoneal administration** in ovarian cancer are under clinical investigation to improve locoregional drug delivery and reduce systemic toxicity (Armstrong et al., 2006).

2. Gold Nanoparticles in Cancer Therapy

2.1 Unique Physicochemical Properties

Gold nanoparticles possess distinctive characteristics that distinguish them from other nanocarriers. Their surface plasmon resonance—the collective oscillation of conduction band electrons upon light excitation—enables strong light absorption and scattering at specific wavelengths, forming the basis for photothermal and photodynamic therapies as well as advanced imaging modalities (Huang et al., 2006).

AuNPs exhibit exceptional biocompatibility, with gold being largely inert in biological environments. Their facile synthesis and surface modification chemistry, particularly through gold-thiol bonds, allow precise control over size (typically 5–100 nm), shape (spheres, rods, shells, cages, stars), and surface functionality (Sperling et al., 2008). The high atomic number of gold ($Z = 79$) also confers radiosensitizing properties, enhancing the efficacy of ionizing radiation (Hainfeld et al., 2004).

2.2 Synthesis Approaches

The synthesis methodology critically influences AuNP properties and subsequent biological interactions.

Chemical synthesis, particularly the Turkevich method employing citrate reduction of chloroauric acid (HAuCl₄), remains the most widely used approach, producing spherical AuNPs of 10–20 nm with controllable size (Turkevich et al., 1951). Seed-mediated growth methods enable fabrication of non-spherical morphologies such as nanorods and nanostars with tunable SPR properties (Nikobakht & El-Sayed, 2003).

Green synthesis has emerged as a biocompatible alternative, utilizing plant extracts, microorganisms, or natural polymers as reducing and stabilizing agents. These approaches avoid toxic chemical residues and offer improved compatibility with biological applications (Iravani, 2011).

Surface functionalization is essential for biological applications. PEGylation enhances colloidal stability and circulation time, while conjugation of targeting ligands (antibodies, peptides, aptamers) enables specific tumor recognition. The strong affinity of thiol groups for gold surfaces facilitates stable covalent attachment of functional molecules (Jazayeri et al., 2016).

2.3 Mechanisms of Anticancer Activity

AuNPs exert anticancer effects through multiple complementary mechanisms:

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Cellular mechanisms involve mitochondrial targeting, reactive oxygen species (ROS) production, and caspase activation leading to apoptosis. AuNPs can induce DNA damage and cell cycle arrest, triggering programmed cell death pathways (Bano et al., 2025).

Photothermal therapy (PTT) leverages AuNP light-to-heat conversion. Upon irradiation with near-infrared (NIR) light—which penetrates deeply into tissues—AuNPs generate localized hyperthermia, achieving tumor ablation while minimizing damage to adjacent healthy tissue (Huang et al., 2008).

Radiosensitization exploits the high atomic number of gold to enhance radiation dose deposition. AuNPs increase photoelectric absorption and secondary electron emission, amplifying DNA damage within tumor cells (Hainfeld et al., 2004). Curcumin-coated AuNPs, for instance, demonstrated a sensitizer enhancement ratio up to 1.82 in prostate cancer cells, significantly improving radiotherapy efficacy (Aborig et al., 2025).

Immunomodulatory effects represent an emerging therapeutic dimension. AuNPs can activate macrophages, regulate cytokine release, and suppress tumor growth and metastasis through immune system engagement (Dykman & Khlebtsov, 2012).

2.4 Applied Uses and Clinical Translation of Gold Nanoparticles

While no pure gold nanoparticle formulation is yet FDA-approved for cancer therapy, several platforms are in advanced clinical development.

AuroLase® (Nanospectra Biosciences) consists of silica-gold nanoshells designed for photothermal ablation of solid tumors. In a pilot study for prostate cancer, AuroLase demonstrated feasibility, safety, and efficacy when combined with focal laser ablation, with minimal adverse events and sustained absence of clinically significant cancer at 12 months (Rastinehad et al., 2019). A pivotal trial for prostate cancer is ongoing (NCT02680535).

NBTXR3 (Hensify®, Nanobiotix) is a hafnium oxide nanoparticle (not gold) that has been approved in Europe for soft tissue sarcoma, but the concept has spurred development of gold-based radioenhancers. Gold nanoparticles are being evaluated in early-phase trials for head and neck cancer and lung cancer as radiosensitizers (NCT02805894, NCT04240665).

CYT-6091 (Aurimune®, CytImmune Sciences) is a PEGylated colloidal gold nanoparticle conjugated with recombinant human tumor necrosis factor (TNF) and pegylated to reduce immunogenicity. Phase I trials demonstrated accumulation in solid tumors, manageable toxicity, and evidence of antitumor activity (Libutti et al., 2010).

Theranostic AuNPs are being investigated in clinical settings for image-guided therapy. Gold nanoparticles can serve as contrast agents for computed tomography (CT), photoacoustic imaging, and surface-enhanced Raman spectroscopy (SERS), enabling real-time monitoring of treatment delivery (Zhuang et al., 2025).

Gold nanoparticle-based photothermal therapy for refractory head and neck cancer, breast cancer, and lung metastases is under investigation in multiple phase I/II studies, with encouraging early results regarding safety and tumor response (O'Neill et al., 2018; Singh et al., 2020).

3. Hybrid Polymer–Gold Nanoparticle Platforms

3.1 Rationale for Hybrid Systems

The integration of polymers with gold nanoparticles creates hybrid platforms that synergistically combine the advantages of both components. Polymers provide biocompatibility, prolonged circulation, controlled drug release, and targeting functionality, while AuNPs contribute photothermal properties, imaging capabilities, and radiosensitization (Kumar et al., 2013).

These hybrid systems enable **multimodal therapy**—the simultaneous or sequential application of multiple therapeutic modalities—to overcome the limitations of any single approach. For example, photothermal therapy can enhance chemotherapy by increasing tumor vascular permeability and drug accumulation, while immunotherapy can be combined to address metastatic disease (Wang et al., 2019).

3.2 Design Strategies

Several architectural designs have been developed for polymer–gold hybrid nanoparticles:

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Polymer-coated AuNPs utilize polymer shells to enhance stability, reduce toxicity, and provide functional groups for ligand conjugation. Carbohydrate polymers including chitosan, hyaluronic acid, gelatin, and starch have been employed to create biocompatible coatings that also confer targeting capabilities (Pissuwan et al., 2011).

AuNP-loaded polymer nanoparticles encapsulate multiple gold nanoparticles within polymer matrices, enabling high AuNP payloads while maintaining controlled release profiles. These systems can incorporate additional therapeutic agents for combination therapy (Park et al., 2016).

Core-shell architectures featuring polymer cores with gold shells, or vice versa, allow precise control over optical and drug delivery properties. The polymer component can be designed for stimuli-responsive drug release, while the gold shell enables photothermal conversion and imaging (Li et al., 2018).

3.3 Therapeutic Synergies and Applied Examples

Hybrid platforms enable sophisticated combination strategies that are being translated toward clinical evaluation.

Photothermal-chemotherapy combines localized hyperthermia with cytotoxic drug delivery. A phase I-compatible chitosan-gold nanorod formulation loaded with doxorubicin showed enhanced tumor accumulation and synergistic efficacy in breast cancer models, with a favorable safety profile (Choi et al., 2020). Clinical translation of such hybrid systems is anticipated within the next several years.

Photodynamic-photothermal therapy employs photosensitizers alongside AuNPs to achieve synergistic tumor ablation through both ROS generation and hyperthermia. Hybrids incorporating indocyanine green (ICG) and gold nanorods within PLGA matrices have been evaluated in orthotopic pancreatic cancer models, demonstrating complete tumor regression in some cohorts (Wang et al., 2019).

Immunomodulatory combinations leverage AuNP-mediated photothermal ablation to induce immunogenic cell death, releasing tumor antigens that activate systemic antitumor immune responses. Polymer carriers can co-deliver immunomodulatory agents such as TLR agonists to enhance this effect (Dai et al., 2020). These platforms are now entering preclinical large-animal studies as a prelude to human trials.

Radiosensitizing hybrids such as curcumin-coated gold nanoparticles (Curc-GNPs) exemplify the potential of polymer-gold hybrids. This system combines the radiosensitizing properties of gold with the antioxidant and anti-inflammatory activities of curcumin. In prostate cancer models, Curc-GNPs demonstrated enhanced cellular uptake, minimal cytotoxicity at therapeutic concentrations, and significant radiosensitization with sensitizer enhancement ratios reaching 1.82 (Aborig et al., 2025). Such formulations are being scaled under GMP for future clinical evaluation.

4. Translational Challenges and Future Perspectives

4.1 Toxicity and Biodistribution

The translation of nanoparticle platforms from bench to bedside requires comprehensive understanding of their in vivo behavior. AuNP toxicity exhibits size-dependent characteristics: ultra-small AuNPs (<5 nm) may induce significant cellular toxicity, including ROS production, DNA damage, and apoptosis, while appropriately surface-functionalized nanoparticles show improved safety profiles (Alkilany & Murphy, 2010).

Biodistribution studies reveal that nanoparticle accumulation depends on multiple factors including size, shape, surface charge, and protein corona formation. PEGylation reduces RES uptake and prolongs circulation, but repeated administration may induce anti-PEG antibodies, leading to accelerated blood clearance (Yang et al., 2016). Long-term biodistribution and clearance mechanisms remain incompletely characterized, requiring systematic investigation.

4.2 Manufacturing and Regulatory Considerations

Scalable manufacturing under good manufacturing practices (GMP) represents a significant hurdle. Batch-to-batch consistency, sterilization, stability, and quality control must be established for any clinically viable formulation (Hua et al., 2018).

Regulatory approval pathways for nanoparticle therapeutics are still evolving. While FDA-approved formulations such as Abraxane® and Doxil® provide precedents, the complexity of hybrid and theranostic

platforms challenges existing regulatory frameworks. Standardized characterization methods and safety assessment protocols are needed to facilitate regulatory review (Tinkle et al., 2014).

4.3 Applied Future Directions

Several emerging directions promise to advance the field toward broader clinical application:

Personalized nanomedicine through computational design enables patient-specific optimization of nanoparticle properties based on tumor characteristics and genetic profiles (Mitchell et al., 2021). Machine learning approaches may accelerate the identification of optimal design parameters.

Tumor microenvironment-responsive systems represent a shift toward active therapeutic engagement with tumor biology. Platforms that respond to hypoxia, redox imbalance, or immune signals can achieve unprecedented specificity (Mi, 2020).

Immuno-nanotherapy integration positions nanoparticles as immune-orchestrating agents rather than passive drug carriers. By reprogramming tumor-associated macrophages, promoting dendritic cell maturation, and enhancing T cell function, nanoparticle platforms can actively modulate the tumor immune microenvironment (Goldberg, 2019).

Time-inspired nanomaterials that adapt their properties dynamically in response to disease progression represent a frontier in precision oncology, enabling therapeutic intervention synchronized with tumor evolution (Cheng et al., 2025).

Combination product approvals may accelerate clinical adoption. Hybrid systems combining an approved polymer formulation with an investigational gold component could follow streamlined regulatory pathways if the polymer component's safety profile is already established.

Conclusion

Polymer-based nanoparticles and gold nanoparticles represent complementary approaches to addressing the limitations of conventional cancer therapy. PNPs excel as versatile drug delivery platforms with controlled release, high loading efficiency, and established clinical translation pathways—exemplified by approved products like Abraxane® and Genexol-PM®. AuNPs contribute unique photophysical properties enabling photothermal therapy, advanced imaging, and radiosensitization; they are now in multiple clinical trials, with AuroLase® leading in photothermal ablation.

The convergence of these technologies into hybrid polymer-gold nanosystems creates opportunities for synergistic therapeutic combinations, multimodal imaging, and integrated theranostic platforms. Recent advances in synthesis methodologies, particularly green synthesis approaches, enhance biocompatibility and enable precise control over nanoparticle properties.

Despite substantial progress, significant challenges remain in toxicity assessment, manufacturing scalability, and regulatory approval. However, with several polymer-gold hybrids approaching clinical readiness and a growing pipeline of nanoparticle-based therapeutics, the field is poised for continued translation. Future directions emphasize personalized design, microenvironment-responsive systems, and immunomodulatory strategies that position nanoparticles as active participants in cancer therapy rather than passive delivery vehicles.

As the field advances toward clinical realization, the integration of polymer engineering, nanotechnology, and immuno-oncology promises to deliver transformative therapeutic options for cancer patients, realizing the vision of precision nano-oncology.

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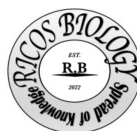
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Data Availability Statement

No original datasets were generated for this review article. All cited data and findings are available within the original research publications referenced in the manuscript, accessible via the provided Digital Object Identifiers (DOIs) or through respective journal platforms.