Nano Nexus & Applications

www.nna.reapress.com

Nano. Nex. App. Vol. 1, No. 1 (2026) 24–35.

Paper Type: Original Article

Gold Nanoparticles in Targeted Drug Delivery: Synthesis, Mechanisms, Applications, and Future Perspectives

Nazanin Malek Mohammadi*

Department of Mechanical Engineering, Morvarid Intelligent Industrial Systems Research Group, Iran; malekmohammadii.nazanin@gmail.com.

Citation:

Received: 19 September 2025 *Revised: 25 November 2025* *Accepted: 29 January 2026*	Malek Mohammadi, N. (2026). Gold nanoparticles in targeted drug delivery: Synthesis, mechanisms, applications, and future perspectives. *Nano nexus & applications, 1*(1), 24-35.

Abstract

Over the past few decades, significant advances in nanotechnology have revolutionized drug delivery systems. Among various nanoscale materials, Gold Nanoparticles (AuNPs) have emerged as particularly promising platforms due to their unique physicochemical characteristics such as excellent chemical stability, tunable surface functionality, outstanding biocompatibility, and distinctive optical properties associated with Surface Plasmon Resonance (SPR). These attributes enable AuNPs to deliver chemotherapeutic agents, nucleic acids, proteins, and other bioactive molecules to target cells with high precision and controllability. This review comprehensively summarizes recent progress in the synthesis strategies and structural features of AuNPs, followed by an in-depth discussion of their drug delivery mechanisms, including passive and active targeting as well as stimuli-responsive systems triggered by pH, light, and enzymatic activity. The therapeutic applications of AuNPs in cancer therapy, gene delivery, antimicrobial treatment, and bioimaging are also highlighted. Finally, the major challenges hindering clinical translation and future perspectives of AuNP-based nanomedicine are critically discussed.

Keywords: Gold nanoparticles, Targeted drug delivery, Nanomedicine, Controlled release, Active targeting, Biocompatibility .

1 | Introduction

Nanotechnology has rapidly evolved into one of the most transformative and interdisciplinary fields of modern science, integrating principles from physics, chemistry, biology, and engineering to manipulate matter at the nanoscale (1–100 nm). Its emergence has opened new frontiers in biotechnology, medicine, materials science, and pharmaceuticals. Within the biomedical domain, nanotechnology plays a particularly crucial role

Corresponding Author: malekmohammadii.nazanin@gmail.com

https://doi.org/10.48314/nna.vi.57

in the design of next-generation drug delivery systems engineered to improve therapeutic precision, minimize systemic toxicity, and overcome the inherent limitations of conventional formulations [1].

Traditional drug delivery methods often suffer from poor bioavailability, rapid systemic clearance, and lack of tissue specificity, leading to suboptimal therapeutic outcomes and significant side effects. Nanomedicine seeks to address these challenges by developing "smart" nanocarriers capable of responding to physiological or external stimuli, selectively accumulating in diseased tissues, and releasing therapeutic payloads in a controlled and site-specific manner [2]. Among the wide spectrum of nanomaterials investigated such as polymeric nanoparticles, liposomes, dendrimers, carbon-based nanostructures, and inorganic nanoparticles Gold Nanoparticles (AuNPs) have emerged as particularly promising candidates due to their unique physicochemical and optical properties [1].

(AuNPs) possess several advantageous characteristics that make them suitable for biomedical applications. These include excellent chemical stability, ease of synthesis with tunable sizes and shapes, straightforward surface functionalization, low intrinsic toxicity at moderate concentrations, and exceptional biocompatibility (*Fig. 1*) [3]. Moreover, their distinctive Surface Plasmon Resonance (SPR) phenomenon arising from collective oscillation of conduction electrons upon light excitation enables various optical applications, such as bioimaging, photothermal therapy, and light-triggered drug release, particularly under Near Infrared (NIR) irradiation [4]. The nirof therapeutic and diagnostic capabilities, known as "theranostics," has further elevated AuNPs as multifunctional platforms in precision nanomedicine [5].

Targeted drug delivery using AuNPs can be broadly categorized into two principal strategies. Passive targeting exploits the Enhanced Permeability And Retention (EPR) effect, which allows nanoparticles to accumulate preferentially within tumor tissues due to leaky vasculature and poor lymphatic drainage [6].

In contrast, active targeting is achieved by conjugating AuNPs with biomolecules such as peptides, antibodies, aptamers, or small-molecule ligands that specifically bind to overexpressed receptors on target cell [7]. This functionalization not only enhances cellular uptake but also increases therapeutic selectivity and reduces off-target cytotoxicity.

Recent studies have revealed that physicochemical parameters such as particle size, geometry (spherical, rod-like, star-shaped), and surface chemistry critically determine the pharmacokinetics, biodistribution, endocytic pathways, and intracellular trafficking of AuNPs [8].

Additionally, the incorporation of AuNPs into hybrid nanostructures such as polymer AuNP composites, liposomal systems, and Metal Organic Frameworks (MOFs) has been shown to improve drug loading efficiency, prolong circulation time, and enable stimuli-responsive release [1].

Despite these advancements, several challenges continue to hinder the clinical translation of AuNP-based nanomedicines. Issues such as bioaccumulation in excretory organs (e.g., liver, spleen), limited biodegradability, potential long term toxicity, and difficulties in large-scale, reproducible synthesis remain critical barriers [2]. Moreover, a comprehensive understanding of the interactions between AuNPs and biological systems including protein corona formation, immune response, and clearance mechanisms is essential to ensure their safety and efficacy in human applications [9].

Nevertheless, the continuous progress in surface engineering, computational modeling, and in vivo imaging technologies offers new opportunities to design safer and more efficient AuNP-based drug delivery systems. The convergence of nanotechnology, molecular biology, and personalized medicine positions (AuNPs) as a cornerstone of future therapeutic strategies—enabling precise, controlled, and patient-specific treatment modalities that could revolutionize modern medicine [10].

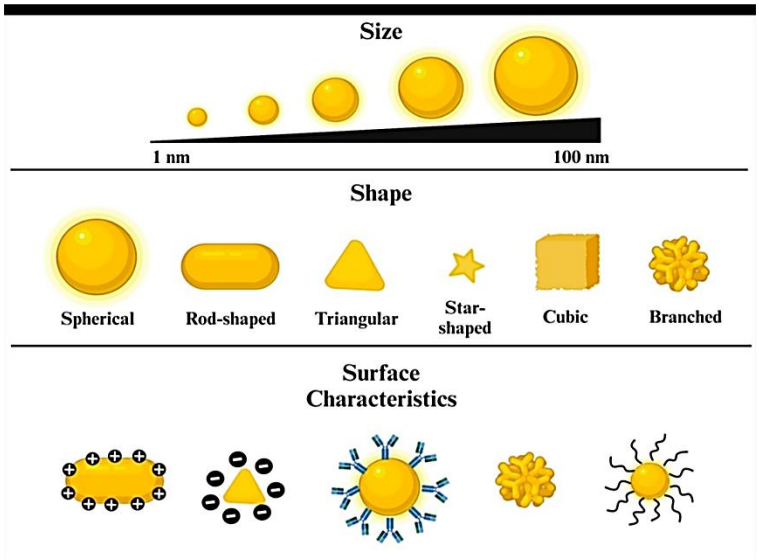


Fig. 1. Physicochemical characteristics of AuNPs.

3 | Synthesis and Physicochemical Properties of Gold Nanoparticles

3.1 | Synthesis Methods

AuNPs can be synthesized through chemical, physical, or biological (green) approaches, each significantly affecting particle size, morphology, surface charge, crystallinity, and ultimately their biological performance [1]. The choice of synthesis method determines not only the physicochemical stability of AuNPs but also their compatibility and efficacy in biomedical applications.

3.1.1 | Chemical methods

Chemical synthesis remains the most commonly employed and versatile approach for producing AuNPs. In this process, trivalent gold ions (Au^{3+}) from gold salts such as Chloroauric Acid ($HAuCl_4$) are reduced to elemental gold (Au^0) using suitable reducing agents, including sodium citrate, sodium borohydride, or ascorbic acid [2].

The Turkevich Frens method is the classical example, generating spherical AuNPs typically in the range of 10–50 nm with a citrate layer that stabilizes the particles electrostatically [9]. More advanced chemical routes such as seed-mediated growth or microemulsion techniques allow the formation of anisotropic morphologies (e.g., rods, prisms, stars) with tunable aspect ratios and optical properties.

3.1.2 | Physical methods

Physical synthesis techniques, including laser ablation, evaporation condensation, and sputtering, are widely utilized for producing high-purity, surfactant-free nanoparticles [10]. Among them, laser ablation offers excellent control over particle size and dispersion without the need for chemical reagents, making it ideal for biomedical applications where chemical contamination must be minimized. However, physical methods are often energy-intensive, costly, and limited in scalability compared to wet-chemical synthesis.

3.1.3 | Green (biological) methods

In recent years, green synthesis has emerged as a sustainable and biocompatible alternative to conventional approaches. This strategy utilizes natural reducing and stabilizing agents derived from plants, microorganisms, or biopolymers [11].

Plant extracts from Camellia sinensis (tea leaves), Aloe vera, or Azadirachta indica (neem) can act simultaneously as reducing and capping agents, yielding stable, environmentally benign AuNPs with biological

coatings [12]. Green-synthesized nanoparticles often exhibit enhanced biocompatibility and reduced cytotoxicity, making them attractive for in vivo biomedical use.

3.2|Physicochemical Properties of Gold Nanoparticles

3.2.1|Shape and morphology (as observed by electron microscopy)

The morphology of AuNPs typically characterized using Transmission Electron Microscopy (TEM) or Scanning Electron Microscopy (SEM) is strongly determined by the synthesis method, reducing agents, and reaction environment. Commonly observed morphologies include:

Spherical nanoparticles

The most prevalent form, with diameters typically between 5–100 nm. In TEM images, they appear as dark, round spots due to gold's high electron density. Usually produced by chemical reduction (e.g., citrate reduction).

Rod-shaped nanoparticles (Nanorods)

Elongated cylindrical particles with aspect ratios >2; synthesized via seed-mediated growth; recognizable in TEM/SEM as short rods.

Triangular or prism-shaped nanoparticles

Formed under tightly controlled conditions of temperature, pH, and surfactant concentration; their sharp edges make them ideal for plasmonic and photonic applications.

Star-shaped or branched nanoparticles

Possess multiple protruding arms or spikes; these complex nanostructures enhance (SPR) and catalytic activity.

Polyhedral / Icosahedral nanoparticle

Highly symmetrical, multi-faceted crystals (e.g., decahedrons, icosahedrons) visible in TEM as polygons with sharp edges and defined facets.

3.2.2|Surface charge and stabilization

The colloidal stability of AuNPs largely depends on their surface charge and the presence of stabilizing or capping agents. Common stabilizers include Polyethylene Glycol (PEG), Polyvinylpyrrolidone (PVP), and sodium citrat [13]. PEGylation, in particular, improves biocompatibility, prevents aggregation, prolongs blood circulation time, and reduces opsonization and macrophage-mediated clearance.

3.2.3|Optical properties (surface plasmon resonance)

One of the most distinctive characteristics of AuNPs is SPR a collective oscillation of surface electrons in response to light. This phenomenon results in strong absorption and scattering in the visible region, typically between 500–600 nm, depending on particle size and shape [14]. SPR underpins many biomedical applications, including optical imaging, photothermal therapy, and light-triggered drug release under Near-Infrared (NIR) irradiation.

3.2.4|Biocompatibility and toxicity

AuNPs are generally considered biocompatible and inert at low to moderate concentrations. However, their toxicity is influenced by several parameters, including particle size, shape, surface coating, dose, and route of administration [15]. Unmodified or "bare" AuNPs may induce oxidative stress or inflammation, whereas surface-functionalized or biologically coated particles (e.g., PEGylated or protein-capped AuNPs) exhibit significantly lower cytotoxicity and improved in vivo safety profiles.

Collectively, understanding the interplay between synthesis conditions and physicochemical properties is crucial for designing AuNP-based nanocarriers optimized for targeted drug delivery, bioimaging, and other clinical applications.

4 | Mechanisms of Drug Delivery Using Gold Nanoparticles

AuNPs serve as versatile carriers capable of delivering therapeutic molecules through different mechanisms that exploit both the unique physicochemical characteristics of AuNPs and the distinct features of pathological microenvironments. The overall efficiency of AuNP-mediated drug delivery depends on how effectively the system can navigate biological barriers, target diseased tissues, and trigger controlled release of therapeutic agents in response to specific stimuli. The major mechanisms are summarized below.

4.1 | Passive Targeting

Passive targeting primarily exploits the EPR effect, a phenomenon typical of solid tumors characterized by leaky vasculature and inefficient lymphatic drainage [16]. These abnormalities enable nanoparticles (typically 20–200 nm) to extravasate and accumulate preferentially within tumor interstitial spaces. AuNPs benefit from this effect by maintaining prolonged circulation time, especially when coated with stabilizing agents such as PEG which reduces renal clearance and enhances tumor accumulation.

However, passive targeting offers limited control and cannot discriminate between different pathological tissues with similar vascular permeability. Moreover, heterogeneous tumor vasculature and variable EPR intensity among patients remain significant challenges that limit its clinical predictability.

4.2 | Active Targeting

Active targeting provides a more selective approach by functionalizing AuNPs with targeting ligands such as monoclonal antibodies, peptides, aptamers, folic acid, or small molecules that specifically recognize and bind to overexpressed receptors on target cells [17]. Once bound, receptor-mediated endocytosis facilitates cellular uptake of the nanoparticle drug conjugate.

For instance, folate-functionalized AuNPs exhibit strong affinity for cancer cells overexpressing folate receptors, whereas HER2-antibody–conjugated AuNPs effectively target breast cancer cells [14]. This approach enhances therapeutic precision, reduces systemic toxicity, and improves intracellular delivery efficiency. Importantly, combining active and passive mechanisms often yields synergistic effects, improving both accumulation and selectivity.

4.3 | PH-Responsive Drug Release

The microenvironment of many tumors is slightly acidic (pH ≈ 6.5), compared to normal physiological pH (≈ 7.4). This difference provides an intrinsic trigger for pH-responsive drug release. AuNPs can be coated or conjugated with pH-sensitive polymers (e.g., poly(histidine), chitosan derivatives) or acid-labile linkers (e.g., hydrazone, imine bonds) that undergo cleavage or structural change under acidic conditions [18]. As a result, the drug detaches selectively in the tumor milieu or in acidic intracellular compartments such as endosomes and lysosomes. This strategy enhances site-specific release while minimizing premature drug leakage in systemic circulation.

4.4 | Light-Responsive Release

AuNPs exhibit strong absorption in the visible and NIR range due to SPR. Upon NIR laser irradiation, AuNPs convert absorbed light into localized heat a process known as photothermal conversion, which can induce structural disruption of surface coatings or thermally cleavable linkers, thereby triggering drug release [19]. This photo-triggered mechanism allows precise spatial and temporal control of drug release, making it particularly suitable for treating deep-seated or drug-resistant tumors. Moreover, when combined with

photothermal therapy, the generated heat can synergistically kill tumor cells, achieving a dual therapeutic effect (chemo-photothermal therapy).

4.5 | Enzyme-Responsive Release

Tumor microenvironments often exhibit elevated expression of specific enzymes such as Matrix Metalloproteinases (MMPs), cathepsins, and phospholipases. Enzyme-responsive AuNP systems exploit this biochemical distinction by incorporating enzyme-cleavable linkers between the nanoparticle surface and the drug molecule [19]. Upon exposure to the target enzyme, the linker is hydrolyzed, releasing the active drug selectively within tumor tissues. For example, MMP-sensitive peptide linkers have been widely used for selective drug release and imaging contrast activation in malignant tissues. This approach ensures localized activation and minimizes systemic exposure.

4.6 | Multi-Responsive and Hybrid Systems

Recent research has focused on designing multi-responsive AuNP-based systems that integrate two or more stimuli (e.g., pH + light, enzyme + redox potential) to achieve greater control over drug delivery. Such hybrid nanoplatforms can respond sequentially or simultaneously to tumor-specific microenvironmental cues, enhancing therapeutic efficacy while minimizing off-target effects. These advanced designs represent a crucial step toward the realization of precision nanomedicine.

5 | Therapeutic Applications of Gold Nanoparticles

AuNPs have emerged as one of the most versatile and multifunctional nanoplatforms in modern medicine. Their unique optical, chemical, and biological characteristics enable their application in diverse therapeutic and diagnostic contexts. The following subsections summarize key biomedical applications of AuNPs in drug delivery and nanomedicine (*Fig. 2*).

5.1 | Cancer Therapy

Among all biomedical applications, cancer therapy remains the most extensively explored domain for AuNPs. Their tunable size, surface chemistry, and optical properties allow precise targeting and controlled drug release within tumor tissues.

AuNPs can effectively deliver chemotherapeutic drugs such as doxorubicin, cisplatin, or paclitaxel directly to malignant cells, thereby reducing systemic toxicity and improving therapeutic index [20]. For example, doxorubicin-loaded AuNPs demonstrate enhanced intracellular accumulation through endocytosis and enable sustained release in acidic tumor environments.

Furthermore, AuNPs can act as photothermal agents due to their SPR effect generating localized heat under NIR irradiation. This combination of chemotherapy and photothermal therapy (chemo-photothermal therapy) leads to synergistic tumor ablation, reduced drug resistance, and improved treatment outcomes *Fig. 1* [21]. Ongoing research also explores the integration of AuNPs with immunotherapy, aiming to stimulate immune recognition of tumor antigens and prevent recurrence.

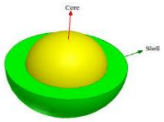
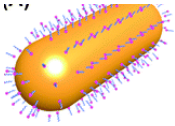
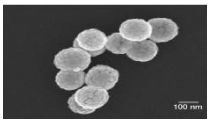
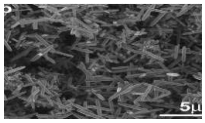
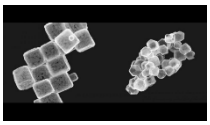
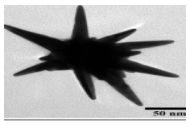
	Nanoshells	Nanorods	Nanocages	Nanostars
Schematic				
SEM				
Size for PTT	~150 nm diameter	~10 nm x 40 nm	~40–60 nm length	~45–120 nm
Stage of development	Clinical trials: lung, head & neck, and prostate cancer	Preclinical	Preclinical	Preclinical
Unique features	Core:shell structure	Two resonance peaks	Drug loading capabilities	Large surface area for bioconjugation

Fig. 1. Comparison of gold nanostructures for photothermal therapy.

5.2 | Gene Therapy

In gene therapy, AuNPs function as robust non-viral vectors for the transport of nucleic acids including DNA, mRNA, and Small Interfering Ribonucleic Acid (SiRNA) into target cells [22]. Their high surface-to-volume ratio allows conjugation with cationic polymers (e.g., polyethyleneimine, PEI), peptides, or thiolated oligonucleotides that facilitate electrostatic binding and cellular uptake. AuNPs protect these genetic materials from enzymatic degradation in the bloodstream and enhance endosomal escape, ensuring efficient nuclear or cytoplasmic delivery [8].

Additionally, AuNP-based gene delivery systems can be engineered for stimuli-responsive release, where environmental cues such as pH or light trigger the controlled liberation of genetic cargo. Recent studies have demonstrated the successful use of AuNPs for gene silencing in cancer and for delivering CRISPR–Cas9 components with high precision, indicating their growing potential in genomic medicine.

5.3 | Antibacterial and Antiviral Applications

With the alarming rise in Multidrug-Resistant (MDR) infections, AuNPs have gained considerable attention for their antimicrobial capabilities. AuNPs exhibit broad-spectrum antibacterial activity through mechanisms such as direct disruption of bacterial membranes, generation of Reactive Oxygen Species (ROS), and interference with essential metabolic pathways [23]. Functionalization with antibiotics (e.g., ampicillin, vancomycin) or peptides further enhances their efficacy and specificity. In antiviral therapy, AuNPs have been shown to inhibit viral attachment, entry, and replication by binding to viral surface proteins or interfering with host–virus interactions. For example, AuNPs conjugated with sulfated ligands have demonstrated inhibitory effects against HIV, influenza, and SARS-CoV-2. Their ability to serve as vaccine adjuvants or carriers for antigenic peptides also makes them promising candidates for next-generation antiviral platforms.

5.4 | Bioimaging and Diagnostics

The unique optical and plasmonic features of AuNPs make them exceptional tools for bioimaging, biosensing, and diagnostic applications. Owing to their strong light-scattering and absorption properties, AuNPs are employed in various imaging modalities such as Optical Coherence Tomography (OCT), Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and fluorescence-based systems [24].

Functionalized AuNPs can selectively accumulate in target tissues, enhancing imaging contrast and enabling real-time monitoring of drug distribution and therapeutic response. Furthermore, AuNPs are integral to the development of theranostic systems, where diagnostic and therapeutic capabilities are combined in a single nanoplatform facilitating early disease detection and personalized treatment strategies.

5.5 | Other Emerging Therapeutic Applications

Beyond oncology and infectious diseases, AuNPs are being investigated for applications in anti-inflammatory therapy, neuroprotection, wound healing, and tissue regeneration. Their ability to modulate oxidative stress and cytokine production offers potential benefits in treating chronic inflammatory disorders. Moreover, AuNP-incorporated scaffolds and hydrogels are increasingly used in regenerative medicine to promote angiogenesis and accelerate wound repair. These expanding roles highlight the versatility of AuNPs as multifunctional agents in modern therapeutics.

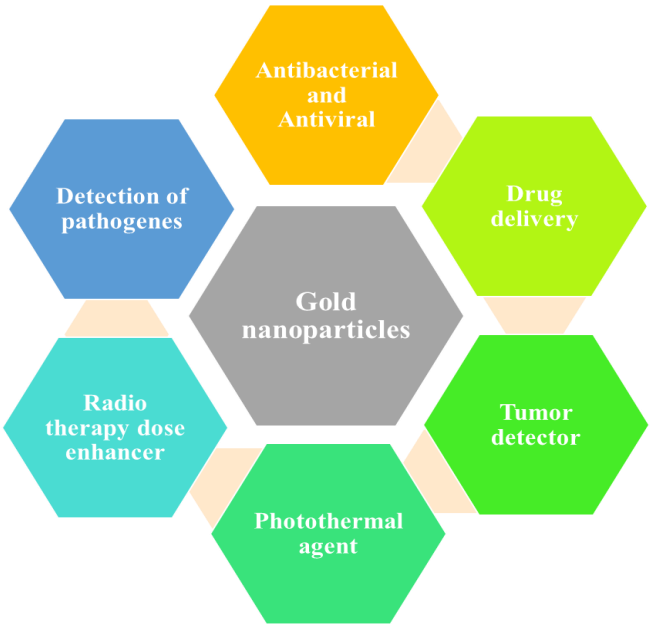


Fig. 2. Therapeutic applications of AuNPs.

6 | Advantages and Challenges of Gold Nanoparticles in Drug Delivery

AuNPs possess a number of unique advantages that make them promising candidates for advanced drug delivery and nanomedicine. However, despite their extensive potential, several critical challenges continue to hinder their full clinical translation. This section summarizes both the major benefits and the key limitations associated with AuNP-based systems.

6.1 | Advantages

6.1.1 | High biocompatibility and low cytotoxicity

AuNPs are generally considered biologically inert and exhibit minimal cytotoxicity at therapeutic concentration [25]. Their biocompatibility can be further enhanced through surface coating with Biopolymers or PEG, which minimizes immune recognition and prolongs circulation time in vivo.

6.1.2 | Surface functionalization and targeting versatility

The gold surface can be readily functionalized with various biomolecules such as ligands, antibodies, aptamers, or peptides, allowing specific interaction with target cell receptors [26]. This structural tunability facilitates active targeting, improved drug retention, and reduced off-target effects.

6.1.3 | Chemical and physical stability

AuNPs demonstrate excellent stability under physiological conditions, maintaining structural integrity and preventing unwanted oxidation or aggregation [27]. This stability ensures that drugs or genetic materials remain protected until they reach their target.

6.1.4 | Unique optical and plasmonic properties

Due to SPR, AuNPs possess strong light absorption and scattering capabilities that enable their dual use in therapy and imaging [28]. This feature forms the foundation for theranostic platforms combining diagnostic and therapeutic functions.

6.1.5 | Controlled and stimuli-responsive drug release

AuNPs can be engineered to release therapeutic agents in response to specific stimuli such as pH changes, enzymatic activity, or NIR light exposure [29]. This spatiotemporal control of drug delivery enhances precision and reduces systemic toxicity.

6.2 | Challenges

Bioaccumulation and cumulative toxicity

Despite their general safety, prolonged retention and accumulation of AuNPs in organs such as the liver, spleen, and kidneys may cause chronic toxicity [30]. Long-term studies are still needed to fully understand their biodistribution and clearance.

Incomplete understanding of bioclearance mechanisms

The excretion pathways and metabolic fate of AuNPs remain poorly characterized, especially for larger or polymer-coated nanoparticles [31]. Identifying these mechanisms is essential for assessing long-term biosafety.

Control over size, shape, and uniformity

Achieving reproducible large-scale synthesis of AuNPs with precise size and morphology remains a major technological challenge [32]. Variations in these parameters significantly affect pharmacokinetics, cellular uptake, and therapeutic efficiency

High production and modification cost

Advanced synthesis procedures, purification steps, and functionalization with biomolecules increase production costs, limiting large-scale commercialization [33]. The development of low-cost, green synthesis approaches could mitigate this limitation.

Potential immune and inflammatory responses

In some formulations, surface-bound biomolecules or aggregation can trigger unintended immune activation or inflammatory reactions [34]. Designing neutral or stealth coatings such as PEGylation can minimize such effects and improve in vivo performance. Overall, while AuNPs hold exceptional promise as multifunctional nanocarriers, addressing these challenges particularly those related to biosafety, scalability, and cost-effectiveness will be essential for their successful transition from laboratory research to clinical practice.

7 | Future Perspectives and Conclusion

7.1 | Future Outlook

With the continuous evolution of nanotechnology, AuNPs are anticipated to serve as a cornerstone of personalized and precision medicine in the coming decades. Future research is expected to focus on improving synthetic strategies to achieve highly monodisperse and size-controlled nanoparticles, along with the development of smart, biocompatible surface coatings that minimize immune recognition and enhance circulation time [20], [33], [35]. The integration of multiple therapeutic and diagnostic functionalities within a single AuNP-based system commonly referred to as a theranostic platform will allow simultaneous disease detection, targeted therapy, and real-time treatment monitoring.

Another key priority is reducing bioaccumulation and improving bioclearance to ensure long-term biosafety and clinical compatibility. Advances in computational modeling, Artificial Intelligence (AI), and machine learning can be employed to predict nanoparticle biological interactions, optimize physicochemical parameters, and accelerate preclinical testing [36], [37]. These tools can also guide the rational design of AuNPs tailored for specific diseases and patient profiles.

Looking beyond oncology, the biomedical applications of AuNPs are expanding into other therapeutic domains, including neurological, cardiovascular, infectious, and autoimmune disorders [38–40]. Their ability to cross biological barriers such as the Blood Brain Barrier (BBB) and to deliver bioactive molecules precisely to target tissues opens new avenues for treating complex and previously intractable diseases. Furthermore, combining AuNPs with other nanomaterials such as polymers, liposomes, and MOFs)may yield hybrid systems with superior mechanical stability, controlled release, and multifunctional capabilities.

8 | Conclusion

In summary, AuNPs represent one of the most versatile and promising nanoplatforms in modern medicine, particularly for targeted and controlled drug delivery. Their unique optical, chemical, and biological properties combined with tunable surface modification enable site-specific drug delivery, enhanced therapeutic efficacy, and minimized off-target toxicity. AuNP-based systems also provide a foundation for multifunctional theranostic applications that unite imaging, therapy, and biosensing within a single platform.

Nevertheless, several critical challenges must still be addressed before clinical realization can be achieved. Long-term toxicity, bioaccumulation, and large-scale manufacturing remain significant barriers. Establishing standardized safety protocols and scalable synthesis techniques will be essential for translating laboratory successes into clinical practice.

Overall, continued interdisciplinary collaboration among chemists, biologists, materials scientists, and clinicians will be vital to unlocking the full therapeutic potential of AuNPs. With the integration of emerging technologies such as AI-driven design, green synthesis methods, and patient-specific nanomedicine, AuNPs are poised to redefine the landscape of targeted therapy and usher in a new era of precision nanomedicine.

Refrences

[1] Georgeous, J., AlSawaftah, N., Abuwatfa, W. H., & Husseini, G. A. (2024). Review of gold nanoparticles: Synthesis, properties, shapes, cellular uptake, targeting, release mechanisms and applications in drug delivery and therapy. *Pharmaceutics, 16*(10), 1332. https://doi.org/10.3390/pharmaceutics16101332

[2] Alam, A., Sahu, A., Nayak, S. (2025). A review on gold nanoparticles: Properties, synthesis and biomedical application in drug delivery and cancer therapy. *International journal of innovative science & research technology (IJISRT), 10*(5), 469–674. https://doi.org/10.38124/ijisrt/25may428%0A%0A

[3] Huang, J., Xu, Z., Jiang, Y., Law, W., Dong, B., Zeng, X., …& Yang, C. (2021). Metal organic framework-coated gold nanorod as an on-demand drug delivery platform for chemo-photothermal cancer therapy. *Journal of nanobiotechnology*, *19*(1), 219. https://doi.org/10.1186/s12951-021-00961-x

[4] Zhao, J., Lee, P., Wallace, M. J., Marites, P. M. (2015). Gold nanoparticles in cancer therapy: Efficacy, biodistribution, and toxicity. *Current pharmaceutical design*, *21*(29), 4240–4251(12). https://doi.org/10.2174/1381612821666150901103032

[5] Chapa, C., Carreón González, J. L., & Garcia Casillas, P. E.(2023). Gold nanoparticles as drug carriers: The role of silica and peg as surface coatings in optimizing drug loading. *Micromachines,14*(2), 451. https://doi.org/10.3390/mi14020451

[6] Yañez-Aulestia, A., Gupta, N. K., Hernández, M., Osorio-Toribio, G., Sánchez-González, E., Guzmán-Vargas, A., … & Lima, E. (2022). Gold nanoparticles: Current and upcoming biomedical applications in sensing, drug, and gene delivery. *Chemical communications*, *58*(78), 10886–10895. https://doi.org/10.1039/D2CC04826D

[7] Mohammed, I. A., & Al-Gawhari, F. J. (2020). Gold nanoparticle: Synthesis, functionalization, enhancement, drug delivery and therapy: A review. *Systematic reviews in pharmacy*, *11*(6), 888-910. http://dx.doi.org/10.5530/srp.2019.2.04

[8] Song, M., Aipire, A., Dilxat, E., Li, J., Xia, G., Jiang, Z., … & Li, J. (2024). Research progress of polysaccharide-gold nanocomplexes in drug delivery. *Pharmaceutics*, *16*(1), 88. https://doi.org/10.3390/pharmaceutics16010088

[9] Sharma, N., Sachan, R. S. K., Singh, A., Karnwal, A., Shidiki, A., & Kumar, G. (2024). Plant-mediated gold nanoparticles in cancer therapy: Exploring anti-cancer mechanisms, drug delivery applications, and future prospects. *Frontiers in nanotechnology*, *6*, 1490980. https://doi.org/10.3389/fnano.2024.1490980

[10] Zhang, R., Kiessling, F., Lammers, T., & Pallares, R. M. (2023). Clinical translation of gold nanoparticles. *Drug delivery and translational research*, *13*(2), 378–385. https://doi.org/10.1007/s13346-022-01232-4

[11] Kim, H. M., Park, J. H., Choi, Y. J., Oh, J. M., & Park, J. (2023). Hyaluronic acid-coated gold nanoparticles as a controlled drug delivery system for poorly water-soluble drugs. *RSC advances, 13*(8), 5529–5537. https://doi.org/10.1039/D2RA07276A

[12] Musmade, N. P., Satpute, D. V. M., & Ghodke, S. R. (2022). Antiretroviral drug loaded gold nanoparticles recent trends and its applications. *Journal of population therapeutics and clinical pharmacology*, *29*(5), 51–70. https://doi.org/10.53555/jptcp.v29i5.6577

[13] Cosma, M., Mocan, T., Delcea, C., Pop, T., Mosteanu, O., & Mocan, L. (2025). Gold nanoparticles as targeted drug delivery systems for liver cancer: A systematic review of tumor targeting efficiency and toxicity profiles. *International journal of molecular sciences*, *26*(16), 7917. https://doi.org/10.3390/ijms26167917

[14] Yusuf, A., Almotairy, A. R. Z., Henidi, H., Alshehri, O. Y., & Aldughaim, M. S. (2023). Nanoparticles as drug delivery systems: A review of the implication of nanoparticles' physicochemical properties on responses in biological systems. *Polymers*, *15*(7), 1596. https://doi.org/10.3390/polym15071596

[15] Duan, L., Li, X., Ji, R., Hao, Z., Kong, M., Wen, X., … & Ma, S. (2023). Nanoparticle-based drug delivery systems: An inspiring therapeutic strategy for neurodegenerative diseases. *Polymers*, *15*(9), 2196. https://doi.org/10.3390/polym15092196

[16] Hajipour, S., & Ghiasvand, A. R. Nanoparticle carriers for drug delivery: An updated review. *Review article pharmaceutical nanotechnology (bentham science)*, *12*. https://doi.org/10.2174/0122117385340986241208123048

[17] Mittal, M., Juneja, S., Pandey, N., & Mittal, R. (2025). Nanoparticle-based drug delivery systems: Current advances and future directions. *Current drug targets, 26*. https://doi.org/10.2174/0113894501393535250903071153

[18] Shivani, S., & Ravindranath, S. (2019). Nanoparticle in pharmaceutical drug delivery system: A review. *Journal of drug delivery & therapeutics*, *9*(3), 487–491. https://doi.org/10.22270/jddt.v9i3.2772

[19] Moinard-Checot, D., Chevalier, Y., Briançon, S., Fessi, H., & Guinebretière, S. (2006). Nanoparticles for drug delivery: Review of the formulation and process difficulties illustrated by the emulsion-diffusion process. *Journal of nanoscience and nanotechnology*, *6*(9–10), 2664–2681. https://doi.org/10.1166/jnn.2006.479

[20] Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. D. P., Acosta-Torres, L. S., … & Seung Shin, H. (2018). Nano based drug delivery systems: Recent developments and future prospects. *Journal of nanobiotechnology*, *16*(1), 71. https://doi.org/10.1186/s12951-018-0392-8

[21] De Jong, W. H., & Borm, P. J. A. (2008). Drug delivery and nanoparticles: Applications and hazards. *International journal of nanomedicine*, *3*(2), 133–149. https://doi.org/10.2147/ijn.s596

[22] Rahman, M. A., Jalouli, M., Bhajan, S. K., Al-Zharani, M., & Harrath, A. H. (2025). A comprehensive review of nanoparticle-based drug delivery for modulating PI3K/AKT/mTOR-Mediated autophagy in cancer. *International journal of molecular sciences*, *26*(5), 1868. https://doi.org/10.3390/ijms26051868

[23] Siddique, S., & Chow, J. C. L. (2020). Gold nanoparticles for drug delivery and cancer therapy. *Applied sciences*, *10*(11), 3824. https://doi.org/10.3390/app10113824

[24] Jia, L., Zhang, P., Sun, H., Dai, Y., Liang, S., Bai, X., & Feng, L. (2021). Optimization of nanoparticles for smart drug delivery: A review. *Nanomaterials*, *11*(11), 2790. https://doi.org/10.3390/nano11112790

[25] Mahdavi, Z., Rezvani, H., & Moraveji, M. K. (2020). Core-shell nanoparticles used in drug delivery-microfluidics: A review. *RSC advances*, *10*(31), 18280–18295. https://doi.org/10.1039/D0RA01032D

[26] Kranti, P., Ramanlal, K., Madhuri, K., & Vinayak, Z. (2021). A review on nanoparticles drug delivery system. *Journal of drug delivery & therapeutics*, *11*(4), 101–104. http://dx.doi.org/10.22270/jddt.v11i4.4865

[27] Mazdaei, M., & Asare-Addo, K. (2022). A mini-review of nanocarriers in drug delivery systems. *British journal of pharmacy*, *7*(1), 1–13. https://search.informit.org/doi/abs/10.3316/informit.497625095829065

[28] Jahan, N., Huda, N. U., Fatima, A., & Shamshad, H. (2023). Recent advances and future challenges of nano-based drug delivery systems. *Nano and medical materials*, *3*(1), 121. https://doi.org/10.59400/nmm.v3i1.121

[29] Li, Z., Xiao, C., Yang, X., & Li, Z. (2025). Progress in the mechanical properties of nanoparticles for tumor-targeting delivery. *Chemical society reviews*, *54*(11), 9391–9420. https://doi.org/10.1039/D3CS00912B

[30] Gressler, S., Hipfinger, C., Part, F., Pavlicek, A., Zafiu, C., & Giese, B. (2025). A systematic review of nanocarriers used in medicine and beyond—definition and categorization framework. *Journal of nanobiotechnology*, *23*(1), 90. https://doi.org/10.1186/s12951-025-03113-7

[31] Haripriyaa, M., & Suthindhiran, K. (2023). Pharmacokinetics of nanoparticles: Current knowledge, future directions and its implications in drug delivery. *Future journal of pharmaceutical sciences*, *9*(1), 113. https://doi.org/10.1186/s43094-023-00569-y

[32] El Yousfi, R., Brahmi, M., Dalli, M., Achalhi, N., Azougagh, O., Tahani, A., … & El Idrissi, A. (2023). Recent advances in nanoparticle development for drug delivery: A comprehensive review of polycaprolactone-based multi-arm architectures. *Polymers*, *15*(8), 1835. https://doi.org/10.3390/polym15081835

[33] Afzal, O., Altamimi, A. S. A., Nadeem, M. S., Alzarea, S. I., Almalki, W. H., Tariq, A., … & Kazmi, I. (2022). Nanoparticles in drug delivery: From history to therapeutic applications. *Nanomaterials*, *12*(24), 4494. https://doi.org/10.3390/nano12244494

[34] Di Stefano, A. (2023). Nanotechnology in targeted drug delivery. *International journal of molecular sciences*, *24*(9), 8194. https://doi.org/10.3390/ijms24098194

[35] Ndung'u, J. W., Muruthi, C. W., Gathirwa, J., Sauli, E., Swai, H. S. (2025). Nanoparticle-based drug delivery system: A review of recent. *International journal of nanobiotechnology (Journalspub)*, *11*(1), 1–12. https://journalspub.com/wp-content/uploads/2025/03/parul.pdf

[36] Tapeh, S. M. T., Baei, M. S., & Keshel, S. H. (2021). Synthesis of thermogel modified with biomaterials as carrier for hUSSCs differentiation into cardiac cells: Physicomechanical and biological assessment. *Materials science and engineering: c*, *119*, 111517. https://doi.org/10.1016/j.msec.2020.111517

[37] Hosseinzadeh, F., & Mehtarifar, H. (2025). Encapsulation of silymarin via Chitosan-PLGA nanoparticles for drug delivery. *Biocompounds (biocompd.)*, *2*(1), 42–52. file:///C:/Users/Admin/Downloads/BIC-2-1-4.pdf

[38] Askarkiaee, S., & Baei, M. S. (2025). Preparation and swelling behaviour of calcium-alginate and calcium alginate-chitosan hydrogel beads. *Biocompounds*, *2*(1), 10–16. https://doi.org/10.48313/bic.vi.30

[39] Niknejad, K., Sharifzadeh Baei, M., Motallebi Tala Tapeh, S. (2018). Synthesis of metformin hydrochloride nanoliposomes: Evaluation of physicochemical characteristics and release kinetics, *9*(3), 298–313. https://ijnd.tonekabon.iau.ir/article_659887.html

[40] Soleimani Moghaddam, M. S., Bahari, A., Houshani, M., Jafari, A., & Motallebi Tala Tapeh, S. (2024). Retracted: A review on progress in the field of conditioning of polymer fuel cell stacks. *Journal of power sources*, *621*, 235300. https://doi.org/10.1016/j.jpowsour.2024.235300