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Gold-Based Nanomaterials for Antimicrobial and Anticancer Applications: A Critical Review

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A B S T R A C T

The rapid emergence of multidrug-resistant pathogens and the inherent limitations of conventional cancer therapeutics have catalyzed the search for novel, multifunctional therapeutic agents. Gold-based nanomaterials have garnered unprecedented attention in biomedical research due to their unique physicochemical properties, exceptional biocompatibility, and highly tunable surface chemistry. This comprehensive review critically evaluates the dual applications of gold nanomaterials in combating microbial infections and malignant tumors. We systematically explore the foundational synthesis methods, ranging from traditional chemical reduction techniques to emerging biologically mediated green synthesis approaches. The mechanisms underlying the antimicrobial efficacy of gold nanoparticles, including physical membrane disruption, oxidative stress induction through reactive oxygen species generation, and intracellular biomolecular interference, are thoroughly analyzed. Furthermore, the anticancer potential of these nanomaterials is examined through the lenses of targeted drug delivery, localized photothermal therapy, and photodynamic therapy, leveraging the enhanced permeability and retention effect as well as active targeting strategies. Despite their immense clinical potential, the translation of gold nanomaterials from the laboratory bench to the bedside faces significant hurdles, primarily concerning long-term in vivo toxicity, biodistribution, and stringent regulatory requirements. By synthesizing current empirical evidence and highlighting existing knowledge gaps, this review aims to provide a robust framework for future research directions in gold-based nanomedicine.

INTRODUCTION

1.1 Background on Nanomedicine

The intersection of nanotechnology and medicine, broadly termed nanomedicine, represents one of the most transformative paradigms in contemporary healthcare and pharmacological research. Over the past few decades, the global health landscape has been increasingly threatened by two distinct yet equally formidable challenges: the relentless proliferation of antimicrobial resistance and the complex, heterogeneous nature of malignant neoplasms. Conventional treatment modalities for bacterial infections heavily rely on monolithic antibiotic therapies, which have inadvertently exerted selective evolutionary pressure on pathogens, leading to the emergence of multidrug-resistant and pan-drug-resistant strains [1]. In a parallel clinical context, traditional cancer interventions, such as systemic chemotherapy and

radiotherapy, are frequently hindered by their non-specific distribution, resulting in severe dose-limiting toxicities, systemic adverse effects, and the eventual development of chemoresistance by tumor cells [2]. Consequently, there is an urgent and critical need for the development of innovative therapeutic platforms capable of circumventing these biological barriers. Nanoscale materials, typically defined by dimensions ranging from one to one hundred nanometers, offer a unique spatial domain where bulk physicochemical properties diverge significantly from those of individual atoms or molecules [3]. At this scale, nanomaterials exhibit an exceptionally high surface area to volume ratio, which inherently facilitates heightened chemical reactivity and provides an expansive platform for the conjugation of therapeutic molecules, targeting ligands, and diagnostic agents. The application of nanomedicine aims to leverage these dimensional advantages to improve the pharmacokinetics, biodistribution, and therapeutic index of existing pharmacological agents, while simultaneously introducing entirely novel mechanisms of therapeutic action [4]. Among the myriad of inorganic, organic, and hybrid nanomaterials currently under investigation, noble metal nanoparticles have distinguished themselves as highly versatile platforms. Within this category, gold-based nanomaterials hold a position of paramount importance, driven by a rich historical context of medical use and an ever-expanding modern repertoire of biomedical applications. The transition of gold from an inert macroscopic noble metal to a highly dynamic nanoscale therapeutic agent underscores a profound evolution in material science and bioengineering [5]. As the scientific community continues to unravel the complexities of host-pathogen interactions and tumor microenvironments, gold nanomaterials are increasingly positioned as multifaceted tools capable of delivering precision medicine [6].

1.2 Unique Properties of Gold Nanomaterials

The immense biomedical utility of gold nanomaterials is fundamentally rooted in their extraordinary and highly tunable physicochemical properties, which are distinctly characteristic of the nanoscale. Chief among these properties is the phenomenon known as localized surface plasmon resonance. When gold nanoparticles are exposed to an incident electromagnetic field, specifically light of a resonant wavelength, the conduction band electrons on the surface of the nanoparticle undergo a collective, coherent oscillation [7]. This resonance results in the strong absorption and scattering of light, phenomena that can be precisely modulated by altering the size, shape, and dielectric environment of the nanoparticle. For instance, while spherical gold nanoparticles typically exhibit a localized surface plasmon resonance absorption peak in the visible region of the electromagnetic spectrum, anisotropic structures such as gold nanorods, nanoshells, and nanostars can be engineered to absorb in the near-infrared biological window [8]. In this near-infrared region, typically between seven hundred and one thousand nanometers, endogenous tissues, blood, and water exhibit minimal light absorption, allowing for deep tissue penetration of the incident light. This optical tunability is the foundational principle underlying the application of gold nanomaterials in photothermal therapy, where the absorbed photonic energy is efficiently converted into localized thermal energy, thereby raising the temperature of the surrounding microenvironment to levels capable of inducing cellular apoptosis or coagulative necrosis [9]. Beyond their optical characteristics, gold nanoparticles possess an exceptionally versatile surface chemistry. The strong affinity between gold and sulfur allows for the facile and robust functionalization of the nanoparticle surface with a wide array of thiolated molecules [10]. This thiol-gold coordination chemistry enables researchers to densely coat the nanoparticles with stabilizing polymers, biological targeting moieties such as antibodies or aptamers, and low molecular weight pharmaceutical agents. Furthermore, compared to other metallic nanomaterials like silver or copper, gold is generally considered to possess superior chemical stability and a higher degree of baseline biocompatibility [11]. The inert core of the gold nanoparticle does not readily undergo oxidation or release toxic metal ions under physiological conditions, which is a significant advantage for systemic in vivo applications. Additionally, the high atomic number and high electron density of gold make these nanoparticles excellent contrast agents for various

diagnostic imaging modalities, including X-ray computed tomography and photoacoustic imaging, thereby facilitating their use as theranostic agents that seamlessly integrate therapeutic and diagnostic functionalities into a single nanoscale entity [12].

2. Literature Review and Background

2.1 Synthesis Strategies for Gold Nanoparticles

The controlled synthesis of gold nanomaterials is a critical prerequisite for their biomedical application, as the physical dimensions and morphological characteristics of the nanoparticles directly dictate their biological interactions, optical behavior, and systemic toxicity. Historically, the synthesis of gold nanoparticles has been dominated by bottom-up chemical reduction methods. The seminal Turkevich method, introduced in the mid-twentieth century, remains one of the most widely utilized and fundamentally understood protocols for synthesizing spherical gold nanoparticles [13]. This method involves the reduction of chloroauric acid in an aqueous solution boiling at one hundred degrees Celsius, utilizing sodium citrate as both the reducing agent and the stabilizing capping agent. The citrate ions reduce the gold cations to zero-valent gold atoms, which subsequently undergo nucleation and growth. The negatively charged citrate molecules then adsorb onto the surface of the newly formed nanoparticles, providing electrostatic repulsion that prevents aggregation [14]. While the Turkevich method is highly effective for synthesizing relatively monodisperse spherical nanoparticles in the size range of ten to twenty nanometers, modifications to the citrate-to-gold ratio and reaction temperature have been continuously developed to expand the achievable size range and improve size distribution. Another cornerstone in chemical synthesis is the Brust-Schiffrin method, which revolutionized the field by enabling the synthesis of extremely small, highly stable, and organic-soluble gold nanoparticles [15]. This two-phase synthesis approach utilizes a phase transfer agent, such as tetraoctylammonium bromide, to transfer the gold precursor from an aqueous phase into an organic solvent, typically toluene. A strong reducing agent, commonly sodium borohydride, is then introduced in the presence of alkanethiols. The resulting gold nanoparticles are inherently stabilized by a dense self-assembled monolayer of the thiol molecules, conferring exceptional stability and allowing the nanoparticles to be dried, stored, and redispersed without loss of structural integrity. Despite the widespread success of these classical chemical methods, the biomedical translation of gold nanomaterials is frequently hindered by the utilization of harsh reducing agents and toxic organic solvents, which can leave hazardous residues on the nanoparticle surface. Consequently, the past decade has witnessed a paradigm shift toward green synthesis or biogenic synthesis strategies [16]. These environmentally benign approaches leverage biological entities, including plant extracts, bacteria, fungi, and algae, to mediate the reduction of gold salts. Plant extracts are particularly advantageous as they contain a rich milieu of phytochemicals, such as flavonoids, terpenoids, alkaloids, and phenolic compounds, which possess strong antioxidant properties [17]. These naturally occurring molecules function dualistically as robust reducing agents to facilitate nanoparticle formation and as robust capping agents to stabilize the particles against agglomeration in physiological buffers. The resulting biogenic gold nanoparticles often exhibit enhanced biocompatibility and inherent biological activity derived from the conjugated phytochemicals, making them highly attractive candidates for both antimicrobial and anticancer applications [18].

2.2 Surface Functionalization and Stability

The bare surface of an inorganic gold nanoparticle is inherently susceptible to aggregation in the complex, high-ionic-strength environment of physiological fluids, and is prone to rapid opsonization by circulating plasma proteins upon intravenous administration. Therefore, the strategic surface functionalization of gold nanomaterials is not merely an option, but an absolute necessity for their deployment in nanomedicine [19]. The most ubiquitous strategy for enhancing the steric stability and extending the systemic circulation time of gold nanoparticles is PEGylation, which involves the covalent attachment of polyethylene glycol chains to the nanoparticle surface. Polyethylene glycol is a highly hydrophilic, non-toxic, and non-

immunogenic polymer that creates a dense, hydrated steric barrier around the gold core [20]. This barrier effectively masks the nanoparticle from the surveillance of the mononuclear phagocyte system, previously known as the reticuloendothelial system, thereby preventing premature clearance by the macrophages of the liver and spleen. The molecular weight, grafting density, and terminal functional groups of the polyethylene glycol chains can be meticulously tailored to optimize the pharmacokinetic profile of the nanomaterial. Beyond passive stabilization, surface functionalization serves as the primary mechanism for imparting active targeting capabilities to gold nanomaterials. By conjugating specific biological recognition elements to the distal ends of the polymer chains or directly to the gold surface, researchers can direct the nanoparticles to bind selectively to receptors that are uniquely expressed or significantly overexpressed on the surface of target cells, such as multidrug-resistant bacteria or malignant tumor cells [21]. A diverse array of targeting ligands has been explored, encompassing monoclonal antibodies, small peptide sequences, aptamers, and small organic molecules like folic acid. For instance, the conjugation of antimicrobial peptides to gold nanoparticles has been shown to synergistically enhance the bactericidal efficacy of the construct by facilitating highly specific binding to the negatively charged components of bacterial cell walls, such as lipopolysaccharides in gram-negative bacteria or teichoic acids in gram-positive bacteria [22]. In the context of oncology, functionalization with ligands targeting the epidermal growth factor receptor or the transferrin receptor has proven highly effective in promoting the selective accumulation and subsequent receptor-mediated endocytosis of gold nanoparticles into cancer cells [23]. Furthermore, the stability of these functionalized constructs must be rigorously evaluated under physiologically relevant conditions. Factors such as the presence of competing intracellular thiols, like glutathione, can induce the displacement of surface ligands in a phenomenon known as ligand exchange. While uncontrolled ligand exchange can lead to premature cargo release and nanoparticle aggregation, intelligently designed delivery systems exploit this exact mechanism. By engineering stimuli-responsive linkages between the gold surface and the therapeutic payload, nanoparticles can be designed to remain completely stable in the systemic circulation but rapidly release their pharmacological cargo upon encountering the highly reducing environment of the tumor cell cytoplasm or the acidic environment of endosomes and lysosomes [24].

3. Antimicrobial and Anticancer Mechanisms

3.1 Mechanisms of Antimicrobial Action

The relentless escalation of antimicrobial resistance necessitates a profound understanding of how novel agents interact with pathogenic microorganisms. Gold nanomaterials exhibit a multi-targeted mechanism of antimicrobial action, fundamentally differing from the specific pathway-inhibition mechanisms characteristic of traditional antibiotics [25]. This multi-targeted approach drastically reduces the probability of bacteria developing resistance, as the pathogens would need to simultaneously acquire multiple simultaneous genetic mutations to survive the assault. The primary mechanism of bactericidal activity is rooted in the direct physical interaction between the gold nanoparticles and the bacterial cell envelope. Due to the high surface energy and specific electrostatic interactions, positively charged gold nanoparticles exhibit a strong affinity for the negatively charged bacterial membrane. Upon contact, the nanoparticles can induce significant physical disruption, altering the structural integrity and permeability of the cell membrane. This structural damage leads to the leakage of critical intracellular components, including electrolytes, proteins, and genetic material, ultimately resulting in rapid cell death [26]. A secondary, yet equally devastating, mechanism of action involves the induction of severe oxidative stress. While bulk gold is chemically inert, nanoscale gold can catalyze the generation of reactive oxygen species, including superoxide radicals, hydroxyl radicals, and hydrogen peroxide, when exposed to cellular microenvironments. The excessive accumulation of reactive oxygen species overwhelms the endogenous antioxidant defense mechanisms of the bacteria. This redox imbalance results in

the widespread oxidation of vital cellular macromolecules, including the peroxidation of membrane lipids, the carbonylation of essential structural and enzymatic proteins, and the induction of single and double-strand breaks in bacterial deoxyribonucleic acid [27]. Furthermore, gold nanoparticles that successfully translocate across the compromised cell membrane can interact directly with internal targets. The high affinity of gold for sulfur and phosphorus allows the nanoparticles to strongly bind to thiol-containing enzymes and the phosphate backbone of nucleic acids, effectively paralyzing cellular respiration, disrupting adenosine triphosphate synthesis, and halting DNA replication and transcription [28].

Table 1: Influence of Nanoparticle Morphology on Antimicrobial Efficacy

Nanoparticle Shape	Primary Synthesis Method	Target Pathogen Model	Dominant Antimicrobial Mechanism
Spherical AuNPs	Citrate Reduction	Escherichia coli	Membrane depolarization and disruption
Gold Nanorods	Seed-mediated Growth	Staphylococcus aureus	Photothermal membrane ablation
Gold Nanostars	Surfactant-free Synthesis	Pseudomonas aeruginosa	Enhanced localized ROS generation
Gold Nanotriangles	Biogenic / Plant Extract	Bacillus subtilis	Physical piercing of peptidoglycan

In addition to combating planktonic bacteria, gold nanomaterials are highly effective against biofilms, which are complex, sessile communities of bacteria encased in a self-produced extracellular polymeric substance matrix. Biofilms represent a significant clinical challenge as they are notoriously impervious to conventional antibiotics and host immune responses. Gold nanoparticles, particularly those optimized for size and surface charge, can successfully penetrate the dense extracellular polymeric substance matrix. Once embedded within the biofilm architecture, the nanoparticles can exert their localized physical and oxidative damage, effectively dismantling the biofilm structure and killing the resident bacteria [29]. The combination of physical membrane disruption, catastrophic oxidative stress, intracellular biomolecular interference, and robust biofilm eradication solidifies gold nanomaterials as exceptionally potent broad-spectrum antimicrobial agents.

3.2 Mechanisms of Anticancer Activity

The application of gold nanomaterials in oncology relies on entirely distinct biological mechanisms and physiological phenomena compared to their antimicrobial use. A foundational concept in tumor targeting is the enhanced permeability and retention effect, a unique characteristic of tumor vasculature. Unlike healthy tissues, rapidly growing malignant tumors typically stimulate the formation of new, highly disorganized blood vessels to supply their increasing metabolic demands. This chaotic angiogenesis results in an irregular vascular architecture characterized by large endothelial fenestrations, lacking a functional lymphatic drainage system [30]. Gold nanoparticles, typically engineered to be between ten and one hundred nanometers in size, can passively extravasate through these leaky vessels and preferentially accumulate within the tumor interstitium. This enhanced permeability and retention effect serves as the primary mechanism for passive targeting, allowing for localized concentration of the therapeutic agent while sparing adjacent healthy tissues from systemic toxicity. However, passive targeting alone is often insufficient for complete tumor eradication. Therefore, researchers frequently employ active targeting strategies by modifying the gold nanoparticle surface with specific ligands, as discussed in the previous section. Once the nanoparticles have accumulated at the tumor site and internalized into the cancer cells via receptor-mediated endocytosis, they can exert their therapeutic effects through several distinct mechanisms.

Figure 1: Mechanims of Gold Nannopapite Action

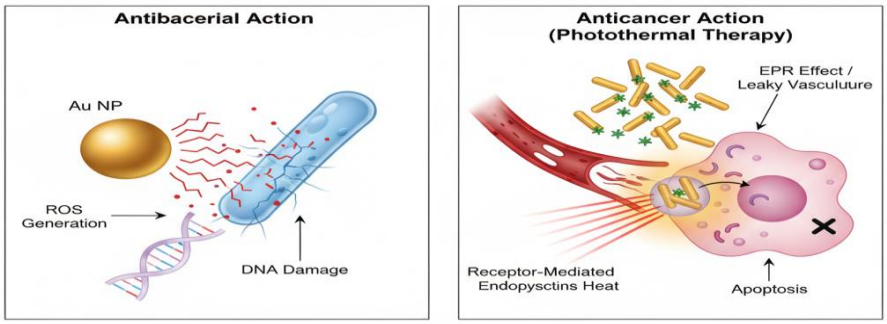


Figure 1: Mechanisms of Gold Nanoparticle Action

The most prominent mechanism is photothermal therapy, leveraging the localized surface plasmon resonance property of gold. When irradiated with a near-infrared laser, the accumulated gold nanoparticles absorb the photonic energy and undergo rapid non-radiative relaxation, dissipating the energy as heat into the surrounding local environment. Cancer cells are inherently more sensitive to heat than healthy cells due to their compromised heat-shock response mechanisms. By precisely controlling the laser intensity and exposure duration, the localized hyperthermia generated by the gold nanoparticles can selectively induce protein denaturation, disruption of the cellular cytoskeleton, and irreversible damage to the cell membrane, ultimately triggering apoptosis or necrosis exclusively within the irradiated tumor volume [31]. Furthermore, gold nanomaterials act as highly efficient delivery vehicles for conventional chemotherapeutic drugs, genetic materials, and radiosensitizers. The vast surface area of the nanoparticles allows for the loading of significant quantities of hydrophobic drugs, which otherwise suffer from poor bioavailability. Through stimuli-responsive linkers, the drug cargo can be stably transported through the bloodstream and released selectively within the acidic endolysosomal compartments of the cancer cells.

Table 2: Representative Gold Nanomaterial Configurations in Experimental Cancer Therapeutics

Nanomaterial Construct	Conjugated Therapeutic Agent	Targeted Cancer Model	Primary Mode of Action
PEGylated Gold Nanoshells	Doxorubicin	Triple-Negative Breast Cancer	Chemo-photothermal therapy
Aptamer-Modified Nanorods	None	Prostate Adenocarcinoma	Targeted photothermal ablation
Peptide-Capped AuNPs	Small interfering RNA (siRNA)	Glioblastoma Multiforme	Gene silencing and radiosensitization
Folic Acid-Targeted AuNPs	Photosensitizer (Ce6)	Ovarian Carcinoma	Targeted photodynamic therapy

Additionally, gold nanoparticles can be utilized in photodynamic therapy by conjugating photosensitizing molecules to their surface. Upon light activation, these photosensitizers generate highly toxic singlet oxygen species. The gold nanoparticle core not only serves as a carrier for the hydrophobic photosensitizers but can also enhance the localized electromagnetic field through plasmonic coupling, thereby amplifying the efficiency of reactive oxygen species generation. The synergistic integration of targeted drug delivery, localized photothermal ablation, and enhanced photodynamic therapy positions gold nanomaterials as incredibly versatile weapons in the modern oncological arsenal.

4. Discussion and Challenges

4.1 Toxicity and Biocompatibility Issues

Despite the extraordinary therapeutic potential of gold-based nanomaterials, their translation into clinical practice is substantially impeded by ongoing concerns regarding their long-term safety, biocompatibility, and complex toxicological profiles. While bulk gold is universally recognized as an inert and highly biocompatible material, the dramatic reduction to the nanoscale fundamentally alters its physicochemical interactions with biological systems. The toxicity of gold nanoparticles is not an intrinsic property of the elemental gold itself, but rather a highly complex consequence of multiple interconnected parameters, including particle size, morphological shape, surface charge, capping agents, and the specific route of administration [1]. Empirical studies have consistently demonstrated a distinct size-dependent toxicity phenomenon. For example, exceptionally small gold nanoparticles, particularly those under five nanometers in diameter, have been shown to penetrate the nuclear membrane, intercalate directly with genetic material, and induce significant cytotoxic and genotoxic effects in healthy cellular models [2]. Conversely, intermediate-sized particles between ten and fifty nanometers generally exhibit higher cellular uptake efficiencies but tend to trigger less immediate cytotoxicity in vitro. Surface charge is another critical determinant of biocompatibility. Cationic gold nanoparticles, which possess a net positive surface charge, generally exhibit higher degrees of cellular toxicity compared to their anionic or neutral counterparts. This is primarily attributed to the strong electrostatic interactions between the positively charged nanoparticles and the negatively charged phospholipid bilayer of mammalian cell membranes [3]. While this interaction is highly beneficial for penetrating bacterial membranes in antimicrobial applications, it can lead to unintended structural disruption, pore formation, and mitochondrial depolarization in non-target healthy mammalian cells. Therefore, the strategic masking of surface charge through dense PEGylation or the use of zwitterionic ligands is essential to mitigate these adverse interactions during systemic circulation. Furthermore, the in vivo biodistribution and long-term fate of gold nanomaterials represent a formidable challenge in toxicological assessments. Following intravenous administration, nanoparticles that evade immediate renal clearance are almost inevitably sequestered by the highly active phagocytic cells of the mononuclear phagocyte system. Consequently, the vast majority of systemically administered gold nanoparticles accumulate heavily in the liver, driven by Kupffer cells, and in the spleen, driven by marginal zone macrophages [4]. Unlike organic or polymeric delivery systems, inorganic gold cores are generally not biodegradable under physiological conditions. This resistance to enzymatic degradation and metabolic breakdown raises significant concerns regarding the potential for chronic intracellular accumulation. While many short-term animal studies report negligible acute systemic toxicity, the long-term physiological consequences of harboring non-degradable metallic aggregates within hepatic and splenic tissues for months or years remain poorly understood. Extensive, longitudinal in vivo studies spanning the entire lifespan of the animal models are urgently required to conclusively determine whether this chronic accumulation triggers delayed inflammatory responses, granuloma formation, or insidious organ dysfunction [5].

4.2 Clinical Translation and Future Perspectives

The journey of gold-based nanomaterials from promising in vitro laboratory results to widespread clinical application is fraught with substantial translational barriers. One of the most prominent obstacles is the extreme difficulty associated with the scale-up and reproducible manufacturing of these complex nanoscale constructs [6]. Most academic syntheses are conducted in small batch volumes where precise control over temperature, stirring rate, and reagent concentration yields highly monodisperse and well-characterized nanoparticles. However, transitioning these delicate synthesis protocols to industrial-scale reactors frequently results in severe batch-to-batch variations, leading to unacceptable heterogeneities in particle size distribution, morphological purity, and surface ligand density. Given that the optical properties, pharmacokinetic profiles, and therapeutic efficacies of gold

nanomaterials are intimately tied to these precise physical parameters, even minor deviations during large-scale manufacturing can drastically alter the clinical performance and safety of the final product [7]. In addition to manufacturing hurdles, the regulatory landscape governing nanomedicines remains highly complex and continuously evolving. Major regulatory bodies demand exhaustive, highly standardized toxicological and pharmacological profiling before approving any clinical trials. Currently, there is a distinct lack of universally standardized protocols for evaluating the complex interactions between functionalized inorganic nanomaterials and biological systems [8]. The discrepancies often observed between in vitro cellular models and complex in vivo physiological systems further complicate the regulatory submission process. For instance, the formation of the protein corona—a dynamic layer of serum proteins that rapidly adsorbs onto the nanoparticle surface upon entering the bloodstream—can completely mask intended targeting ligands, alter the systemic biodistribution, and trigger unintended immunological recognition [9]. Characterizing and controlling this biomolecular interface in a predictive manner is crucial for satisfying stringent regulatory safety and efficacy requirements. Looking toward the future, the successful clinical translation of gold nanomaterials will depend heavily on the integration of advanced multidisciplinary approaches. The development of ultra-small gold nanoclusters that maintain therapeutic efficacy while falling below the renal clearance threshold offers a promising avenue to circumvent the issue of long-term hepatic accumulation [10]. Furthermore, leveraging advanced computational modeling and artificial intelligence to predict the biological identity and pharmacokinetic behavior of specific surface modifications could significantly streamline the optimization process. By embracing green synthesis methodologies, standardizing toxicological assays, and focusing on scalable, reproducible engineering techniques, the scientific community can eventually bridge the gap between experimental promise and clinical reality [11].

5. Conclusion

In summary, the exploration of gold-based nanomaterials has undeniably ushered in a new frontier in the ongoing battle against multidrug-resistant pathogens and complex oncological diseases. This critical review has synthesized the current body of knowledge surrounding the precise engineering of gold nanoparticles, highlighting how variations in size, morphology, and surface chemistry can be meticulously optimized to achieve targeted therapeutic outcomes. In the realm of antimicrobial applications, the multifaceted mechanisms of gold nanoparticles—ranging from catastrophic physical membrane disruption to the catastrophic induction of intracellular oxidative stress—provide a robust strategy to bypass traditional enzymatic resistance pathways and effectively eradicate resilient bacterial biofilms. Concurrently, in anticancer applications, the extraordinary optical properties of gold nanomaterials enable highly localized and potent photothermal and photodynamic therapies, while their versatile surface chemistry facilitates the delivery of complex chemotherapeutic payloads directly to the tumor microenvironment via the enhanced permeability and retention effect and active targeting pathways. However, the realization of gold nanomedicine in routine clinical practice is contingent upon successfully navigating significant toxicological and regulatory challenges. The long-term retention of non-biodegradable metallic cores within clearance organs necessitates rigorous, longitudinal safety evaluations and the continued innovation of renally clearable nanocluster designs. Moreover, the industrial scale-up of these highly sophisticated nanostructures demands unprecedented precision in manufacturing to ensure absolute batch-to-batch consistency. Despite these formidable hurdles, the inherent versatility and potent multimodal therapeutic capabilities of gold nanomaterials present an overwhelming imperative for continued research. Through sustained interdisciplinary collaboration bridging materials science, pharmacology, and clinical oncology, gold-based nanomaterials hold the profound potential to fundamentally revolutionize modern therapeutic protocols and significantly improve patient survival outcomes in both infectious diseases and cancer [12].

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