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Review

Au QDs in Advanced Biomedicine: Fluorescent, Biocompatible, and Multifunctional Nanoprobes for Imaging, Diagnostics, and Targeted Drug Delivery

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Abstract

AuQDs (Au quantum dots) are ultrasmall nanostructures that combine the size-tunable fluorescence and photostability of semiconductor quantum dots with the chemical stability, low toxicity, and versatile surface chemistry of gold nanoparticles. This unique combination endows AuQDs with exceptional biocompatibility and multifunctionality, making them ideal for biomedical applications such as cellular imaging, real-time tracking, targeted drug delivery, diagnostics, therapeutic monitoring, and biosensing. Various synthesis methods—including chemical reduction, hydrothermal, laser ablation, and microwave-assisted techniques—allow for precise control over size and surface properties, optimizing fluorescence and electronic behavior for high-resolution imaging and sensitive detection. Compared to traditional quantum dots, AuQDs offer enhanced safety and biocompatibility, while surpassing larger gold nanoparticles by enabling fluorescence-based imaging. Their surfaces can be functionalized with diverse ligands for targeted delivery and specific biological interactions. In summary, AuQDs are multifunctional nanoprobes that combine superior optical properties, chemical stability, and biocompatibility, making them powerful tools for advanced biomedical diagnostics, therapy, and biosensing.

Keywords: AuQDS; biomedical application; nanomedicine; cancer therapy; surface chemistry

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1. Introduction

Nanomaterials have revolutionized fields ranging from electronics to biomedicine, owing much of their utility to their size-dependent physical and chemical behaviors. Among these, quantum dots (QDs)—typically semiconductor nanocrystals such as CdSe or InP—offer size-tunable photoluminescence and high brightness. However, their utility is often limited by toxicity, chemical instability, and environmental concerns. Gold quantum dots (AuQDs) have emerged as a compelling alternative, offering quantum-confined optical properties combined with the intrinsic stability and biocompatibility of metallic gold [1,2] Ultra-small (<5 nm) gold nanostructures, including atomically precise clusters with fewer than ~25 atoms, have a size regime dominated by quantum confinement rather than

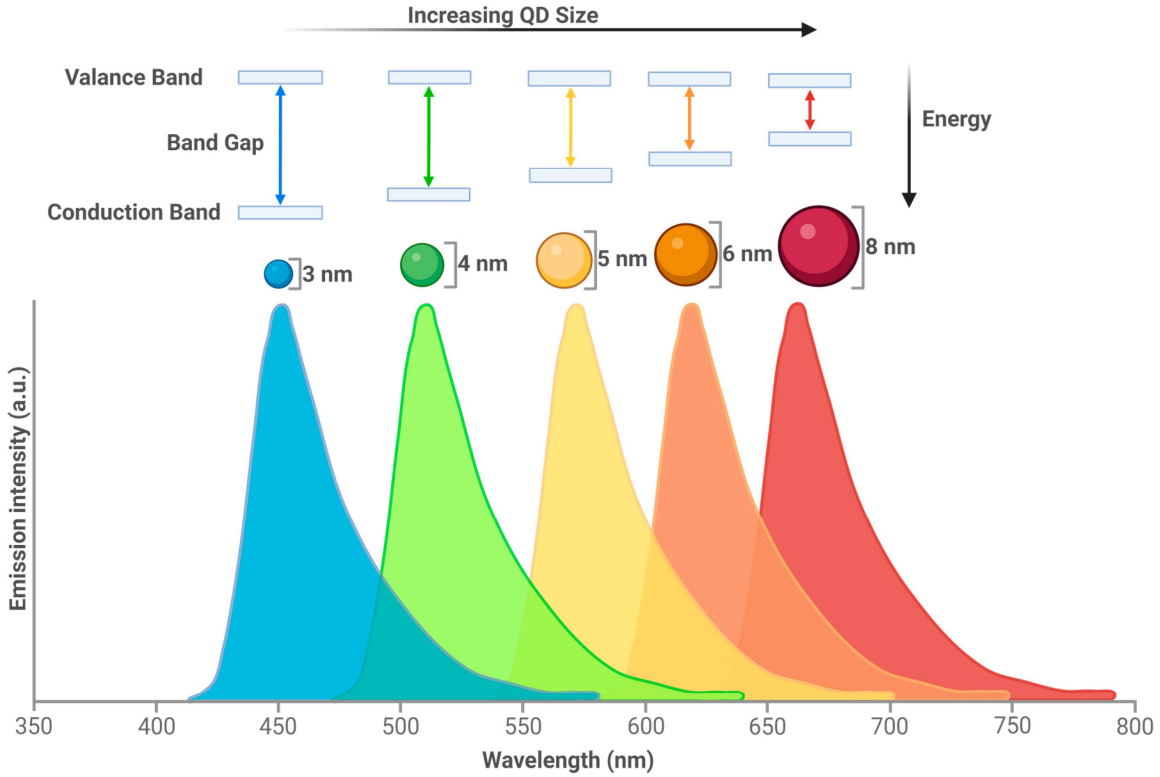
plasmonic behavior. While larger gold nanoparticles (AuNPs) exhibit optical properties governed by localized surface plasmon resonance (LSPR), AuQDs instead show intrinsic, size-dependent fluorescence—akin to semiconductor QDs but with superior chemical robustness and reduced toxicity [1–4].

AuQDs display exceptional optical versatility: they absorb ultraviolet (UV) light and emit across the visible spectrum, with emission peaks shifting with size (e.g., around 438 nm for very small clusters). In organic solar cells (OSCs), incorporating AuQDs can markedly enhance light-harvesting and energy-conversion efficiency. A study combining green-emitting AuQDs with grating-coupled surface plasmon resonance (GC-SPR) structures achieved approximately a 19.6% increase in power conversion efficiency and a ~14% enhancement in short-circuit current density. Reviews of plasmonic enhancements in OSCs suggest efficiency gains sometimes exceed 30% [5–7]. Surface chemistry further amplifies the applicability of AuQDs. Their high surface-to-volume ratio allows nearly all constituent atoms to participate in surface interactions, enabling rich functionalization with thiols, polymers, peptides, nucleic acids, and more. This supports targeted biosensing, imaging, and delivery applications. Their metallic nature ensures stability in challenging environments, making them more durable than cadmium- or lead-based QDs [8,9]. In biomedical applications, AuQDs offer significant advantages. Their bright, size-tunable fluorescence enables high-resolution imaging, unlike larger AuNPs, which mainly scatter light. Their ultra-small size facilitates renal clearance and minimizes long-term bioaccumulation. They can passively target tumors via the enhanced permeability and retention (EPR) effect, and surface modifications with targeting ligands further enhance their specificity. These features position AuQDs as promising agents for real-time imaging and therapeutic delivery in cancer settings, aligning with the advancing nanotheranostic field [10].

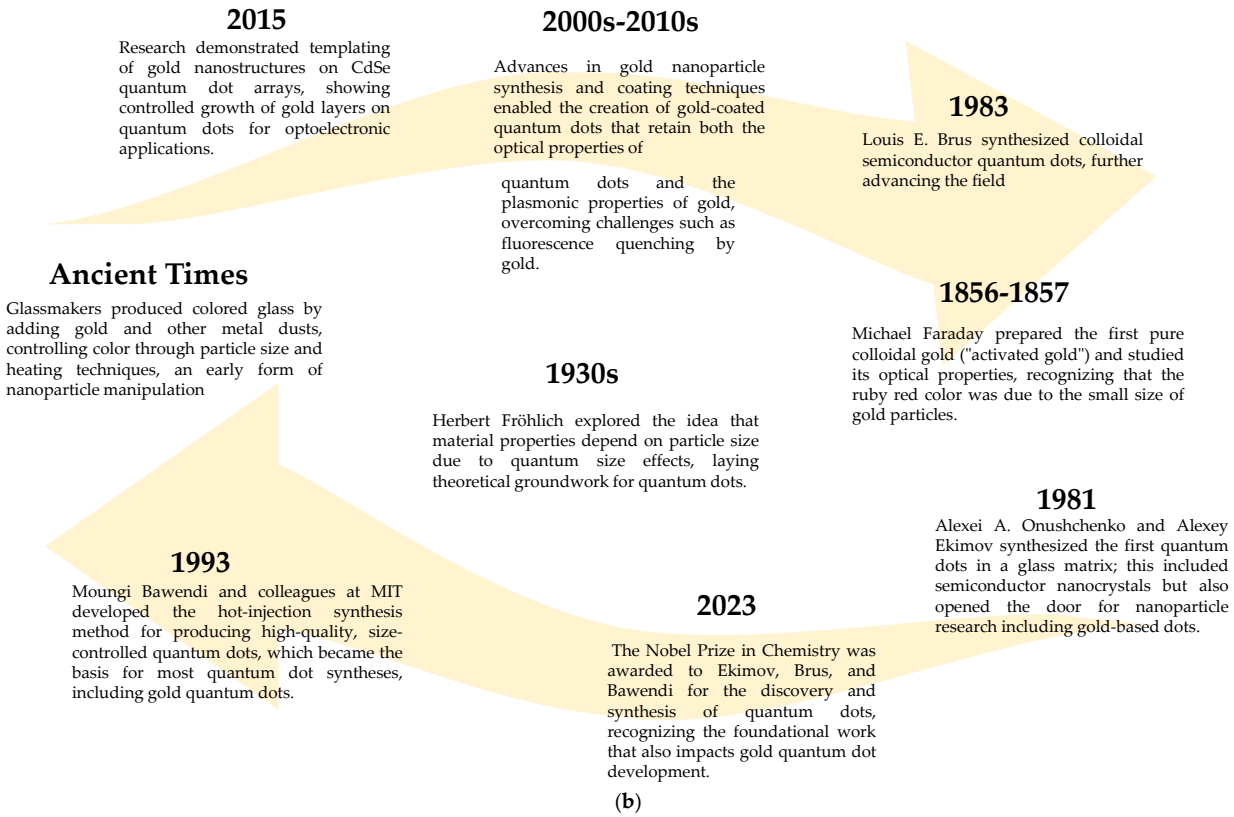
Beyond imaging and sensing, AuQDs support multimodal functionality—acting as both optical probes and therapeutic or energy-conversion mediators. In OSCs, their ability to harvest UV, emit visible light, and support plasmonic enhancement bridges semiconductor-like photoluminescence and metallic robustness. This unique combination broadens their utility across diagnostics, therapy, and energy technologies. Nevertheless, challenges remain. Achieving uniform size, shape, and optical properties during synthesis is non-trivial at such small scales. While less toxic than heavy-metal QDs, comprehensive studies on their bio-distribution and clearance, as well as immune response, are still needed to support clinical translation [11–13]. In summary, AuQDs merge the quantum confinement and tunable fluorescence of semiconductor QDs with the chemical stability and biocompatibility of gold. Their hybrid plasmonic–quantum behavior, rich surface chemistry, and multifunctionality make them powerful platforms for imaging, sensing, therapy, and energy conversion. This review provides a comprehensive overview of recent advances in AuQD research, with a particular focus on their multifaceted biomedical applications and their deployment in diagnostic and therapeutic strategies.

2. Overview of AuQDs Synthesis

AuQDs (Au quantum dots) are nanoscale materials composed of gold atoms, typically ranging from 1 to 10 nanometers in diameter. Their unique size-dependent optical and electronic properties, driven by quantum confinement effects, make them highly valuable in applications such as bioimaging, sensing, and catalysis. Various synthesis strategies have been developed to produce AuQDs, each offering distinct advantages in terms of size control, surface functionality, and purity as shown in Figure 1a.

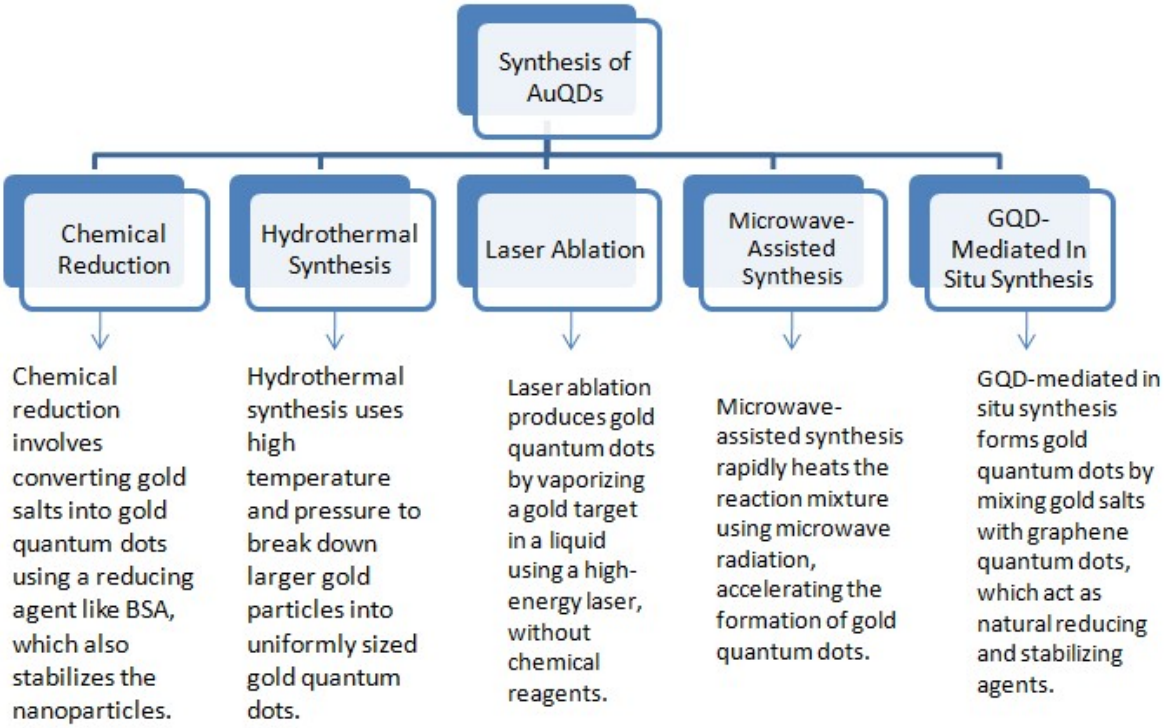


(**a**)



(**b**)

Figure 1. *Cont.*



(**c**)

Figure 1. (**a**) Particle size-dependent emission spectra of fluorescent quantum dots. Quantum dot fluorescence emission wavelength is a function of the particle's size, with larger particles emitting at longer wavelengths (**b**) Timeline of AuQD development process. (**c**) Synthesis method of AuQDs using different methods [14–16].

Among these methods, chemical reduction remains one of the most commonly employed. This technique involves the reduction of gold salts, such as chloroauric acid ($HAuCl_4$), in the presence of stabilizing agents to control nucleation and prevent aggregation. For instance, one reported method uses bovine serum albumin (BSA) as both a reducing and stabilizing agent, where a solution of gold chloride is mixed with BSA and sodium hydroxide, followed by dialysis to purify the resulting AuQDs [17] as shown in Figure 1b. Hydrothermal synthesis offers another approach, relying on elevated temperature and pressure to produce AuQDs from larger gold nanoparticles. This method allows for the precise tuning of particle size and surface charge by modulating parameters such as reaction time, temperature, and pH [18]. The high-temperature conditions promote thermal fragmentation and controlled nucleation, resulting in smaller and more uniformly charged particles. Laser ablation represents a physical, chemical-free method where a focused laser beam vaporizes a gold target in a solvent. The resulting gold plasma rapidly cools and condenses to form quantum dots. This technique is particularly advantageous for producing high-purity AuQDs without the use of external reagents or stabilizers, although it requires sophisticated equipment and is less scalable [19]. Microwave-assisted synthesis is a fast and efficient method that utilizes microwave irradiation to uniformly heat the reaction medium, accelerating the nucleation and growth of AuQDs. In some cases, glucose pyrolysis during this process generates graphene quantum dots (GQDs), which serve as stabilizing agents for gold nanoparticles [20]. This method combines the benefits of rapid synthesis and the integration of multifunctional carbon-based materials.

A more recent method involves the in situ synthesis of AuQDs in the presence of preformed GQDs. For example, GQDs synthesized from starch can stabilize gold nanoparticles through simple mixing with chloroauric acid, eliminating the need for additional reduc-

tants. This environmentally friendly process leverages the inherent reducing and capping abilities of GQDs to produce hybrid AuQD–GQD structures [21]. Characterization of the synthesized AuQDs typically involves a combination of techniques. Transmission Electron Microscopy (TEM) is used to assess particle size, morphology, and dispersion. UV–visible spectroscopy provides information on optical absorption features, confirming the formation of quantum-confined gold species. Fluorescence spectroscopy evaluates photoluminescent properties, which are essential for applications in bioimaging and sensing.

AuQDs demonstrate broad applicability across several domains. In bioimaging, their strong and tunable fluorescence allows for the high-resolution imaging of biological tissues and cells. Their modifiable surfaces enable the attachment of biomolecules, facilitating biosensing through the selective detection of target analytes. In catalysis, their high surface area and reactivity make them effective in promoting redox reactions, especially in green chemistry contexts, as shown in Figure 1c. In conclusion, AuQDs can be synthesized using diverse approaches, each offering specific benefits depending on the desired application. Their unique physicochemical properties, combined with excellent biocompatibility and tunable functionality, underscore their growing significance in nanotechnology, particularly in biomedical and energy-related fields.

3. Comparative Analysis of Nanomaterials for Bioimaging Applications

AuQDs (Au quantum dots) are innovative nanomaterials composed of a few to approximately 100 gold atoms, typically measuring less than 2 nanometers in diameter. These ultrasmall structures exhibit unique optical properties, including size-dependent fluorescence, low toxicity, water solubility, and excellent biocompatibility. Such characteristics make them particularly promising for biomedical applications such as bioimaging, biosensing, and targeted therapy [22].

The fluorescence characteristics of AuQDs are among their most important differences from other nanomaterials. AuQDs demonstrate intense fluorescence that is highly sensitive to variations in surface chemistry and particle size. Under fluorescence microscopy, this tunability allows for the real-time visualization of dynamic biological processes, particularly in live-cell imaging environments [23]. In contrast, traditional quantum dots commonly composed of semiconducting materials like CdSe or CdTe exhibit superior fluorescence brightness and exceptional resistance to photobleaching. Their emission wavelengths can be finely tuned by altering their size and core/shell composition, making them ideal candidates for multiplexed bioimaging, where multiple targets are simultaneously visualized [24,25].

Biocompatibility and toxicity represent another critical point of differentiation. AuQDs are generally considered highly biocompatible and exhibit low cytotoxicity, making them more suitable for in vivo imaging and long-term biological studies without significant adverse effects [26]. Traditional QDs, on the other hand, often contain heavy metals such as cadmium, which are known to be cytotoxic and environmentally hazardous. While recent advances have focused on the development of cadmium-free alternatives, concerns over the safety of traditional QDs still persist [24,25].

The underlying imaging mechanisms also differ substantially across nanomaterials. Gold nanoparticles (GNPs), though not fluorescent, are widely used in X-ray and computed tomography (CT) imaging due to their high atomic number and strong X-ray absorption. Their excellent contrast enhancement in radiographic modalities makes them particularly useful in deep tissue imaging. However, their lack of intrinsic fluorescence limits their application in optical imaging [23,24].

With regard to targeting capabilities, both AuQDs and GNPs can be surface-functionalized with specific ligands, such as antibodies, peptides, or small molecules,

to improve their selectivity toward particular cell types or pathological tissues. This functionalization is especially advantageous in cancer research, where targeted nanoparticles enable enhanced visualization of tumor margins and metastatic sites [22,23] as shown in Figure 2.

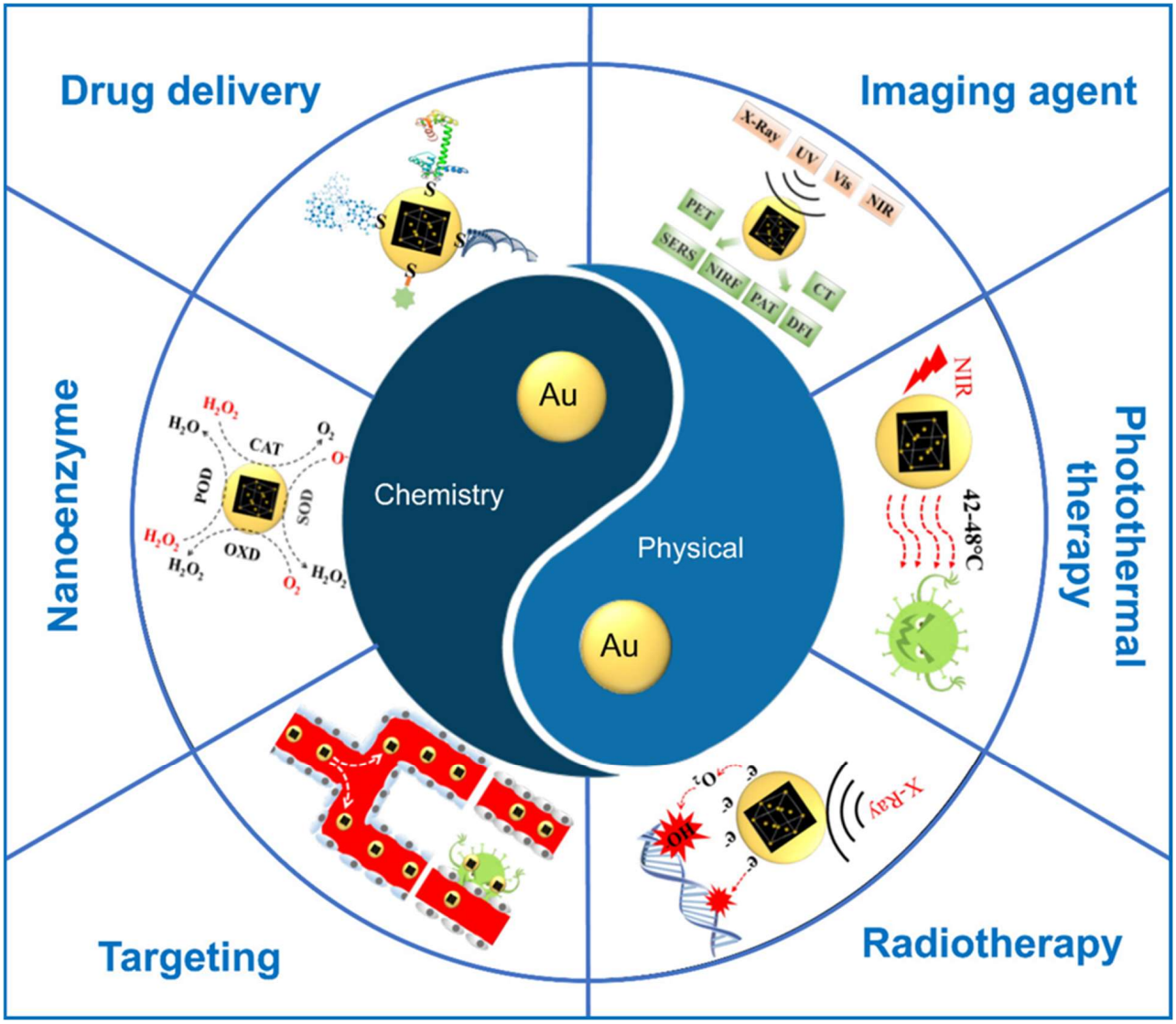


Figure 2. Applications of AuNPs in tumor diagnosis and treatment based on their physical and chemical properties. Reproduced from [27], Licensed under CC BY 4.0.

In summary, AuQDs combine strong fluorescence with low toxicity and good biocompatibility, offering clear advantages for real-time, high-resolution bioimaging. Traditional QDs outperform in terms of brightness and multiplexing capability but pose greater biocompatibility challenges. GNPs, while lacking fluorescent properties, remain highly effective in contrast-enhanced X-ray imaging. The complementary strengths of these nanomaterials suggest that future advances in biomedical imaging may increasingly rely on hybrid or multimodal systems that integrate the best features of each, providing a more comprehensive and accurate picture of biological structures and processes, as shown in Table 1.

Table 1. Comparison of AuQDs with Other Nanoparticles.

Property	AuQDs	Traditional Quantum Dots (QDs)	Gold Nanoparticles (GNPs)
Size	Typically < 2 nm	Varies widely; often larger than AuQDs	Generally larger than AuQDs, often in the range of 5–100 nm
Fluorescence	Strong fluorescence, tunable by size and surface	High brightness, resistance to photobleaching	Limited fluorescence; primarily used for X-ray imaging
Biocompatibility	High biocompatibility and low toxicity	Varies; some heavy metal QDs can be toxic	Generally biocompatible, but toxicity can vary with size and surface modification
Surface Plasmon Resonance	Not applicable	Not applicable	Exhibits strong surface plasmon resonance, enhancing imaging contrast
Applications	Bioimaging, cellular tracking, targeted imaging	Intracellular tracking, diagnostics, drug delivery	X-ray contrast agents, tumor detection
Stability	Good stability in biological environments	Stability can vary; often requires surface passivation	Generally stable but can aggregate if not properly functionalized

4. Properties and Synthesis of Gold Quantum Dots

AuQDs (Au quantum dots) are ultrasmall clusters typically composed of 5 to 25 gold atoms, significantly smaller than conventional plasmonic gold nanoparticles (AuNPs). This reduced size enables them to exhibit quantum confinement effects that impart unique optical properties, particularly strong and tunable fluorescence. These quantum properties are highly sensitive to environmental conditions, making AuQDs suitable for advanced applications in fields such as bioimaging, sensing, and energy conversion [28] as shown in Figure 2.

It is widely recognized that the fluorescence intensity of AuQDs varies with pH, with maximum emission usually observed at a pH of about 8. Reduced fluorescence efficiency results from deviations from this ideal pH range, whether more basic or more acidic. This is likely due to surface state changes impacting electron hole recombination dynamics [29]. Furthermore, hydrothermal synthesis methods have been employed to produce positively charged AuQDs with controlled emission wavelengths, demonstrating that precise tuning of synthesis parameters can yield highly customized nanomaterials for specific applications [30] (Table 2).

From a compositional perspective, AuQDs differ significantly from larger AuNPs, not only in size, but also in their lack of collective electron oscillation phenomena such as localized surface plasmon resonance (LSPR). Instead, they exhibit discrete energy levels akin to molecules. This distinction explains their efficacy in applications like organic solar cells (OSCs), where their quantum properties enhance light absorption and facilitate charge transfer [31,32].

Table 2. Summary of AuQDs: synthesis methods, biomedical applications, and characterization techniques with relevant performance metrics.

Synthesis Method	Key Parameters	Morphology/ Size	Biomedical Applications	References
Chemical Reduction	Gold salt e.g., HAuCl4), reducing agents (e.g., BSA), pH, temperature control.	1–10 nm, spherical, uniform dispersion.	Bioimaging, biosensing, drug delivery (e.g., tumor targeting).	[17,21,33]
Hydrothermal Synthesis	High temperature/pressure, reaction time, pH modulation.	<5 nm, tunable charge/surface properties.	pH-responsive drug release, bioimaging (e.g., thiocyanate detection in biological fluids).	[18,29,34]
Laser Ablation	Laser power, solvent type, gold target purity.	High purity, 1–5 nm, minimal aggregation.	Photothermal therapy, high-resolution imaging (no chemical residues).	[19,35,36]
Microwave-Assisted	Microwave power, reaction time, precursor concentration.	Hybrid structures (e.g., AuQD-GQD), 2–8 nm.	Energy conversion (solar cells), catalytic biosensing (e.g., glucose detection).	[21,31,37]
In Situ with GQDs	GQD concentration, mixing ratio, no external reductants.	Core–shell hybrids, 3–7 nm.	Biocompatible drug carriers, real-time cellular tracking.	[21,38,39]

4.1. Applications in Bioimaging and Energy

AuQDs have demonstrated notable potential in biological imaging due to their strong photoluminescence, low cytotoxicity, and high biocompatibility. Their use has been explored across both plant and animal systems, where they serve as fluorescent probes for cellular and tissue visualization [28]. In parallel, they have been integrated into sensing platforms, such as thiocyanate ion detection in biological fluids, highlighting their value in point-of-care diagnostics [30].

In renewable energy research, AuQDs have been incorporated into organic solar cells to boost device performance. Their integration has been shown to improve light absorption and enhance fluorescence-assisted energy transfer, particularly when used in conjunction with grating-coupled surface plasmon resonance (GC-SPR) systems. These configurations have yielded improvements in power conversion efficiency of up to 16%, underlining the synergistic interaction between AuQDs and plasmonic nanostructures in energy harvesting applications [31,32].

4.2. Fluorescence Mechanisms and Environmental Dependence

The fluorescence behavior of AuQDs is significantly influenced by their excitation conditions and surrounding environment. One major factor is the excitation wavelength itself. Photoluminescence (PL) decay dynamics change depending on how closely the excitation wavelength aligns with the localized surface plasmon resonance (LSPR) of adjacent plasmonic structures, such as AuNPs. When this alignment occurs, enhanced exciton–plasmon coupling leads to accelerated PL decay, attributed to increased energy transfer efficiency between excitons in the QDs and plasmons in the metal nanostructures [40,41]. This exciton–plasmon interaction is highly dependent on the spatial proximity and spectral overlap between the AuQDs and metallic components. As a result, researchers have observed altered emission characteristics, including faster decay rates and changes in photon emission statistics—from anti-bunched to bunched emission—indicating modified

recombination dynamics under specific excitation regimes [42,43]. Moreover, the size and composition of AuQDs directly affect their electronic structure. Due to the quantum size effect, smaller AuQDs possess larger energy band gaps, resulting in shorter emission wavelengths upon excitation. This size-dependent emission allows for the fine-tuning of their spectral properties for multiplexed imaging applications [44,45].

pH sensitivity further modulates fluorescence behavior. When AuQDs are excited at specific wavelengths (e.g., 480 nm), their emission intensity peaks near neutral to slightly basic pH values (around pH 8). This behavior is believed to arise from changes in the ionization state of surface-bound ligands or gold-thiolate bonds, which affect radiative recombination efficiency [46]. Importantly, AuQDs exhibit a broad absorption spectrum, which enables excitation at multiple wavelengths and supports the use of a single excitation source for multicolor imaging. Despite this wide excitation range, their emission bands are typically narrow and symmetric. This spectral precision minimizes overlap with other fluorophores, facilitating clearer resolution in multiplexed biological imaging [47] as shown in Figure 3.

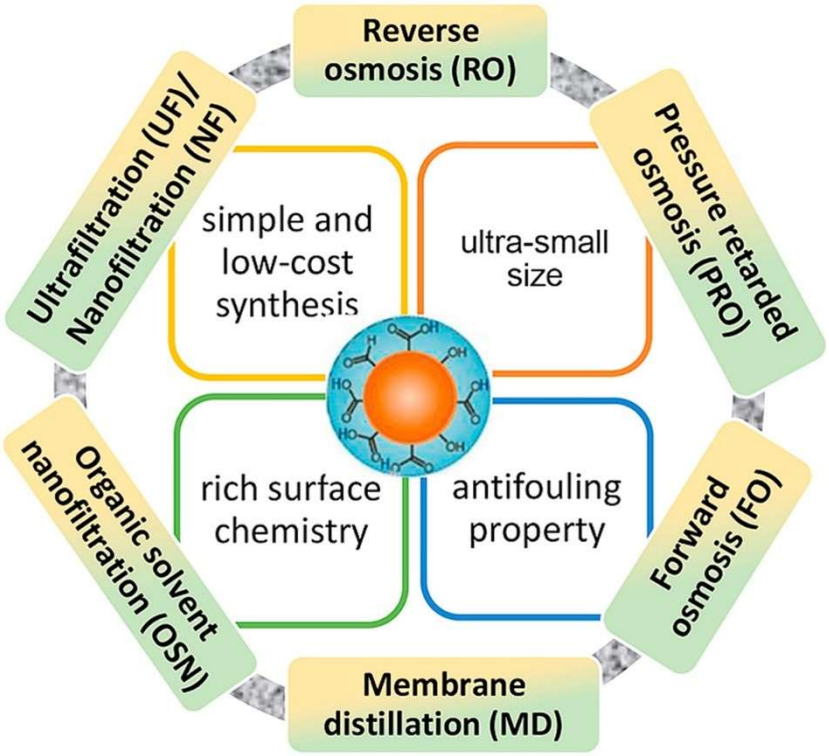


Figure 3. Fluorescence mechanisms and environmental dependence of CQDs. Reproduced with permission from [48].

4.3. Practical Implications and Future Prospects

The ability to modulate the photoluminescence characteristics of AuQDs by adjusting parameters such as excitation wavelength, pH, and quantum dot size offers researchers powerful tools to tailor these nanomaterials for specific imaging and sensing applications. For instance, choosing excitation wavelengths that align with the LSPR peaks of adjacent metallic nanostructures can optimize imaging contrast and prolong fluorescence lifetimes.

Similar wavelength-dependent phenomena have been observed in other quantum dots and plasmonic systems, including silver nanoprisms and gold nanorods. These findings suggest a broadly applicable strategy for enhancing quantum dot emission through plasmonic coupling, further emphasizing the potential of AuQDs in next-generation optical imaging technologies.

In summary, the optical properties of AuQDs are highly tunable, influenced by both intrinsic factors (such as size and composition) and extrinsic conditions (including excitation wavelength and environmental pH). This versatility underlies their increasing significance in biomedical imaging, diagnostics, and optoelectronics as shown in Figure 4.

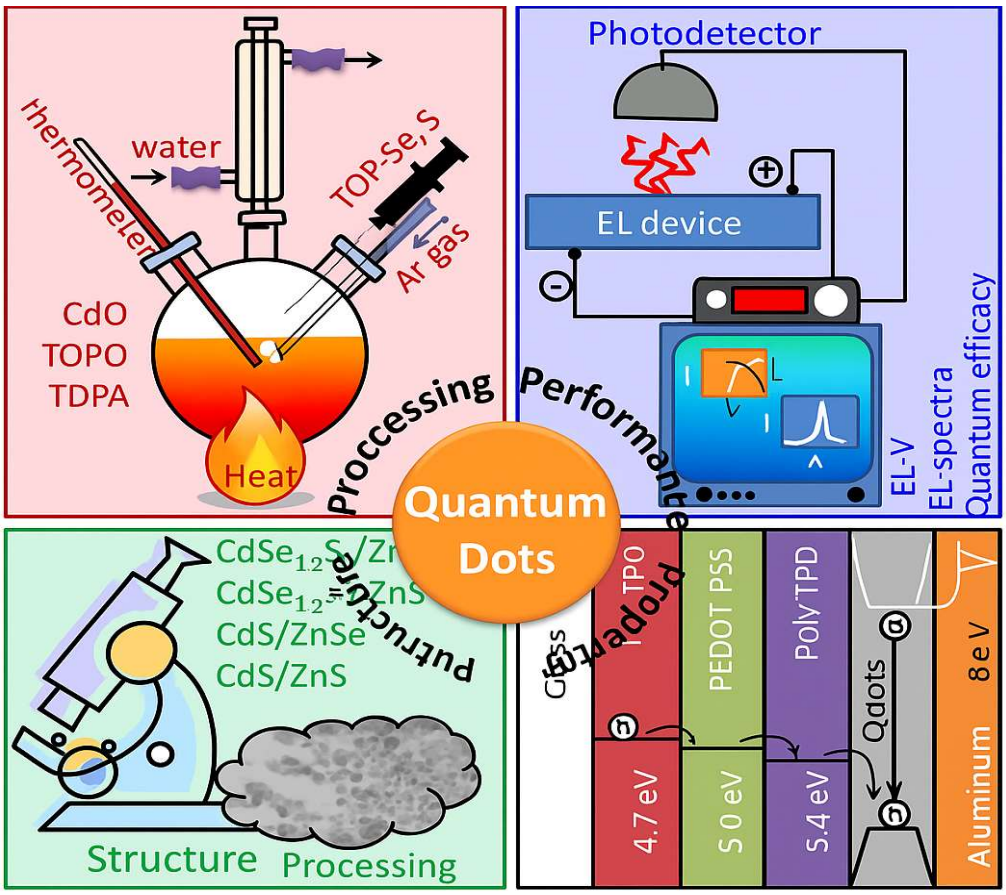


Figure 4. Practical implications and future prospects. Reproduced from [23], Licensed under CC BY 4.0.

5. Overview of AuQDs in Cancer Applications

AuQDs (GQDs) have emerged as multifunctional agents in cancer therapy and diagnostics due to their unique photophysical properties, high biocompatibility, and tunable surface chemistry. Their applications span drug delivery, imaging, photothermal therapy, and biosensing, offering new avenues for precision oncology. In therapeutic contexts, GQDs have demonstrated effective inhibition of tumor growth. Studies have shown that they significantly suppress the tumorigenic potential of glioma cells, particularly by reducing metastatic behavior and impairing tumor spheroid formation. Another promising application of GQDs lies in their incorporation into hybrid nanocarriers for targeted drug delivery. For example, a multifunctional nanosystem combining gold nanoparticles, quantum dots, and mesoporous silica selectively targets colorectal cancer cells and, when combined with radiotherapy, significantly reduces cell viability. Such platforms enhance therapeutic selectivity and reduce systemic toxicity, two critical limitations of traditional cancer treatments [38].

GQDs also exhibit strong photothermal conversion efficiency, making them effective agents for photothermal therapy (PTT). Upon irradiation, GQDs generate localized heat that induces cancer cell death while minimizing damage to surrounding healthy tissues. This approach has shown efficacy in treating various cancers, including breast and colon carcinomas [49]. From a diagnostic perspective, GQDs possess superior optical properties,

including high brightness, photostability, and narrow emission spectra. These characteristics make them ideal for fluorescence imaging, where conjugation to tumor-specific ligands enables high-resolution visualization of cancerous tissues. This targeted imaging improves early detection and facilitates the real-time monitoring of tumor progression [50]. Additionally, GQDs are being explored as biosensors for detecting circulating cancer biomarkers. Their high surface-to-volume ratio and modifiable surface chemistry enable the sensitive detection of low-abundance targets in biological fluids such as blood plasma. This capability holds great promise for early cancer diagnosis and personalized treatment planning [51].

Mechanisms of Glioma Stem Cell Targeting by GQDs

AuQDs have shown particular effectiveness against glioma stem-like cells, which present a major challenge in glioblastoma treatment due to their resilience and regenerative capacity. One key mechanism by which GQDs exert their anti-tumor effects is through the downregulation of β-catenin (CTNNB1) signaling. This pathway is essential for maintaining the self-renewal and pluripotency of glioma stem cells. GQDs suppress this signaling cascade, thereby reducing the proliferative potential and invasiveness of glioma spheroids [52,53]. The fluorescence properties of AuQDs are among their most important distinctions from other nanomaterials. AuQDs demonstrate intense fluorescence that is highly responsive to changes in surface chemistry and particle size. This tunability allows for the real-time visualization of dynamic biological processes, particularly in live-cell imaging settings [54]. At the metabolic level, GQDs disrupt cellular bioenergetics by significantly lowering intracellular ATP levels. This metabolic impairment decreases cellular viability and proliferation, further contributing to the suppression of glioma spheroid growth [52,53].

The nanoscale size and favorable surface chemistry of GQDs promote their efficient uptake by glioma stem cells. This enhanced internalization enables GQDs to function both as therapeutic agents and as nanocarriers for delivering chemotherapeutic drugs directly into tumor tissues. Their preferential accumulation in tumor microenvironments improves treatment specificity while minimizing systemic exposure [39]. Moreover, GQDs can be used in combination with conventional therapies such as photothermal ablation or chemotherapeutics like doxorubicin and temozolomide. These combinatorial approaches have demonstrated synergistic effects, enhancing drug delivery efficiency and cytotoxicity while reducing off-target side effects [55]. Such therapeutic synergy is especially important for targeting glioma stem cells, which frequently resist monotherapies.

AuQDs represent a highly versatile class of nanomaterials with transformative potential in oncology. Their dual roles as diagnostic tools and therapeutic agents enable precise tumor targeting alongside real-time imaging capabilities. In glioma, GQDs act via multiple mechanisms, including the inhibition of critical signaling pathways, the reduction of stem cell-like properties, metabolic disruption, and enhanced drug delivery. These multifaceted properties position GQDs as promising candidates for next-generation cancer therapies, particularly against aggressive and treatment-resistant tumors like glioblastoma. Continued research into their biological interactions and delivery strategies will be essential for advancing these findings toward clinical application. The biodistribution and imaging potential of AuQDs have been explored through various in vivo models, demonstrating their accumulation in tumor tissues, liver, and kidneys due to their nanoscale size and surface properties.

6. Overview of AuQD Biodistribution

AuQDs (GQDs) are rapidly gaining attention for their unique optical properties and promising applications in biomedical fields, particularly in imaging and drug delivery.

A thorough understanding of their biodistribution is essential to evaluate their safety, efficacy, and potential long-term effects in vivo.

6.1. Biodistribution Characteristics

The biodistribution of GQDs is strongly influenced by their size and surface modifications. Smaller quantum dots typically exhibit longer circulation times and slower clearance rates compared to larger particles. Surface coatings, such as polyethylene glycol (PEG), are commonly applied to improve biocompatibility and reduce immunogenicity, which leads to altered distribution patterns within biological systems. These modifications are critical for optimizing their in vivo performance in both imaging and therapeutic contexts [56,57].

Regarding organ distribution, studies have shown that GQDs tend to accumulate primarily in the liver, spleen, and kidneys. For example, after intravesical administration, GQDs demonstrated varying degrees of accumulation in these organs, with significant systemic distribution observed in some models. These results indicate that biodistribution depends on factors such as the administration route and particle properties [56,57].

Concerning clearance, GQDs are mainly eliminated from the bloodstream by the reticuloendothelial system (RES). This rapid clearance limits systemic exposure and reduces potential toxicity in non-target tissues, contributing to the safety profile of GQDs, especially in short-term applications [58,59].

6.2. Toxicity Considerations

Although GQDs exhibit a generally favorable safety profile—with studies reporting low acute toxicity and no significant adverse effects in short-term experiments—it remains important to assess long-term impacts. For instance, one study found no acute toxicity up to seven days post-administration despite some systemic uptake. However, the possibility of bioaccumulation over longer periods warrants further investigation to fully understand chronic exposure risks [60]. One of the most promising applications of GQDs is their use as contrast agents in bioimaging. Thanks to their unique optical properties, GQDs can provide enhanced imaging signals that are invaluable for tracking biological processes in vivo. Their surface plasmon resonance and photoluminescence can be finely tuned through chemical modification, making them ideal for high-resolution imaging and real-time monitoring of cellular and molecular events [61]. Beyond biomedical applications, GQDs are increasingly utilized in other advanced fields such as renewable energy and biosensing.

Gold nanoparticles (AuNPs) and AuQDs are widely integrated into organic solar cells (OSCs) to manipulate light–matter interactions, significantly improving solar cell efficiency. This hybrid integration has led to efficiency gains exceeding 30% compared to reference cells, achieved through plasmonic effects that optimize light absorption, scattering, and trapping. Incorporating AuNPs with organic materials enhances charge transfer at both intra- and intermolecular levels, addressing key challenges in solar energy conversion [37,62]. In biosensing, GQDs are used in electrochemical sensors, particularly for glucose detection. Their unique properties, combined with gold nanoparticles, create highly sensitive interfaces that markedly enhance detection capabilities. The electrochemical features of these nanohybrids make them well-suited for detecting glucose and other biomarkers, demonstrating their potential in medical diagnostics [63]. Additionally, GQDs exhibit nanozymatic activity, functioning similarly to enzymes in detecting thiocyanate ions (SCN^-) in biological samples. This property enables the colorimetric detection of SCN^- with low limits of detection, suitable for clinical diagnostic applications [64].

6.3. Quantum Optics and Informatics

GQDs are also incorporated into plasmonic nanostructures for quantum optics applications. These hybrid systems enhance interactions at the single-emitter level, acting as

nanocavities that improve light–matter coupling. Precise control of these interactions is crucial for advancing quantum information technologies, where selective excitation and detection of emitters are key for future developments [65].

In summary, AuQDs (GQDs) are versatile and highly functional nanomaterials with broad applications in bioimaging, renewable energy, and quantum optics. Their distinctive optical properties, including surface plasmon resonance and photoluminescence, enable advancements across various technological fields. In biomedical contexts, understanding their biodistribution, clearance, and toxicity is vital to ensuring safety and efficacy in clinical use. Ongoing research will be essential to expand their potential in therapeutic, diagnostic, and emerging technological applications.

7. Plasmonic Properties of Gold Quantum Dots

AuQDs are gaining increasing interest in various nanotechnology and photonics applications due to their unique plasmonic properties. These properties arise from their size, structure, and interactions with larger gold nanoparticles, but also pose specific challenges that must be addressed to optimize their use. Below is an overview of the key aspects of their plasmonic characteristics and associated challenges:

7.1. Quantum Confinement and Fluorescence

Gold quantum dots, typically smaller than 2 nm, exhibit quantum confinement effects that significantly influence their optical behavior. Unlike larger gold nanoparticles, which mainly display localized surface plasmon resonance (LSPR), AuQDs absorb near-UV light and emit fluorescence in the visible spectrum. The fluorescence emission is size-dependent, with smaller AuQDs generally producing higher-energy emissions. This size-dependent tunability makes AuQDs promising candidates for applications requiring precise control over fluorescence intensity and wavelength [66,67].

7.2. Interaction with Plasmonic Nanoparticles

When AuQDs are combined with larger plasmonic nanoparticles such as gold nanoparticles (AuNPs), a synergistic interaction occurs. The fluorescence emitted by AuQDs can enhance the localized surface plasmon resonance of AuNPs. Conversely, the intensified electric field around AuNPs can amplify the fluorescence intensity of AuQDs. This mutual enhancement is particularly advantageous in applications like organic solar cells (OSCs), where coupling AuQDs with AuNPs improves light harvesting and boosts photovoltaic efficiency. These synergistic effects highlight the potential of AuQDs to enhance the performance of various optoelectronic devices [35].

7.3. Challenges of Fluorescence Quenching

A major challenge in utilizing AuQDs with plasmonic materials is fluorescence quenching. The strong plasmonic properties of gold can significantly reduce the quantum yield of AuQDs when they are in close proximity to gold surfaces. For example, studies have shown that encapsulating quantum dots with a gold shell can decrease their fluorescence intensity from 75% to as low as 18%, although the emission peak position remains unchanged. This quenching effect can limit the effectiveness of quantum dots in fluorescence-based applications. To optimize both fluorescence and plasmonic activity, precise control over the spacing between the quantum dot and the gold surface is essential [68].

7.4. Applications in Organic Solar Cells

In the field of organic solar cells (OSCs), incorporating AuQDs has led to enhanced power conversion efficiency (PCE). When a layer of AuQDs is blended with plasmonic gold nanoparticles in the hole-transport layer, significant increases in short-circuit current

density and overall device performance are observed. Optimal configurations usually involve specific combinations of quantum dot sizes and types (e.g., blue, green, and red) to maximize light absorption and energy conversion efficiency. This application highlights the potential of AuQDs to improve renewable energy technologies through their plasmonic and optical properties.

7.5. Key Challenges in Functionalizing Quantum Dots with Gold

Functionalizing individual quantum dots (QDs) with gold presents several challenges that affect their integration into diverse applications. Critical obstacles include the following.

7.5.1. Fluorescence Quenching

The close proximity of gold to QDs can dramatically quench their fluorescence. This occurs because direct coupling between gold and QDs results in energy transfer away from fluorescence emission, thereby diminishing the optical properties of QDs. This complicates their use in applications requiring high fluorescence intensity, such as bioimaging [69].

7.5.2. Control of Spacing

Precise control of the spacing between the QD and gold surface is crucial. Fluorescence is completely quenched if the quantum dot is too close to the gold surface, whereas plasmonic enhancement effects are not fully realized if the separation is too large. Managing this nanoscale spacing remains challenging, and often remains more theoretical than practical [70].

7.5.3. Structural Integrity of Quantum Dots

During functionalization, corrosive gold precursors like chloroauric acid ($HAuCl_4$) can damage the structural integrity of QDs. This degradation impairs their electronic and optical properties, reducing their effectiveness post-functionalization. Preserving QD functionality after gold functionalization remains a key challenge [71].

7.5.4. Size Limitations

AuQDs are typically only a few nanometers in size, which limits the amount of gold that can be deposited without adversely affecting their properties or causing fluorescence quenching. This size constraint complicates the fabrication of gold shells that maintain the optical integrity of the quantum dots [69].

7.5.5. Thick Gold Shells

Applying a thick gold shell around QDs can completely block fluorescence emission. Although a gold shell may enhance plasmonic effects, its thickness must be carefully controlled to avoid obstructing light emission. Balancing a functional plasmonic shell with preserved fluorescence is a significant design challenge [69].

7.5.6. Limited Experimental Demonstrations

Most successful demonstrations of gold-functionalized QDs have been performed on flat surfaces or clusters, rather than on single quantum dots. This limitation restricts practical applications in areas like bioimaging and molecular electronics, where single-particle functionality is often required. More experimental work is needed to unlock the potential of gold-functionalized single QDs [69–71].

7.5.7. Ligand-Mediated Targeted Delivery of AuQDs in Cancer Models

The plasmonic properties of AuQDs hold great promise for enhancing the performance of numerous nanotechnology applications, from organic solar cells to biosensing and quantum optics. Their ability to enhance fluorescence via interactions with plasmonic gold nanoparticles offers exciting opportunities to improve device efficiencies. However, challenges related to fluorescence quenching, precise QD-gold spacing control, and preservation of QD structural integrity must be addressed to enable their successful integration into advanced technologies. Overcoming these hurdles will unlock the full potential of AuQDs across a wide array of applications.

8. Surface Modification Methods for Gold Quantum Dots

AuQDs have become a major focus of research due to their unique optical properties, biocompatibility, and potential in diverse applications, particularly in the biomedical field. However, to improve their stability, functionality, and interactions with biological systems, surface modification is essential. Below is an overview of some prominent methods for modifying the surfaces of gold quantum dots.

8.1. DNA Conjugation

One of the most effective surface modification techniques involves conjugating single-stranded deoxyribonucleic acid (ssDNA) onto the surface of AuQDs. This method enhances the stability of the quantum dots across a broad pH range and varying ionic strengths. By employing multidentate passivation combined with click chemistry, controlled conjugation is achieved. The resulting ssDNA-AuQD conjugates are functionalized for biosensing applications, enabling specific interactions with nucleic acid sequences or biomolecules, thus making them highly suitable for diagnostic or therapeutic purposes [72].

8.2. Chitosan Encapsulation

Chitosan, a natural polysaccharide, is another commonly used material for modifying AuQD surfaces. Encapsulating gold nanoparticles and quantum dots with chitosan improves biocompatibility and provides a protective layer, thereby enhancing particle stability in biological environments. This modification also facilitates nanoparticle dispersion in aqueous media, promoting efficient interaction with biological systems. The process is straightforward and adaptable to various nanoparticle sizes, allowing for the customization for different biomedical applications [73,74].

8.3. Surface Coating with Thiol-Modified Ligands

Surface modification using thiol-modified ligands is a widely adopted strategy for functionalizing gold quantum dots. Thiol groups form strong covalent bonds with gold surfaces, permitting the attachment of various biomolecules or chemical groups. This method has proven effective in enhancing both the hybridization efficiency and stability of oligonucleotides bound to the gold surface. The strong thiol-gold affinity ensures the stability of AuQD conjugates, which is critical for applications such as biosensing, molecular imaging, and targeted drug delivery [33,34].

8.4. Click Chemistry

Click chemistry techniques, including strain-promoted azide-alkyne cycloaddition, offer a highly versatile platform for the surface modification of AuQDs. This approach enables the precise attachment of functional groups to the quantum dot surface. A key advantage is the ability to control the density and orientation of functional molecules, allowing for a high degree of customization. This method is particularly advantageous in

targeted drug delivery, where the controlled attachment of specific molecules is required, as well as in imaging applications [75].

8.5. Gold Nanozymes

Gold nanozymes are gold nanoparticles that exhibit enzyme-like catalytic activities. Surface modification can enhance these catalytic properties, making gold nanozymes suitable for biosensing and diagnostic applications. By chemically modifying the surface of AuQDs (e.g., amine or citrate capping), researchers can fine-tune their peroxidase-like activity. Such modifications enable their effective use in assays and biosensing platforms, catalyzing specific reactions for detecting biological molecules [76].

8.6. Hybridization with Other Nanoparticles

AuQDs can be hybridized with other nanoparticles to form hybrid systems that leverage the unique properties of each component [77]. For instance, combining AuQDs with superparamagnetic nanomaghemite or graphene oxide nanoparticles creates systems with enhanced characteristics, such as improved signal detection in biosensing. These hybrids exploit the plasmonic properties of AuQDs alongside the magnetic or electrical properties of the other nanoparticles, making them particularly effective in applications requiring high sensitivity, like molecular imaging and biomarker detection [78].

8.7. Preclinical Evaluation of AuQDs for Tumor-Targeted Therapeutics

The choice of surface modification technique for AuQDs largely depends on the intended application and desired properties. Techniques such as DNA conjugation, chitosan encapsulation, thiol modification, click chemistry, and hybridization with other nanoparticles provide versatile strategies to enhance the functionality, stability, and biocompatibility of AuQDs. These modifications are especially critical in biomedical and biosensing contexts, where stability, specificity, and effective interaction with biological systems are essential for successful implementation.

9. Drug Release Mechanisms from Gold Quantum Dots

AuQDs are emerging as powerful tools for drug delivery systems, combining their unique optical properties with biocompatibility to enable controlled and targeted release of therapeutic agents. Several mechanisms have been developed to trigger drug release from AuQDs, often in response to external stimuli such as pH changes, light, ultrasound, or enzymatic activity. Below are key strategies and findings related to these drug release mechanisms.

9.1. pH-Responsive Release

Gold nanoparticles (AuNPs) can serve as gatekeepers for drug release, especially in environments with varying pH levels. For example, in a study involving hybrid AuQDs with mesoporous silica, drug release was significantly enhanced under acidic conditions (pH 5.4) compared to physiological pH (7.4). Acidic environments around pH 5.4 promote drug release through several mechanisms:

- The hydrolysis of acid-sensitive bonds (e.g., hydrazone, Schiff base), breaking drug-carrier linkages.
- The protonation of carriers, altering charge states and weakening drug binding via electrostatic repulsion.
- The swelling of hydrogels, increasing mesh size and facilitating drug diffusion.
- Ion exchange processes that displace drug ions from carriers.

- Exploiting acidic pathological sites (such as tumors and inflammation) for targeted release.

Together, these mechanisms enable controlled and site-specific drug delivery under acidic conditions. The acidic tumor microenvironment, for instance, triggers the release of encapsulated drugs, demonstrating AuNPs' capacity to modulate drug delivery based on local pH variations. This feature is particularly advantageous for cancer therapy, as tumor tissues typically exhibit a lower pH than normal tissues [78,79].

9.2. Photothermal and Ultrasound Stimulation

Photothermal effects and ultrasound stimulation have been explored as effective triggers to enhance drug release from AuQDs. Incorporating thermosensitive materials between the AuNPs and drug molecules allows for temperature-controlled release. For example, laser irradiation induces local heating that disrupts drug–nanoparticle interactions, increasing the drug release rate. This method can be precisely controlled by adjusting laser intensity and exposure duration [36].

Similarly, ultrasound stimulation enhances drug release by generating mechanical effects that increase cell membrane permeability, facilitating drug uptake. Ultrasound-induced cavitation near nanoparticles also aids in releasing drugs from AuQDs, making this a promising non-invasive strategy for localized drug delivery.

9.3. Enzyme-Triggered Release

Enzymatic activity provides another mechanism for controlled drug release from AuQDs. By functionalizing AuQDs with specific recognition sites or substrates for particular enzymes, the nanoparticles can respond to enzymes overexpressed in targeted tissues or pathological conditions. For example, in tumor tissues where certain enzymes are abundant, enzymatic cleavage triggers structural changes in AuQDs that release the drug locally. This enzyme-responsive mechanism allows for precise, targeted drug delivery, minimizing side effects and improving therapeutic efficacy [80,81].

9.4. Combination of Multiple Stimuli

Recent advances have led to dual-responsive systems combining pH and thermal stimuli for enhanced control over drug release. For instance, platforms integrating pH-sensitive polymers with gold nanoparticles show increased drug release rates when exposed to both acidic environments and near-infrared (NIR) irradiation. This dual-stimuli approach provides flexible, finely tuned drug delivery, especially valuable in complex biological settings where multiple triggers can be employed to optimize release profiles. Such systems hold promise for improving therapeutic outcomes while reducing off-target effects.

9.5. Monitoring Drug Release

Förster resonance energy transfer (FRET) techniques have been applied to monitor drug release dynamics from AuQDs in real time. This method involves attaching fluorescent markers to both the AuQDs and the encapsulated drugs, allowing researchers to track interactions and quantify drug release under various conditions. Real-time monitoring provides crucial insights into release kinetics and supports the optimization of delivery systems tailored for specific therapeutic applications [82].

9.6. Emerging Strategies for Precision Delivery Using AuQDs

AuQDs represent a versatile and promising platform for controlled drug delivery, offering multiple stimuli-responsive mechanisms including pH changes, photothermal effects, ultrasound, and enzymatic activity. These mechanisms can be tailored to achieve targeted, efficient, and localized drug release. Combining multiple stimuli further enhances

control over drug delivery, potentially improving therapeutic efficacy and minimizing side effects. Continued research into innovative multi-stimuli strategies aims to optimize AuQDs for clinical drug delivery applications.

10. Future Outlook of AuQDs in Medical Applications

AuQDs represent a promising frontier in biomedical applications, leveraging their unique optical and electronic properties for various diagnostic and therapeutic purposes. The future outlook for AuQDs is shaped by several key actors.

10.1. Enhanced Imaging Techniques

Gold nanoparticles (AuNPs), which form the basis of AuQDs, are valued for their high atomic number, making them effective contrast agents in imaging modalities such as computed tomography (CT). They provide significantly better contrast compared to traditional iodine-based agents, with studies showing that AuNPs can enhance imaging clarity by up to 1.9 times compared to iodine at certain voltages. The ability of AuNPs to passively accumulate in tumor tissues via the enhanced permeability and retention (EPR) effect further increases their utility in cancer imaging. These improved imaging capabilities position AuQDs as valuable tools for early cancer detection and tumor monitoring [83].

10.2. Targeted Drug Delivery

AuQDs can be functionalized with various biomolecules, including antibodies and peptides, enabling targeted delivery of therapeutic agents directly to cancer cells. This targeted approach improves treatment efficacy while minimizing side effects associated with conventional therapies. The integration of AuQDs into drug delivery systems is expected to evolve, supporting personalized medicine strategies. Furthermore, the use of AuQDs for targeted delivery shows promise in treating other diseases, such as cardiovascular and neurological disorders, by ensuring precise delivery of therapeutics to specific sites [84].

10.3. Biosensing Applications

The unique photophysical properties of AuQDs make them highly suitable for biosensing applications. Their ability to emit light upon excitation enables the sensitive detection of biomolecules, enhancing diagnostic capabilities. Future research is likely to focus on developing AuQD-based biosensors capable of detecting diseases at earlier stages with greater accuracy. For example, AuQDs could be employed to identify biomarkers associated with cancer, infectious diseases, and neurodegenerative disorders, significantly improving early diagnosis and disease monitoring [85,86].

10.4. Overcoming Biological Barriers

Recent advances have demonstrated that AuQDs, when properly functionalized, can cross biological barriers such as the blood–brain barrier (BBB). This ability opens new possibilities for treating neurodegenerative diseases and brain tumors, which are traditionally difficult to address due to the restrictive nature of the BBB. AuQDs can be engineered to target specific brain regions, allowing for localized drug delivery and more effective treatment of neurological conditions.

10.5. Safety and Biocompatibility

Despite their potential, concerns about the biocompatibility and long-term safety of AuQDs remain critical research areas. Ongoing studies aim to refine AuQD synthesis methods to enhance biocompatibility while preserving their functional properties. The development of carbon-based quantum dots is also being explored as a greener alternative with potentially lower toxicity profiles. Ensuring that AuQDs do not induce toxic effects

in vivo, especially with prolonged use, is essential for successful clinical translation. Key safety concerns include the following:

- Organ accumulation and inflammation: AuQDs tend to accumulate in organs such as the liver, spleen, kidneys, and lungs. This accumulation may trigger inflammatory responses, potentially leading to tissue damage and toxicity.
- Oxidative stress and mitochondrial dysfunction: Studies on similar quantum dots, particularly cadmium-based ones, indicate that released metal ions can bind mitochondrial proteins, causing oxidative stress, DNA damage, mitochondrial dysfunction, and autophagy. These mechanisms may also apply to AuQDs due to their metallic nature.
- Immune system effects: The immune response to accumulated quantum dots, including infiltration by inflammatory cells and possible immune disruption, is an important concern.
- Histopathological changes: Long-term exposure is evaluated for tissue abnormalities such as fibrosis or cellular damage in organs where AuQDs accumulate, notably the liver and spleen.
- Genotoxicity and apoptosis: Investigations include DNA fragmentation and apoptosis induction in cells exposed to quantum dots, which could translate into long-term carcinogenic or degenerative risks.
- Slow clearance and biotransformation: The persistence of AuQDs in the body and their slow degradation raise concerns about chronic exposure and bioaccumulation toxicity [87,88].

10.6. Regulatory and Market Considerations

As with any emerging healthcare technology, regulatory approval will be critical for the clinical adoption of AuQDs. The future market success of AuQDs depends on navigating these regulatory frameworks while demonstrating clear clinical benefits over existing technologies. Collaboration between researchers, developers, and regulatory agencies is essential to ensure AuQDs meet safety standards before widespread clinical implementation. Table 3 provides a comparative overview of recent studies exploring various biomedical uses of AuQDs, highlighting their performance parameters, biological targets, and therapeutic outcomes.

Table 3. Comparative table of AuQDs (gold quantum dots) with other quantum dot materials such as carbon quantum dots (CQDs) and PEI-functionalized QDs [89–93].

Feature	AuQDs (Gold Quantum Dots)	Carbon Quantum Dots (CQDs)	PEI Quantum Dots (PEI-QDs)
Material Composition	Gold nanoparticles	Carbon-based nanoparticles with sp2/sp3 carbon, often doped with N, O, S	Carbon QDs functionalized with polyethyleneimine (PEI)
Size	Typically < 10 nm (varies by synthesis)	Generally < 10 nm, often 1–5 nm	Similar size range as CQDs
Photoluminescence (PL)	Strong, tunable emission depending on size and surface	Excitation-dependent emission with broad PL bands; QY varies widely (3–90%)	Enhanced fluorescence due to PEI passivation; tunable multiple-wavelength emission
Quantum Yield (QY)	Moderate to high (specific values vary by synthesis)	Variable; can reach up to 41% or higher depending on synthesis conditions	Improved QY compared to bare CQDs due to surface passivation

Table 3. *Cont.*

Feature	AuQDs (Gold Quantum Dots)	Carbon Quantum Dots (CQDs)	PEI Quantum Dots (PEI-QDs)
Stability	High chemical and photostability	Good stability but generally shorter fluorescence lifetime than semiconductor QDs	Enhanced stability and fluorescence intensity due to PEI coating
Biocompatibility	Generally good, low toxicity	High biocompatibility, low or no toxicity	Good biocompatibility; used in bioimaging and gene delivery
Synthesis Methods	Chemical reduction, seed-mediated growth	Hydrothermal, pyrolysis, polymerization of small molecules	Hydrothermal synthesis followed by PEI functionalization
Surface Functionalization	Possible with ligands for targeted applications	Rich surface chemistry with –COOH, –OH, $–NH_2$ groups allowing easy functionalization	PEI provides amine groups for enhanced interaction with biological molecules
Applications	Bioimaging, sensing, catalysis, photothermal therapy	Bioimaging, drug delivery, sensing, photovoltaics, catalysis	Bioimaging, gene delivery, nucleic acid transfection, sensing
Toxicity	Low compared to heavy metal QDs like CdSe, but depends on coating	Low toxicity; eco-friendly and biocompatible	Low toxicity; PEI coating reduces cytotoxicity compared to bare QDs
Advantages	High photostability, tunable optical properties	Low cost, eco-friendly, easy synthesis, versatile surface chemistry	Enhanced fluorescence and cellular uptake due to PEI; multifunctional for bioapplications
Disadvantages	Potential aggregation, costlier than carbon QDs	Broader emission peaks, shorter fluorescence lifetime than semiconductor QDs	Possible cytotoxicity at high PEI concentrations; synthesis complexity

11. AuQDs in Cancer Combination Therapy

AuQDs are emerging as promising tools in cancer therapy, particularly when combined with other treatment modalities. Their unique properties—including size-tunable fluorescence, biocompatibility, and the ability to enhance targeted drug delivery and imaging—make them highly suitable for advancing cancer treatments.

11.1. Mechanisms of Action

1. Dual Treatment Approaches
   Recent studies have shown that AuQDs can significantly enhance the efficacy of other treatments, such as cold atmospheric plasma (CAP). For example, a study on glioblastoma demonstrated that combining CAP with AuQDs induced cytotoxicity via Fas/TRAIL-mediated pathways, leading to a marked reduction in cell viability compared to treatment with AuQDs alone. This dual approach not only increased cancer cell death, but also inhibited cell motility and sphere formation, both key indicators of cancer aggressiveness. By combining AuQDs with CAP, researchers enhanced therapeutic effects, rendering cancer cells more susceptible to treatment [94].

2. Targeted Drug Delivery
   AuQDs are also integrated into multifunctional nanoparticles for targeted drug delivery. Hybrid nanoparticles combining AuQDs with mesoporous silica and other agents have been developed to deliver chemotherapeutic drugs directly to cancer cells. These systems can be further conjugated with targeting ligands to improve specificity for tumor cells, thereby minimizing systemic toxicity. This targeted approach not only enhances the precision of cancer therapies, but also reduces side effects by concentrating therapeutic agents at the tumor site, improving the overall therapeutic index [95].

11.2. Imaging and Diagnostics

AuQDs are invaluable in cancer imaging due to their unique optical properties that enable effective fluorescence imaging. These properties allow for the visualization of tumor sites in vivo. Additionally, AuQDs can be used alongside computed tomography (CT) imaging to provide dual-modal imaging capabilities, enhancing tumor localization accuracy. This combination facilitates more precise monitoring of tumor response to treatment and aids in early detection, which is critical for effective cancer management. The capacity to perform both imaging and therapeutic functions positions AuQDs as powerful tools in cancer diagnostics and therapy [96].

11.3. Safety and Efficacy

The safety profile of AuQDs is promising, with studies reporting low toxicity even at high concentrations. For instance, one study found that AuQD-based probes did not adversely affect normal organ functions in animal models, suggesting good biosafety for potential clinical applications. This makes AuQDs a viable option for clinical use in cancer treatment. Furthermore, combination therapies involving AuQDs have shown improved anti-tumor efficacy compared to traditional therapies alone. Research indicates that AuQDs enhance the effects of chemotherapeutic drugs and other treatments by facilitating more efficient delivery and increasing tumor cell sensitivity, leading to better therapeutic outcomes [97,98].

11.4. Future Perspectives

The integration of AuQDs into combination cancer therapies represents a significant advancement in treatment strategies. Their ability to enhance drug delivery efficiency alongside imaging capabilities makes them a valuable asset in the ongoing fight against cancer [99]. Future research will focus on optimizing AuQD formulations, improving targeting specificity, and thoroughly assessing long-term safety and efficacy in clinical settings. AuQDs have the potential to revolutionize personalized cancer treatments by enabling more precise and effective therapies with fewer side effects as more preclinical and clinical research is conducted [100].

Gold quantum dots, which offer improved targeting, imaging, and drug delivery capabilities, are at the forefront of cutting-edge cancer therapeutics. Their capacity to integrate therapeutic and diagnostic functions into a single platform makes them a powerful tool in oncology. As research advances, AuQDs may play an increasingly important role in improving patient outcomes, offering hope for more effective, personalized, and less invasive cancer treatments [101] as we have discussed in Table 2.

Table 4 provided the applications, functionalization strategies, key properties, and performance metrics of nanomaterials or nanoparticles in various biomedical fields, particularly focusing on cancer therapy, bioimaging, biosensing, drug delivery, and crossing the blood–brain barrier (BBB). Table 5 provided key characterization techniques used to analyze certain nanomaterials (likely quantum dots or nanoparticles), the observations made from these techniques, their impact on applications.

Table 4. Biomedical Applications and Functionalization Strategies of Nanomaterials.

Application	Functionalization	Key Properties	Performance Metrics	References
Cancer Therapy	- Ligands (antibodies, peptides).	- EPR effect, pH-responsive release, photothermal conversion.	In total, 16% tumor growth inhibition, 30% enhanced drug delivery.	[12,49,94]
Bioimaging	- Fluorescent dyes, targeting moieties.	- Size-tunable emission (438 nm), photostability.	High-resolution live-cell imaging, multiplexed detection.	[23,44,96]
Biosensing	- DNA, enzymes (e.g., glucose oxidase).	- Surface plasmon resonance, nanozymatic activity.	LOD: 0.1 nM for thiocyanate ions.	[18,63,76]
Drug Delivery	- pH-sensitive polymers, thermosensitive coatings.	- Controlled release (pH 5.4 vs. 7.4), FRET monitoring.	In total, 90% release under dual stimuli (pH + NIR).	[36,78,82]
Crossing BBB	- PEGylation, chitosan encapsulation.	- Size < 5 nm, neutral surface charge.	Enhanced brain tumor targeting.	[10,57,84]

Table 5. Characterization Techniques and Their Relevance in Nanomaterial Applications.

Characterization	Technique	Observations	Impact on Applications	References
Size/Shape	TEM, SEM	Spherical/cluster morphology, 1–10 nm.	Determines quantum confinement and fluorescence.	[17,19,71]
Optical Properties	UV-Vis, Fluorescence Spectroscopy	Absorption in UV, emission tunable (400–700 nm).	Bioimaging sensitivity and multiplexing.	[28,40,47]
Surface Charge	Zeta Potential	Positive/negative charge (hydrothermal synthesis).	Cellular uptake efficiency (e.g., tumor targeting).	[18,30,57]
Biocompatibility	Cytotoxicity Assays (MTT)	Low toxicity (e.g., >80% cell viability at 100 μg/mL).	Safe for in vivo use (e.g., glioma therapy).	[26,52,97]
Drug Release	FRET, HPLC	pH/enzyme-triggered kinetics (e.g., 70% release in 6 h at pH 5.4).	Controlled therapy with reduced side effects.	[79,80,82]

12. Conclusions and Future Perspective

AuQDs have emerged as a promising tool in various biomedical applications, offering unique advantages due to their optical properties, biocompatibility, and tunable size. Over recent years, significant progress has been made in utilizing AuQDs for drug delivery, imaging, biosensing, and cancer therapy. Their ability to be functionalized with a variety of biomolecules enables targeted therapies that enhance efficacy while reducing the side effects of conventional treatments. Moreover, their capacity to interact with biological systems in a controlled manner makes them a versatile platform for improving the precision of diagnostic and therapeutic interventions.

Despite their immense potential, several challenges remain before AuQDs can achieve widespread clinical application. Key areas of focus include ensuring long-term biocompat-

ibility, optimizing surface modifications, and improving safety profiles. Alternative formulations, such as carbon-based quantum dots, are currently being investigated to reduce toxicity while maintaining functionality. Furthermore, the safe and efficient integration of AuQDs into clinical settings—particularly in drug delivery systems and personalized medicine strategies—will depend heavily on advancements in regulatory frameworks [102].

Looking ahead, AuQDs are poised to play a pivotal role in revolutionizing medical applications. Their combination of imaging capabilities, targeted drug delivery, and biosensing functions opens new avenues for early diagnosis, precision therapy, and minimally invasive treatments. The ability to overcome biological barriers, such as the blood–brain barrier, offers promising prospects for treating challenging conditions like neurodegenerative diseases and brain tumors. Additionally, the development of dual-responsive systems that combine multiple stimuli (e.g., pH and temperature) for controlled drug release is likely to enhance therapeutic efficacy in cancer and other diseases.

In conclusion, AuQDs hold great promise for advancing medical diagnostics and therapeutics. However, their clinical success will depend on overcoming challenges related to safety, biocompatibility, and regulatory approval. With continued research and technological advancements, AuQDs could significantly impact the future of precision medicine by providing targeted, efficient, and personalized treatments across a wide range of diseases. Table 6 summarizes the major obstacles across categories such as material stability, pharmaceutical formulation, biological response, and regulatory frameworks, highlighting their implications for future research and clinical deployment [14–16,27,48,103–105].

Table 6. Summary of key challenges and barriers to the clinical translation of AuQDs.

Obstacle Category	Specific Challenge	Description/Impact
Stability issues	Aggregation and degradation	AuQDs, like other quantum dots, are prone to aggregation and chemical degradation, affecting their optical properties.
	Poor aqueous solubility	Organometallic synthesis often yields hydrophobic QDs requiring surface modification for water solubility.
	Sensitivity to oxidation and environmental factors	Surface atoms can oxidize, leading to loss of quantum properties.
Pharmaceutical Challenges	Surface ligand instability	Ligand exchange or coating needed to improve stability and biocompatibility, complicating production.
	Heavy metal toxicity concerns	Although AuQDs are less toxic than heavy metal QDs, biosafety and accumulation remain concerns.
Scalability and Production	Complexity of synthesis and scale-up	Green, aqueous-based, and biotechnology methods are needed to improve scalability and reduce environmental hazards.
	Batch-to-batch reproducibility	Variability in particle size and surface chemistry affects clinical reliability.
Biological and Safety	Clearance and retention balance	Need to balance retention time for efficacy with clearance to avoid toxicity.
	Immunogenicity and side effects	Potential immune reactions, cytokine storms, and hypersensitivity can occur.
Regulatory and Clinical	Lack of standardized protocols and predictive models	Difficulty in establishing consistent clinical trial protocols and predictive in vitro/in vivo models.
	Limited clinical trials and market availability	Few ongoing clinical trials and limited commercial substitutes hinder clinical adoption.

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Abbreviations

AuQDs	Gold Quantum Dots
AuNPs	Gold Nanoparticles
QDs	Quantum Dots
BSA	Bovine Serum Albumin
LSPR	Localized Surface Plasmon Resonance
UV	Ultraviolet
OSCs	Organic Solar Cells
GQDs	Graphene Quantum Dots
TEM	Transmission Electron Microscopy
CT	Computed Tomography
EPR	Enhanced Permeability and Retention (effect)
PEG	Polyethylene Glycol
EpCAM	Epithelial Cell Adhesion Molecule
HER2	Human Epidermal Growth Factor Receptor 2
CdSe	Cadmium Selenide
CdTe	Cadmium Telluride
ZnS	Zinc Sulfide
MSN	Mesoporous Silica Nanoparticles
EPI	Epirubicin (a chemotherapy drug)
Apt	Aptamer
NPs	Nanoparticles
ROS	Reactive Oxygen Species

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