Review

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Glowing Hope: Radioactive Gold Nanoparticles for Targeted Therapy. A Comprehensive Review on Nanoparticle Geometry and Synthesis

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The amalgamation of radioactivity and nanoparticles has catalyzed profound innovations across scientific and medical domains. This study offers a comprehensive exploration of synthesis methodologies, safety assessments, and formulation tactics pertaining to radioactive gold nanoparticles within the domain of precision medicine. The convergence of radioactivity and nanotechnology has instigated novel approaches to combat various diseases, notably cancer. Radioactive elements emit ionizing radiation, enabling targeted destruction of diseased cells, while nanoparticles provide unique benefits such as customizable properties and efficient payload delivery. Synthesis techniques for radioactive gold nanoparticles encompass a spectrum of methods, including chemical reduction, radiation-induced synthesis, and surface functionalization.

These methodologies afford precise control over nanoparticle attributes like size, morphology, and surface chemistry, thereby influencing their biological interactions and therapeutic efficacy. Synthesis methods are numerous in the literature and each one yields differently shaped gold nanoparticles, the particular geometry of these offers them different roles and functions with specific advantages and disadvantages. Safety considerations are paramount in nanoparticle-based therapies. Despite the inherent cytotoxicity of radioactivity, meticulous surface modifications and biocompatible coatings mitigate off-target effects, enhancing the safety profile of radioactive nanoparticles and optimizing therapeutic outcomes. Formulation strategies play a pivotal role in tailoring the delivery and targeting of radioactive gold nanoparticles. Strategies such as encapsulation within polymeric matrices, conjugation with targeting ligands, and integration into nanocarriers offer versatility in modulating pharmacokinetics and maximizing therapeutic efficacy.

The fusion of radioactivity and nanotechnology presents significant potential for disease treatment. By elucidating synthesis, safety considerations, and formulation strategies of radioactive gold nanoparticles, this article aims to advance precision medicine and facilitate the development of personalized therapeutic interventions.

Keywords: radiation; target medicine; nanoparticles; gold nanoparticles; nanogeometry

Introduction

In the dynamic realm of contemporary medicine, radiomedicine emerges as a beacon of innovation, heralding a transformative approach to disease diagnosis and treatment. At its core lies the integration of nanoparticles, particularly gold nanoparticles, into targeted therapies, promising a realm of more precise, effective, and personalized treatments that could redefine healthcare.

Radiomedicine represents a fusion of radiology and medicine, harnessing radiation for therapeutic and diagnostic purposes. Unlike conventional treatments which often exhibit systemic toxicity and non-specific effects on healthy tissues, radiomedicine aims to deliver radiation precisely to the disease site while minimizing harm to surrounding tissue (Fig. 1). This precision is facilitated through nanoparticles, serving as carriers for delivering therapeutic payloads with unparalleled accuracy.

Among the plethora of radio-nanoparticles explored for medical applications, gold nanoparticles stand out as promising candidates. Their distinctive properties, such as biocompatibility, ease of functionalization, and customizable size and shape, make them ideal for targeted therapies. Gold nanoparticles can be precisely tailored to bind to specific molecular targets, like receptors overexpressed on cancer cells, facilitating highly selective drug delivery [1–3].

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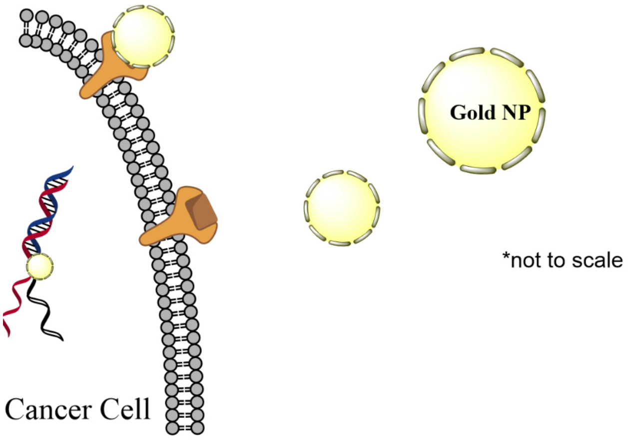

Fig. 1. General mechanism of radioactive nanoparticles (made with ChemDraw (https://perkinelmer-chemdraw-professional.software.informer.com/16.0/)). * structures not to scale.

One of the most compelling applications of gold nanoparticles in radio medicine is targeted cancer therapy. Traditional cancer treatments, such as chemotherapy and radiotherapy, often result in significant collateral damage to healthy tissues and severe side effects. In contrast, gold nanoparticles can be functionalized with anticancer drugs or radioisotopes and guided directly to tumor sites through passive or active targeting mechanisms. Once localized, these nanoparticles can release their payload, delivering a lethal dose of therapy specifically where needed, sparing healthy tissue and minimizing adverse effects [4,5].

Moreover, gold nanoparticles hold immense potential in theranostics, which combines therapeutic and diagnostic capabilities within a single platform. By incorporating imaging agents into gold nanoparticles, clinicians can not only deliver targeted therapies but also monitor their efficacy in real-time. This dual functionality enables early assessment of treatment response, facilitating timely adjustments and personalized medicine approaches tailored to individual patient needs [6].

The versatility of gold nanoparticles extends beyond cancer therapy, encompassing a wide range of medical applications. In cardiovascular medicine, gold nanoparticles can be used for targeted drug delivery to atherosclerotic plaques, reducing the risk of cardiovascular events. In neurology, they show promise for crossing the blood-brain barrier to deliver therapeutics for neurodegenerative diseases. Additionally, gold nanoparticles are being explored for applications in regenerative medicine, diagnostics, and antimicrobial therapy, highlighting their multifaceted utility in healthcare [7,8].

However, translating gold nanoparticle-based therapies from research to clinical practice presents challenges. Issues such as nanoparticle stability, biodistribution, and long-term safety profiles require meticulous attention to ensure clinical success. Moreover, navigating the regulatory landscape surrounding nanomedicine demands rigorous preclinical and clinical evaluation to establish efficacy and safety standards.

Despite these challenges, the potential of radiomedicine and gold nanoparticle-based therapies to revolutionize healthcare remains undeniable.

As research progresses and technologies evolve, the vision of personalized, precision medicine tailored to individual patient characteristics moves closer to realization. By harnessing the unique properties of gold nanoparticles and leveraging the power of targeted therapies, radiomedicine holds the promise of transforming disease diagnosis, treatment, and ultimately, patient outcomes [9,10].

As we stand on the brink of a new era in healthcare, the fusion of nanotechnology with medicine offers a beacon of hope for patients and clinicians alike, ushering in a future where precision and efficacy converge to redefine the boundaries of healing.

Materials and Methods

This review article was meticulously prepared by selecting and analyzing only recently published articles from the scientific literature. The process for selecting these articles involved several systematic steps, aimed at ensuring the inclusion of high-quality, relevant, and current research in the field of radiomedicine, specifically focusing on the integration of gold nanoparticles.

A comprehensive literature search was conducted using prominent scientific databases including PubMed, Web of Science, and Google Scholar. The search was restricted to articles published within the last five years to ensure the review reflects the latest advancements and trends. Keywords used in the search included “radiomedicine”, “gold nanoparticles”, “targeted therapy”, “nanoparticles in medicine”, and “nanoparticle synthesis”. Boolean operators (AND, OR, NOT) were used to refine the search results and ensure a broad yet focused collection of articles.

The initial search yielded a substantial number of articles. Titles and abstracts of these articles were screened for relevance. Full texts of potentially relevant articles were then retrieved and assessed based on the inclusion and exclusion criteria. This process was conducted independently by two reviewers to minimize bias, with any discrepancies resolved through discussion or consultation with a third reviewer.

Key information such as study objectives, methodologies, findings, and conclusions were noted. Special attention was given to the synthesis methods, functionalization techniques, and therapeutic applications of gold nanoparticles in radiomedicine. This information was then synthesized to provide a comprehensive overview of the current state of research, highlight significant advancements, and identify areas for future study.

In selecting scientific articles for this review, inclusion criteria encompassed peer-reviewed studies focusing on the synthesis, characterization, and applications of gold nanoparticles (AuNPs) with various shapes, such as spheres, rods, stars, shells, cages, and prisms. Studies were chosen based on their relevance to the field, robustness of experimental design, and novelty of findings. Exclusion criteria were based on papers lacking detailed methodological descriptions, those with inconclusive or poorly supported results, and studies not available in English. Over 150 articles were initially selected, but after rigorous evaluation, only 52 met the stringent criteria for relevance and quality and were included in the final review.

Results and Discussions

Various methods exist for synthesizing gold nanoparticles, often classified as top-down or bottom-up protocols, and further categorized into physical, chemical, and biological approaches. These methods yield nanoparticles with diverse morphologies tailored for specific applications [11].

Physical methods rely on energy transfer, induced by radiation, such as photochemical processes, ionizing radiation, and microwave radiation, to initiate reduction reactions and nucleate metallic particles. Chemical routes, the most prevalent, utilize reducing agents like sodium borohydride, hydrazine, or citrate to trigger nanoparticle nucleation. Porous supports aid in achieving size control, with the matrix pores influencing nanomaterial morphology [12,13].

Different Synthesis Methods

Green synthesis methods are gaining traction due to their environmental friendliness. Examples include microwave-induced plasma-in-liquid processes, which break water molecules without toxic reducing agents, and radiolysis by gamma radiation or X-rays, which generate reducing agents from water molecules. Phytochemicals from plant extracts, like epigallocatechin and mangiferin, serve as both reducing agents and stabilizers, promoting nanoparticle synthesis in a green approach [14].

Laser sources and antioxidants from tea leaves, such as catechins and theaflavins, also play roles in gold nanoparticle synthesis. These compounds demonstrate excellent reducing and stabilizing properties, yielding biocompatible nanoparticles. Additionally, microorganisms like bacteria and fungi offer eco-friendly biological methods, synthesizing gold nanoparticles without organic solvents.

In practice, a common method for synthesizing gold nanospheres involves the reduction of tetrachloroaurate ion ($AuCl_4^-$) using citrate in an aqueous environment, known as the *Turkevitch* method (Fig. 2). Here, citrate serves as both a reducing agent and an anionic stabilizer, yielding nanospheres approximately 15 nm in diameter [15,16].

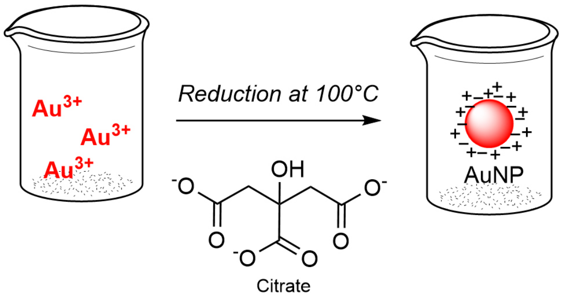

Fig. 2. Visual representation of the *Turkevitch* method (made with ChemDraw (https://perkinelmer-chemdraw-professional.software.informer.com/16.0/)).

Various methods were explored to synthesize gold nanoparticles (AuNPs) with tailored properties suitable for therapeutic applications. Chemical reduction techniques, utilizing agents like sodium borohydride and citrate, were commonly employed for their simplicity and high yield. These methods allowed precise control over nanoparticle size and shape, crucial for achieving desired therapeutic effects. Green synthesis approaches using phytochemicals from plant extracts showed promise as eco-friendly alternatives, producing biocompatible AuNPs without toxic reducing agents [17].

Nanoparticle Geometry and Specific Properties

Gold nanoparticles have garnered significant attention in the fields of chemistry, physics, and materials science due to their unique optical, electronic, and catalytic properties. These properties can be finely tuned by manipulating the size, shape, and surface characteristics of the nanoparticles, making them highly versatile for various applications, including medical diagnostics, drug delivery, and environmental sensing. One of the most critical aspects influencing the functionality of gold nanoparticles is their geometry. This article delves into the synthesis of gold nanoparticles with different geometries, highlighting the methods and conditions that lead to the formation of spheres, rods, cubes, and other complex shapes [18,19].

Overlooking geometry, several other factors significantly influence the function of gold nanoparticles. The surface chemistry is an important characteristic, that plays a vital role in biomedical applications, including the nature of the ligands used and functional groups attached to the gold surface, plays a crucial role in determining the stability, solubility, and biocompatibility of the NPs. Gold NPs functionalized with polyethylene glycol (PEG) exhibit enhanced biocompatibility and reduced clearance by the immune system, making them suitable for drug delivery and imaging applications [1–3,5,6].

The size of gold NPs also affects their optical, electronic and catalytic properties, with smaller particles generally exhibiting more pronounced quantum effects. Smaller gold NPs (around 5–10 nm) have been found to penetrate deeper into tumors compared to larger ones, improving their efficacy in cancer treatment. On the other hand, larger gold NPs (20–50 nm) are often preferred in photothermal therapy due to their superior light absorption and conversion properties. The environment in which the gold NPs are used, such as the potential of hydrogen (pH), ionic strength, and presence of other biomolecules, can impact their aggregation state and reactivity. For example, gold NPs designed for use in acidic tumor microenvironments often have pH-sensitive coatings that enable targeted drug release under these conditions [3,11].

Recent studies from the literature have highlighted the importance of surface charge and zeta potential in influencing cellular uptake and toxicity profiles. Moreover, the synthesis method and subsequent surface modifications can introduce defects and influence the crystallinity of the nanoparticles, thereby affecting their functional performance. Understanding these multifaceted factors is crucial for optimizing gold NPs for specific applications *in vivo* [1,2,4,10].

Spherical gold nanoparticles are the most commonly synthesized form due to their simplicity and the well-established methods available for their production. The Turkevich method, developed in the 1950s, remains a cornerstone in the synthesis of spherical AuNPs. This method involves reducing gold salts commonly chloroauric acid ($HAuCl_4$) with a reducing agent such as citrate in an aqueous solution. The citrate ions not only reduce the gold ions to elemental gold but also act as capping agents, stabilizing the nanoparticles and preventing their aggregation [20].

The size of the spherical nanoparticles can be controlled by varying the concentration of the reducing agent and the gold precursor. Higher concentrations of citrate lead to smaller nanoparticles, typically in the range of 10–20 nm, due to more nucleation sites being formed. Conversely, lower concentrations result in fewer nucleation sites and thus larger particles.

Gold nanorods exhibit unique optical properties due to their anisotropic shape, which causes them to have two plasmon resonance modes: longitudinal and transverse. The seed-mediated growth method is widely used for synthesizing gold nanorods. This method involves two main steps: the creation of small spherical gold seeds and their subsequent growth into rod shapes in the presence of a surfactant, typically cetyltrimethylammonium bromide (CTAB) [21].

In the growth solution, the gold salt is reduced by a weak reducing agent such as ascorbic acid. The presence of CTAB directs the growth of the seeds into rod shapes by preferentially adsorbing onto certain crystallographic facets, thereby controlling the aspect ratio of the rods. By adjusting the concentration of the gold precursor, the reducing agent, and the CTAB, researchers can fine-tune the aspect ratio of the nanorods, resulting in precise control over their optical properties [22].

Cubic gold nanoparticles are another geometry that offers distinct properties, particularly in catalysis and surface-enhanced Raman spectroscopy (SERS). The synthesis of cubic AuNPs often involves the reduction of gold salts in the presence of strong reducing agents and capping agents that favor the formation of {100} facets, which are characteristic of cubic shapes [23,24].

One common method for synthesizing cubic gold nanoparticles is through the use of silver ions as a shape-directing agent. In this process, a small amount of silver nitrate is added to the gold salt solution, and the reduction is carried out using ascorbic acid. The silver ions preferentially bind to the {100} facets, inhibiting their growth and promoting the formation of cubes.

Other polyhedral shapes, such as octahedra and icosahedra, can be synthesized by carefully controlling the reduction kinetics and the concentration of the capping agents. For instance, using polyvinylpyrrolidone (PVP) as a capping agent can stabilize different facets, leading to the formation of various polyhedral structures.

Star-shaped and branched gold nanoparticles are particularly interesting due to their high surface area and multiple sharp tips, which enhance their catalytic and SERS activities. These nanoparticles are typically synthesized through seed-mediated growth methods, similar to the synthesis of nanorods, but with modifications to promote branching [25–27].

The use of surfactants like CTAB, along with silver ions and other additives, can direct the growth of gold seeds into branched structures. The growth conditions, such as temperature, pH, and the concentration of the reactants, are critical in determining the final shape of the nanoparticles. For example, higher temperatures and specific potential of hydrogen (pH) conditions can favor the formation of multiple branches [28].

The ability to synthesize gold nanoparticles with various geometries opens up a plethora of possibilities for their application in science and technology, Table 1 presents the most common AuNPs geometries with their specific advantages and disadvantages. Each geometry offers unique properties that can be exploited in different fields, from medicine to electronics. The synthesis methods discussed—ranging from simple reduction processes to more complex seed-mediated growth techniques—demonstrate the intricate control researchers have over nanoparticle shape and size. As the field of nanotechnology continues to evolve, the development of new methods for synthesizing gold nanoparticles with tailored geometries will undoubtedly lead to further advancements and novel applications [29,30].

Applications for Specifically Shaped Gold Nanoparticles

Gold nanoparticles have emerged as promising candidates for various therapeutic applications, including drug

Table 1. Different gold nanoparticle geometries, their advantages, disadvantages and biomedical uses.

Geometry	Advantages	Disadvantages	Differences	Common uses
Spheres	- Easy to synthesize and functionalize - Good control over size distribution	- Limited surface area-to-volume ratio - May aggregate in biological environments	- Uniform optical properties - Isotropic scattering and absorption	- Drug delivery, imaging, biosensing
Rods	- Tunable aspect ratios and optical properties - Enhanced photothermal efficiency	- More complex synthesis - Less stable compared to spheres	- Anisotropic properties - Enhanced near-infrared absorption	- Photothermal therapy, imaging, catalysis
Stars	- High surface area - Multiple tips enhance catalytic and sensing abilities	- Complex synthesis - Less stable and more prone to aggregation	- High surface plasmon resonance - Multi-branched structure	- Sensing, imaging, catalysis
Shells	- Tunable core-shell structure for multifunctionality	- Complicated and expensive synthesis process	- Core-shell interaction	- Drug delivery, imaging, photothermal therapy
Core-Shell	- Enhanced stability and biocompatibility	- Potential core material degradation	- Enhanced stability and biocompatibility	
Cages	- High surface area with hollow structure - Tunable porosity	- Fragile and less stable - Complex synthesis and functionalization	- High porosity - Enhanced catalytic activity	- Drug delivery, catalysis, imaging
Prisms	- Tunable optical properties with sharp corners	- Difficult to synthesize uniformly	- Anisotropic optical properties	- Sensing, imaging, photothermal therapy
Triangles	- High aspect ratio	- Stability issues in biological environments	- Shape-dependent optical absorption	

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delivery, photothermal therapy, and diagnostic imaging. Their unique physicochemical properties, such as high surface area-to-volume ratio and tunable surface chemistry, make them ideal platforms for targeted drug delivery and image-guided therapy. AuNPs can be functionalized with therapeutic agents, such as anticancer drugs or nucleic acids, and targeted to specific cells or tissues using ligands or antibodies, thereby minimizing off-target effects and enhancing therapeutic efficacy [31,32].

In drug delivery applications, AuNPs can serve as carriers for chemotherapeutic drugs, allowing controlled release and targeted delivery to tumor sites. Surface modification of AuNPs with tumor-targeting ligands or antibodies enables selective accumulation in cancer cells, reducing systemic toxicity and improving therapeutic outcomes. Additionally, AuNPs can be used for photothermal therapy, where they absorb near-infrared light and convert it into heat, leading to localized hyperthermia and tumor ablation. This approach offers a non-invasive and targeted alternative to conventional cancer therapies, with potential for synergistic combination with other treatment modalities [33,34].

The optical properties of gold nanoparticles are highly dependent on their shape, which affects the surface plasmon resonance (SPR) phenomenon. SPR is the collective oscillation of electrons in response to light, leading to strong absorption and scattering at specific wavelengths. Spherical nanoparticles exhibit a single SPR peak, while anisotropic shapes like rods, cubes, and stars show multiple SPR peaks corresponding to different plasmon modes [35].

For instance, gold nanorods have two SPR peaks: one in the visible region due to transverse oscillation and another in the near-infrared (NIR) region due to longitudinal oscillation. This tunability is essential for applications like imaging, where specific wavelengths are targeted for enhanced efficacy and minimal damage to surrounding tissues [36].

The catalytic activity of gold nanoparticles is also influenced by their shape which can range from nanocubes, spheres and rods to more complex ones like nanostars, cages and clusters. Different geometries expose different crystallographic facets, which have varying catalytic properties. For example, cubic nanoparticles with {100} facets exhibit higher catalytic activity in certain reactions compared to spherical nanoparticles. Star-shaped nanoparticles, with their high surface area and numerous active sites, offer even greater catalytic efficiency, making them ideal for applications in environmental remediation and chemical synthesis [37].

The interaction of gold nanoparticles with biological systems is geometry-dependent. Spherical nanoparticles tend to be internalized by cells more efficiently than rod-shaped or star-shaped nanoparticles. However, rod-shaped nanoparticles can penetrate cell membranes more effectively due to their anisotropic shape, which is advantageous for drug delivery and gene therapy, improving their ability to reach tumor sites as well. Additionally, the enhanced surface area of branched nanoparticles improves their interaction with biomolecules, increasing their effectiveness in applications like biosensing and targeted therapy [38,39].

Gold nanoparticles are widely used in medical imaging and diagnostics due to their excellent biocompatibility and unique optical properties. Spherical gold nanoparticles are commonly employed in techniques like colorimetric assays, where their SPR response changes color upon binding to specific analytes. This property is utilized in pregnancy tests and other diagnostic assays for rapid and sensitive detection.

Gold nanorods, with their tunable NIR absorption, are used in imaging techniques like photoacoustic imaging and optical coherence tomography. These methods provide high-resolution images of biological tissues, enabling early diagnosis of diseases such as cancer. The ability to tune the absorption wavelength of gold nanorods allows for deeper tissue penetration and improved contrast, enhancing the accuracy of these imaging techniques [40].

Photothermal therapy (PTT) leverages the ability of gold nanoparticles to convert absorbed light into heat, destroying cancer cells through localized hyperthermia. Gold nanorods and nanoshells are particularly effective in PTT due to their strong absorption in the NIR region, where biological tissues are more transparent. This enables deeper penetration of light into tissues, allowing for the treatment of tumors located deeper within the body [41].

Gold nanoparticles with different geometries are employed in environmental applications, including water purification and pollutant detection. Cubic and star-shaped nanoparticles, with their high catalytic activity, are used in catalytic converters to reduce harmful emissions from industrial processes and vehicles. Their ability to accelerate chemical reactions at lower temperatures makes them ideal for energy-efficient environmental remediation [42–44].

In water purification, gold nanoparticles are used to detect and remove contaminants. Spherical and cubic nanoparticles functionalized with specific ligands can selectively bind to heavy metals and organic pollutants, allowing for their efficient removal from water sources. The high surface area of star-shaped nanoparticles enhances their adsorption capacity, making them effective in purifying large volumes of water [45].

Biosensors based on gold nanoparticles leverage their unique optical and electronic properties for the detection of biological molecules. Spherical nanoparticles are commonly used in surface-enhanced Raman scattering (SERS) sensors, where they enhance the Raman signal of target molecules, enabling ultra-sensitive detection. Cubic and star-shaped nanoparticles, with their high surface area and multiple active sites, further improve the sensitivity and selectivity of these sensors, making them valuable tools in medical diagnostics, food safety, and environmental monitoring [46].

When used in dental applications, radioactive AuNPs can be precisely directed to malignancies within the oral cavity, minimizing damage to surrounding healthy tissues. The primary mechanism involves the use of radioactive isotopes, such as Gold-198 or Gold-199, integrated into the nanoparticles. Once administered, these nanoparticles accumulate preferentially in tumor tissues due to the enhanced permeability and retention (EPR) effect. The localized radiation emitted from the nanoparticles induces cellular damage specifically in the cancer cells, sparing adjacent normal cells.

This targeted approach not only enhances the efficacy of cancer treatment but also reduces the side effects typically associated with conventional radiation therapy. Additionally, AuNPs can be conjugated with various targeting molecules, such as antibodies or peptides, to further increase specificity towards cancerous tissues. Beyond cancer treatment, radioactive gold nanoparticles hold potential for diagnostic purposes in dental medicine, aiding in the precise imaging of oral diseases.

This dual functionality of therapeutic and diagnostic (theranostic) capabilities positions radioactive AuNPs as a versatile tool in advancing dental health care and personalized treatment strategies. A study published by Zhang *et al*. (2022) [47] highlights the successful application of gold nanoparticles in enhancing the imaging and treatment of oral cancer, underscoring their potential to revolutionize dental oncology.

The synthesis of gold nanoparticles with various geometries is of paramount importance for optimizing their properties and performance in different applications. By tailoring the shape of gold nanoparticles, researchers can exploit their unique optical, catalytic, and biological interactions, leading to significant advancements in medical imaging, therapy, drug delivery, environmental remediation, and biosensing. As nanotechnology continues to evolve, the development of new methods for synthesizing gold nanoparticles with precise geometries will drive innovation and expand their potential applications across diverse fields [48].

Different Types of Radioactive Nanoparticles

In addition to traditional radioactive gold nanoparticles, various advanced types and configurations enhance their therapeutic and diagnostic potential. Radioactive isotope-embedded AuNPs, such as those with Au-198 and Au-199, emit beta and gamma radiation effective for cancer therapy and imaging. Other isotopes like Iodine-131 (I-131) and Rhenium-188 (Re-188) can also be embedded in AuNPs, combining gold's properties with specific radiation characteristics. Multifunctional radioactive AuNPs, like theranostic nanoparticles, integrate therapeutic and diagnostic functions. For instance, AuNPs conjugated with radioactive isotopes can be coated with targeting ligands for simultaneous treatment and imaging. Ultra-small radioactive gold nanoclusters exhibit unique luminescence properties useful in bioimaging and targeted radiotherapy [49].

Surface-functionalized radioactive AuNPs further expand their medical applications. Functionalizing AuNPs with targeting molecules, such as antibodies or peptides, allows them to selectively bind to specific cells, delivering localized radiation therapy while minimizing damage to healthy tissue. Hybrid radioactive nanocomposites, such as gold-silica and gold-iron oxide nanoparticles, provide additional functionalities. Gold-silica nanoparticles combine therapeutic effects with drug or imaging agent delivery, while gold-iron oxide nanoparticles offer radiotherapy, magnetic hyperthermia therapy, and enhanced imaging through magnetic resonance imaging (MRI). These advanced radioactive gold nanoparticles significantly expand their application range, offering innovative solutions for targeted cancer therapy, diagnostic imaging, and multifunctional theranostics [50].

Bioavailability and Toxicity

The bioavailability and toxicity of AuNPs are critical considerations for their therapeutic use. Green synthesis methods using phytochemicals offer biocompatible AuNPs with enhanced bioavailability and reduced toxicity compared to conventional methods. Phytochemicals act as both reducing agents and stabilizers, promoting the formation of stable AuNPs suitable for biomedical applications. Biological synthesis methods involving microorganisms yield AuNPs with low toxicity, enhancing their biocompatibility and therapeutic potential.

Research on the toxicity of gold nanoparticles in humans has provided valuable insights into their biocompatibility and safety profiles. One significant study involved a clinical trial assessing the toxicity and biodistribution of PEGylated gold nanoparticles in cancer patients. The trial demonstrated that AuNPs accumulated primarily in the liver and spleen but were largely non-toxic at the administered doses. Blood tests and liver function tests showed no significant adverse effects, suggesting that PEGylated AuNPs are well-tolerated in humans [51].

Another study focused on inhalation exposure, where healthy volunteers were exposed to aerosolized gold nanoparticles. The results indicated no acute toxicity, with normal respiratory function and no significant changes in blood parameters post-exposure. These findings, corroborated by *in vivo* imaging and post-exposure monitoring, underscore the potential for safely using AuNPs in therapeutic and diagnostic applications, although long-term studies are still necessary to fully understand chronic exposure effects.

Toxicity assessments of AuNPs synthesized using green approaches revealed favorable safety profiles, with minimal adverse effects observed *in vitro* and *in vivo*. Phytochemicals demonstrate excellent biocompatibility and low cytotoxicity, making them promising candidates for therapeutic AuNP synthesis. Furthermore, biological synthesis methods offer eco-friendly alternatives, eliminating the need for toxic chemicals and organic solvents [52].

Conclusions

In conclusion, radiomedicine stands at the forefront of modern healthcare, embodying the innovative integration of nanoparticles to revolutionize disease diagnosis and treatment. Gold nanoparticles, with their remarkable properties of biocompatibility, ease of functionalization, and customizable size, emerge as key players in this transformation. Their ability to precisely target disease sites while minimizing damage to healthy tissues promises a new era of precision and personalized medicine.

The unique capabilities of gold nanoparticles in targeted cancer therapy exemplify their potential. Traditional treatments like chemotherapy and radiotherapy often cause extensive collateral damage, but gold nanoparticles offer a targeted approach, delivering therapeutic agents directly to tumor cells and sparing healthy tissues. This precision not only enhances treatment efficacy but also reduces adverse effects, significantly improving patient outcomes.

Beyond cancer therapy, gold nanoparticles hold versatile applications across various medical fields. In cardiovascular medicine, they offer targeted drug delivery to atherosclerotic plaques, potentially reducing cardiovascular events. In neurology, their ability to cross the blood-brain barrier paves the way for treating neurodegenerative diseases. Moreover, their role in regenerative medicine, diagnostics, and antimicrobial therapy underscores their multifaceted utility.

The synthesis of gold nanoparticles, whether through chemical, physical, or green methods, is crucial for optimizing their properties for specific applications. Green synthesis methods, utilizing phytochemicals and biological approaches, stand out for their environmental friendliness and biocompatibility, presenting a sustainable path forward.

Despite the challenges in translating these advancements from research to clinical practice, such as ensuring nanoparticle stability and navigating regulatory landscapes, the potential benefits are immense. The fusion of nanotechnology with medicine, exemplified by gold nanoparticles in radiomedicine, heralds a future where disease diagnosis and treatment are more precise, effective, and tailored to individual patient needs. As research and technology continue to evolve, the promise of personalized, precision medicine is poised to become a reality, offering new hope and improved outcomes for patients worldwide.

Availability of Data and Materials

All experimental data included in this study can be obtained by contacting the first author if needed.

Author Contributions

LGH, MGD, AS, TC and IIL designed the research study. GC, CDH and CM performed the research. EC and GC analyzed the data. EC and AS supervised and provided help and advice on the drafting process. TC, GC, IIL, AS and CM drafted this manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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