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GOLD NANOPARTICLES: A COMPREHENSIVE REVIEW OF THEIR SYNTHESIS, PROPERTIES AND BIOMEDICAL APPLICATIONS

Deshika Karunanithi[1], Pavithra Ramesh[1], K. Gilbert Tony[1], T. Arasu[1], Bharathi Mohan*[1], Kannabirran Vaikundam[1], Rajalingam Dhakshinamoorthy[1]

[1*]Department of Pharmaceutics, Kamalakshi Pandurangan College of Pharmacy, Ayyampalayam, Tiruvannamalai-606 603, India.

ABSTRACT

Gold nanoparticles have emerged as one of the most versatile and extensively studied nanomaterials in modern medicine and biotechnology. Their unique physicochemical properties-including localized surface plasmon resonance, high biocompatibility and ease of functionalization-have positioned gold nanoparticles at the forefront of nanomedicine. This review provides a comprehensive overview of gold nanoparticles, beginning with their synthesis through physical, chemical and green methods and the wide range of characterization techniques employed to assess their size, shape, crystallinity and surface modifications. Functionalization strategies such as PEGylation, ligand conjugation, and drug or nucleic acid attachment are highlighted as key approaches to enhance therapeutic efficacy and circulation stability. Biomedical applications span drug delivery, imaging, biosensing, photothermal and photodynamic therapies, nucleic acid delivery and antimicrobial interventions. Particular emphasis is placed on translational aspects, including toxicity profiles, biodistribution, regulatory challenges and progress toward clinical trials and commercialization. A comparative perspective against other nanocarrier systems underscores the unique advantages of gold nanoparticles in theranostics. The future directions in personalized nanomedicine, smart and stimuli-responsive gold nanoparticles and their potential integration with artificial intelligence and bioelectronics. Overall, gold nanoparticles represent a promising platform that bridges fundamental nanoscience with transformative clinical applications, though challenges in safety, scalability and regulation remain to be addressed.

KEYWORDS

Gold nanoparticles, Nanomedicine, Drug delivery, Theranostics and Photothermal therapy.

Author for Correspondence:
Bharathi Mohan,
Department of Pharmaceutics,
Kamalakshi Pandurangan College of Pharmacy,
Tiruvannamalai, India.

Email: deshikaruna2003@gmail.com

INTRODUCTION

Nanotechnology has revolutionized medicine by offering innovative tools for diagnosis, therapy, and drug delivery as shown in Figure No.1. Among the various nanomaterials developed, AuNPs have attracted particular attention due to their unique physicochemical and optical properties. Their tunable size, shape and surface chemistry, along

with excellent biocompatibility, make them an attractive platform for applications ranging from drug delivery and molecular imaging to photothermal therapy and biosensing. In recent years, AuNPs have become central to theranostics, where therapeutic and diagnostic modalities are integrated into a single system. This dual capability positions AuNPs as a cornerstone in the advancement of precision nanomedicine.

Gold nanoparticles possess remarkable physicochemical properties, including exceptional stability, low electrical resistance, a high surface-to-volume ratio and excellent conductivity, making them highly suitable for bridging biorecognition systems with signal transduction and for use in advanced biosensing platforms. Their inherent chemical inertness, biocompatibility, and non-toxicity further support their safety and eco-friendliness in medical applications. Importantly, variations in size, shape and surface modifications can significantly influence their sensitivity and selectivity in biological detection.

Gold nanoparticles are nanoscale particles of gold, generally ranging in size from 1 to 100 nanometers, which endows them with unique physical, chemical, and optical properties distinct from bulk gold.They can be synthesized in diverse morphologies such as nanospheres, nanorods, nanoshells, nanoprisms, nanopyramids, nanobipyramids, nanocages, nanorings, nanodisks, nanostars, nanorice, nanobowls, nanoflowers,nanochips,nanoparticles and nanocrescents. Each of these shapes exhibits distinct optical behaviors, including tunable localized surface plasmon resonance (LSPR), variations in light absorption and scattering, enhanced fluorescence, and strong surface-enhanced Raman scattering (SERS), which collectively expand their versatility across diagnostic and therapeutic applications.

The phenomenon of LSPR imparts gold nanoparticles with unique optical properties, including strong light absorption and scattering. These features arise from the collective oscillation of conduction electrons when excited by specific wavelengths of light. Such properties make AuNPs highly attractive for biomedical imaging, biosensing, and photothermal therapy. Their tunable LSPR behavior, governed by size, shape and surface chemistry, further enhances their versatility in nanomedicine.

SYNTHESIS OF GOLD NANOPARTICLES (AuNPs)

Gold nanoparticles (AuNPs) are among the most widely studied nanomaterials due to their unique optical, electronic and catalytic properties. Their applications span biomedicine (drug delivery, imaging, diagnostics), electronics and catalysis. The synthesis method determines particle size, shape, monodispersity, and surface functionality, which in turn governs their properties. They can be synthesized via physical, chemical, or green approaches as shown in Figure No.2.

Physical Methods

Physical routes rely on top-down approaches, breaking down bulk gold into nanoscale particles.

Laser Ablation

Pulsed laser ablation in liquid (PLAL) is a physical technique in which a pulsed laser beam is directed onto a gold target immersed in a liquid medium, causing localized heating and ablation that lead to the ejection of gold atoms or clusters, which subsequently cool and nucleate to form AuNPs. This method offers significant advantages, such as the synthesis of highly pure nanoparticles without the use of chemical reagents and the ability to precisely control particle characteristics by varying laser parameters (wavelength, pulse duration and energy) and the surrounding medium. However, its practical application is limited by high energy consumption and poor scalability, restricting its use for large-scale production.

Sputtering

Argon plasma sputtering is a physical vapor deposition technique in which argon plasma ions bombard a gold target, leading to the ejection of gold atoms that subsequently condense to form nanoparticles either in a liquid medium or on a solid substrate. This method allows the synthesis of highly pure gold nanoparticles with excellent

control over thickness, uniformity and morphology. However, the technique requires sophisticated vacuum equipment and generally produces a relatively low yield, which limits its suitability for large-scale nanoparticle production.

Chemical Methods

Bottom-up synthesis by reducing gold precursors with chemical agents.

Turkevich Method

The Turkevich method involves the reduction of chloroauric acid by trisodium citrate under boiling conditions, leading to the formation of spherical gold nanoparticles with sizes typically ranging from 10 to 20nm. The process is visually indicated by a distinct color change from yellow to blue or gray and finally to a characteristic wine-red hue, signifying nanoparticle formation, while the particle size can be finely tuned by adjusting the citrate-to-gold ratio. In comparison, the Brust–Schiffrin method utilizes a two-phase system consisting of water and toluene, where tetraoctylammonium bromide (TOAB) acts as a phase transfer agent, sodium borohydride serves as the reducing agent, and thiol ligands function as stabilizing agents. This approach produces highly stable gold nanoparticles of 1–5 nm that are soluble in organic solvents, making it particularly suitable for surface functionalization and organic-phase applications.

Seed-Mediated Growth

The seed-mediated growth method involves two main steps: in the first step, small gold seed particles of about 1–3 nm are synthesized, which act as nucleation centers. In the second step, these seeds are introduced into a growth solution containing a gold salt, the surfactant cetyltrimethylammonium bromide (CTAB), and a mild reducing agent, which together promote controlled anisotropic growth. This technique enables the synthesis of gold nanoparticles with various shapes, such as rods, cubes, prisms and stars. Furthermore, the optical properties of the resulting nanoparticles can be tuned by adjusting their aspect ratio, with longer nanorods exhibiting a red-shifted surface plasmon resonance.

Green Synthesis

Eco-friendly methods using biological reducing and stabilizing agents.

Plant Extracts

In the green synthesis method, biomolecules such as polyphenols, alkaloids, sugars, and proteins act as natural reducing and stabilizing agents, facilitating the reduction of gold ions to elemental gold for the formation of AuNPs. Plant extracts from sources such as tea, aloe vera, neem and coffee are commonly used in this environmentally friendly approach. The size and shape of the resulting nanoparticles are influenced by factors including the biochemical composition of the extract, pH, and reaction temperature. This method is not only cost-effective and eco-friendly but also offers good scalability for large-scale nanoparticle synthesis.

Microorganisms

Microbial synthesis of AuNPs utilizes microorganisms such as bacteria, fungi, and algae, which enzymatically reduce gold ions to elemental gold through either intracellular or extracellular mechanisms. In intracellular synthesis, gold ions are reduced within the microbial cells, whereas in extracellular synthesis, secreted enzymes facilitate reduction outside the cells. This biologically driven approach yields highly biocompatible gold nanoparticles; however, it is often limited by slower synthesis rates and challenges in achieving consistent reproducibility.

Control of Size, Shape and Surface Properties

Size Control

The choice of reducing agent plays a crucial role in determining the size and distribution of gold nanoparticles. Strong reducing agents such as sodium borohydride promote rapid nucleation, leading to the formation of smaller nanoparticles, whereas weaker reducing agents like citrate or plant extracts result in slower nucleation and consequently larger particle sizes. Additionally, reaction parameters such as temperature and time significantly influence the size distribution and uniformity of the synthesized nanoparticles.

Shape Control

Surfactants such as cetyltrimethylammonium bromide (CTAB) play a crucial role in directing the anisotropic growth of gold nanoparticles, leading to the formation of various shapes such as nanorods and prisms. The concentration of seed particles significantly influences the degree of branching and structural complexity, while factors like pH and ionic strength further affect the morphology and uniformity of the resulting nanoparticles.

Surface Properties

Surface functionalization of AuNPs is a crucial step in enhancing their stability, biocompatibility and functionality for various applications. Thiol ligands are commonly used to improve nanoparticle stability, while polymers such as PEG enhance biocompatibility and reduce non-specific interactions. Additionally, biomolecules such as antibodies and DNA can be conjugated to the nanoparticle surface to enable targeted delivery and biosensing applications. Furthermore, the surface charge, often represented by the zeta potential, plays a significant role in determining the colloidal stability and cellular uptake behavior of the nanoparticles.

CHARACTERIZATION OF GOLD NANOPARTICLES (AuNPs)

Characterizing AuNPs is essential to confirm their size, shape, crystallinity, surface charge, and stability. Different complementary techniques are typically employed:

UV–Vis Spectroscopy (Surface Plasmon Resonance, SPR)

Gold nanoparticles exhibit strong visible light absorption due to localized surface plasmon resonance, which arises from the collective oscillation of conduction electrons when excited by light. Spherical AuNPs display a characteristic red-wine color, while a red shift indicates particle growth or aggregation and multiple bands appear for anisotropic shapes such as rods. This property provides a rapid and non-destructive way to monitor nanoparticle synthesis, stability, and aggregation behavior.

Dynamic Light Scattering (DLS) and Zeta Potential

DLS (Hydrodynamic Diameter)

Dynamic light scattering measures the Brownian motion of nanoparticles in suspension to determine their hydrodynamic size, which includes the core particle, solvent layer, and any attached surface ligands. This technique is highly sensitive to changes in particle size and is particularly useful for detecting nanoparticle aggregation in colloidal systems.

Zeta Potential

Zeta potential analysis reflects the surface charge at the nanoparticle-liquid interface and serves as an important indicator of colloidal stability. High absolute zeta potential values generally correspond to strong electrostatic repulsion between particles, ensuring good stability, whereas low values indicate weaker repulsion and a higher tendency for nanoparticle aggregation.

Microscopy Techniques (Morphology and Size Distribution)

Transmission Electron Microscopy (TEM)

Transmission electron microscopy provides high-resolution imaging down to the atomic scale, allowing precise determination of nanoparticle size, shape and crystallinity through the observation of lattice fringes. However, the technique requires careful sample preparation, typically involving drop-casting the nanoparticle suspension onto specialized grids.

ii. **Scanning Electron Microscopy (SEM):**

Scanning electron microscopy is used to analyze the three-dimensional surface morphology and larger-scale particle distribution of nanoparticles. Although it offers lower resolution compared to TEM, SEM provides easier and more efficient imaging for bulk surface characterization.

X-Ray Diffraction (XRD)

X-ray diffraction analysis is based on the principle that crystalline AuNPs produce characteristic diffraction peaks corresponding to their face-centered cubic lattice structure. This technique is used to confirm the crystallinity and phase purity of the nanoparticles, while peak broadening in the

diffraction pattern can provide insights into nanoscale crystal size, as described by the Scherrer equation.

Fourier Transform Infrared Spectroscopy (FTIR) and Raman Spectroscopy (Surface Functionalization)

Functionalization of gold nanoparticles with ligands, polymers, or biomolecules is critical for stability, biocompatibility and targeted applications. Vibrational spectroscopy techniques like FTIR and Raman provide direct information about chemical groups attached to AuNP surfaces.

Fourier Transform Infrared Spectroscopy (FTIR)

Fourier-transform infrared spectroscopy operates on the principle that molecules absorb infrared radiation at specific frequencies corresponding to the vibrational modes of their functional groups. In the context of AuNPs, FTIR is widely used to identify surface ligands such as thiols, amines, carboxylates and polymers and to confirm surface functionalization by comparing spectra before and after modification. For example, the disappearance of the –SH stretching band indicates thiol binding to gold, while PEGylation or biomolecule conjugation can be confirmed through the presence of characteristic C–O, N–H, and C=O vibrational modes.

Raman Spectroscopy

Raman spectroscopy is based on the principle of inelastic scattering of monochromatic light, typically from a laser source, which provides a unique molecular fingerprint corresponding to the vibrational modes of surface groups. In gold nanoparticles, it is employed to detect surface-bound molecules through their characteristic vibrational bands and its sensitivity is greatly enhanced by surface-enhanced Raman scattering, where localized plasmon fields of AuNPs amplify the Raman signal. This technique enables ultrasensitive detection of biomolecules, drugs and environmental pollutants and serves as a valuable complement to FTIR spectroscopy, being more responsive to symmetric vibrations and less influenced by water interference.

FUNCTIONALIZATION AND SURFACE MODIFICATION OF GOLD NANOPARTICLES (AUNPS)

Surface modification of AuNPs is crucial for enhancing stability, circulation, biocompatibility, and specificity. Functionalization strategies include coating with polymers, attaching targeting ligands, and conjugating therapeutic molecules. PEGylation prolongs circulation time, while targeting ligands such as antibodies, peptides, folate, or aptamers enable selective delivery to diseased cells. In addition, AuNPs can be conjugated with drugs or nucleic acids for therapeutic applications as shown in Figure No.3.

PEGylation (Polyethylene Glycol Coating)

Polyethylene glycol (PEG) functionalization, or PEGylation, of gold nanoparticles is employed to improve colloidal stability and reduce opsonization, thereby minimizing clearance by the immune system. The presence of PEG chains forms a hydrophilic "stealth" corona around the nanoparticle surface, which prevents protein adsorption and the subsequent formation of a protein corona. This modification enhances biocompatibility, reduces aggregation in physiological media, and significantly increases the blood circulation half-life of AuNPs, making them more suitable for biomedical applications.

Targeting Ligands

AuNPs can be surface-modified with biological recognition elements to achieve active targeting of cancer cells, bacteria, or diseased tissues.

Antibodies (immuno-AuNPs)

Bind specific cell-surface antigens. Used in diagnostics and targeted therapy.

Peptides

Small targeting motifs for receptor-mediated uptake. Example: RGD peptide binds integrins.

Folate

Targets folate receptor, overexpressed in many cancers.

Aptamers

Short DNA/RNA sequences with high binding specificity. Useful for molecular recognition and sensing.

Drug and Biomolecule Conjugation

AuNPs serve as versatile carriers for therapeutics and genetic material:

Chemotherapeutics

Doxorubicin, paclitaxel, cisplatin can be loaded or conjugated to AuNPs that targeted delivery with reduced systemic toxicity.

siRNA/miRNA/DNA

AuNPs protect nucleic acids from degradation and enhance cellular uptake.

Photothermal/Photodynamic agents

Functionalized AuNPs can combine therapy with imaging ("theranostics").

BIOMEDICAL APPLICATIONS OF GOLD NANOPARTICLES (AUNPS)

Due to their unique optical, electronic, and surface properties, AuNPs are widely explored for applications in drug delivery, imaging, diagnostics, therapy, and antimicrobial treatments as shown in Figure No.4.

Drug Delivery

Gold nanoparticles (AuNPs) enable highly controlled and targeted drug release through pH-, enzyme-, or light-responsive mechanisms that ensure precise delivery at disease sites, thereby enhancing therapeutic efficiency. Additionally, functionalized AuNPs have shown the ability to overcome multidrug resistance (MDR) by bypassing cellular efflux pumps and increasing intracellular drug accumulation, offering a promising strategy for improving treatment outcomes in resistant cancers.

Examples

Doxorubicin- or paclitaxel-conjugated AuNPs show enhanced cytotoxicity in resistant cancer cells.

AuNP-drug conjugates can combine chemotherapy with photothermal therapy for synergistic effects.

Imaging and Diagnostics

Gold nanoparticles (AuNPs) offer exceptional versatility in biomedical imaging and diagnostics, with their strong plasmonic scattering making them highly effective for optical imaging techniques such as dark-field microscopy and optical coherence tomography (OCT). Their high atomic number (Z = 79) provides superior X-ray attenuation, positioning AuNPs as promising contrast agents for computed tomography (CT), while functionalization with gadolinium or iron enhances their utility in magnetic resonance imaging (MRI). In diagnostics, AuNPs form the basis of numerous point-of-care biosensors, including colorimetric assays used in pregnancy and COVID-19 rapid tests and their integration into surface-enhanced Raman scattering (SERS) platforms enables ultrasensitive molecular detection across a wide range of applications.

Photothermal and Photodynamic Therapy (PTT/PDT)

Gold nanoparticles (AuNPs) play a central role in light-based cancer therapies, notably in photothermal therapy (PTT), where they absorb near-infrared (NIR) light and convert it into heat to induce localized hyperthermia and selective tumor cell destruction. They also enhance photodynamic therapy (PDT) by serving as carriers for photosensitizers that generate reactive oxygen species (ROS) upon light activation. The combination of PTT or PDT with conventional treatments such as chemotherapy or radiotherapy offers synergistic therapeutic benefits, resulting in improved efficacy and more comprehensive tumor control.

Gene and Nucleic Acid Delivery

Gold nanoparticles (AuNPs) are widely employed as nucleic acid delivery platforms, offering protection for siRNA and miRNA against nuclease degradation while enhancing cellular uptake to achieve effective gene silencing. They also serve as versatile carriers for DNA and mRNA in applications such as CRISPR-based gene editing and mRNA vaccine delivery. These capabilities arise from surface modification with cationic ligands, which enables strong electrostatic binding of nucleic acids and promotes efficient intracellular transport.

Antimicrobial and Antiviral Applications

Gold nanoparticles (AuNPs) exhibit broad-spectrum antimicrobial activity, functioning as potent antibacterial agents by disrupting microbial cell membranes, interfering with essential protein

functions, and inducing reactive oxygen species (ROS) that lead to cell death. In addition to their antibacterial effects, AuNPs also demonstrate significant antiviral potential, where they can inhibit viral attachment, entry, and replication; this has been explored in the context of major viral pathogens such as HIV, influenza viruses and coronaviruses, including SARS-CoV-2 (COVID-19).

TOXICITY AND BIOCOMPATIBILITY OF GOLD NANOPARTICLES (AUNPS)

While gold nanoparticles exhibit promising biomedical potential, their safety profile is influenced by size, shape, surface chemistry and dose. Careful evaluation of toxicity and biocompatibility is essential for clinical translation.

Size- and Shape-Dependent Toxicity

Size

The biological impact of gold nanoparticles (AuNPs) is strongly influenced by their size, with smaller particles (<5nm) capable of penetrating cellular organelles such as the nucleus and mitochondria, where they may induce genotoxic effects and oxidative stress, whereas larger AuNPs (>50nm) exhibit limited intracellular penetration but tend to accumulate within specific tissues, raising concerns regarding long-term biodistribution and retention.

Shape

Nanoparticle shape also plays a critical role in biological interactions, with rod-shaped and sharp-edged AuNPs exhibiting stronger membrane-disruptive effects compared to spherical particles, while spherical AuNPs are generally regarded as more biocompatible due to their smoother geometry and reduced mechanical stress on cellular membranes.

Biodistribution and Clearance

Gold nanoparticles (AuNPs) typically distribute throughout the reticuloendothelial system (RES), with predominant accumulation in the liver and spleen, and their clearance from the body is largely governed by particle size and surface chemistry, which together influence uptake, circulation time and elimination pathways.

Clearance of gold nanoparticles (AuNPs) is highly size-dependent, with ultrasmall particles below 5nm efficiently eliminated through renal filtration, whereas larger AuNPs exceeding 10nm are predominantly cleared via hepatic pathways; additionally, surface coatings play a crucial role in modulating circulation time, biodistribution and organ retention.

Accumulation in Organs

Liver and Spleen

High uptake due to macrophage activity in RES.

Kidneys

Very small AuNPs can cross the glomerular barrier and be excreted in urine.

Brain

Generally low accumulation due to blood–brain barrier (BBB), unless functionalized for CNS targeting.

Strategies to Reduce Toxicity

Surface engineering plays a crucial role in improving the biocompatibility and therapeutic performance of gold nanoparticles (AuNPs), with PEGylation providing a hydrophilic “stealth” layer that reduces immune recognition and protein corona formation, while biodegradable coatings such as chitosan, dextran and other biomolecules enhance clearance and limit long-term tissue accumulation. Furthermore, targeted functionalization using antibodies, peptides, or aptamers helps minimize off-target interactions and careful optimization of dosing and exposure duration is essential to reduce systemic toxicity and ensure safe biomedical application.

INDUSTRIAL AND TRANSLATIONAL ASCEPTS

Gold nanoparticles (AuNPs) have emerged as a promising platform in nanomedicine, owing to their unique physicochemical properties. However, their translation from laboratory research to clinical application involves navigating several industrial, regulatory and clinical challenges.

Regulatory Challenges: FDA and EMA Perspectives

FDA

The U.S. Food and Drug Administration (FDA) has recognized the necessity for specialized regulatory guidance concerning nanotechnology-based products and in 2007, its Nanotechnology Task Force highlighted several key challenges, including limitations in traditional product characterization methods that may not adequately define nanomaterials, the inadequacy of existing safety assessment strategies for evaluating nanoscale behaviors and the broader need for updated regulatory frameworks that reflect the unique physicochemical properties of nanotechnology. The FDA has stated that it will continue to provide additional guidance as needed to address these evolving regulatory considerations.

EMA

The European Medicines Agency (EMA) has similarly recognized the regulatory complexities associated with nanomedicines and its Horizon Scanning initiative has identified several pressing challenges, including difficulties in defining and categorizing nanomedicines within existing regulatory frameworks, the need for dedicated guidelines to ensure appropriate assessment of their safety and efficacy and the requirement for clearer, nanotechnology-specific approval pathways. In response to these concerns, the EMA continues to work toward developing robust and comprehensive regulatory frameworks tailored to the unique characteristics of nanomedicines.

Scale-Up and Reproducibility Issues

Scaling up the production of gold nanoparticles (AuNPs) from laboratory research to industrial manufacturing presents significant challenges, as many synthesis methods optimized for small-scale experiments do not readily translate to high-volume production, making it difficult to maintain uniformity in particle size, shape and surface characteristics across batches. Additionally, achieving regulatory compliance, particularly with Good Manufacturing Practice (GMP) standards for nanomaterials, adds further complexity. Overcoming these obstacles will require the advancement of scalable synthesis technologies and the establishment of rigorous quality control systems to ensure consistency, safety and reliability in large-scale AuNP production.

Current Patents and Commercial Products

A growing number of patents and commercial products reflect the expanding applications of gold nanoparticles (AuNPs), including innovations focused on medicinal preparations that incorporate AuNPs with chemically bound targeting or modifying agents to enhance therapeutic performance. In addition, several commercial formulations using AuNPs are currently in development, particularly within drug delivery and diagnostic imaging. Overall, the landscape of AuNP-related patents and products is rapidly evolving, driven by ongoing research and technological advancement in the nanomedicine field.

Clinical Trials Involving AuNPs

Clinical trials have increasingly investigated the therapeutic potential of gold nanoparticles (AuNPs) across a range of medical conditions, including cancer therapy, where they have been evaluated for targeted drug delivery and photothermal treatment; neurological disorders such as multiple sclerosis and Parkinson's disease, where their neurotherapeutic applications are being explored; and vaccine delivery, where AuNPs are studied for their ability to enhance immune responses.

FUTURE PROSPECTS OF GOLD NANOPARTICLES (AUNPS) IN THERANOSTICS

Personalized Nanomedicine and Precision Oncology

Gold nanoparticles (AuNPs) offer significant promise in personalized cancer therapy, as their size, shape, and surface chemistry can be precisely tailored to match patient-specific tumor characteristics. Functionalization with targeting ligands such as antibodies, aptamers and peptides enables high selectivity and accumulation within cancer tissues, thereby reducing systemic toxicity

and enhancing therapeutic efficacy. Moreover, AuNPs can be engineered to respond to biomarker-defined molecular signatures, supporting the development of biomarker-driven and highly individualized oncology treatments.

Theranostic AuNPs (Dual Diagnostic and Therapeutic Use)

Gold nanoparticles (AuNPs) uniquely integrate diagnostic and therapeutic capabilities, combining imaging modalities such as CT, photoacoustic imaging and SERS with therapeutic approaches including photothermal therapy, photodynamic therapy and radiosensitization. Current advancements focus on developing single-platform nanosystems that enable real-time monitoring of drug delivery and treatment response, while the incorporation of multimodal imaging agents-including MRI contrast materials, fluorescent probes and PET tracers-onto AuNP surfaces provides comprehensive and highly precise disease mapping.

Smart / Stimuli-Responsive AuNPs

Stimuli-responsive gold nanoparticles (AuNPs) are emerging as advanced platforms for controlled and site-specific drug delivery, with pH-sensitive systems leveraging the acidic tumor microenvironment to achieve localized release and temperature-responsive AuNPs enabling externally triggered activation through near-infrared-induced photothermal heating. Enzyme-sensitive formulations further enhance precision by responding selectively to tumor-associated enzymes such as matrix metalloproteinases (MMPs) and cathepsins, ensuring drug activation only at diseased sites. Additionally, multi-stimuli-responsive designs that integrate pH, redox and thermal triggers offer superior control, improved therapeutic efficiency, and enhanced safety in complex biological environments.

Integration with Emerging Technologies

Artificial Intelligence (AI)

Artificial intelligence is increasingly transforming the development of gold nanoparticle (AuNP) therapeutics, with AI-driven design approaches enabling precise optimization of particle size, shape, and ligand density for enhanced performance. Machine learning models further contribute by predicting biodistribution, toxicity profiles and therapeutic outcomes, thereby accelerating the design of safer and more effective AuNP-based nanomedicines.

Nanorobotics

Gold nanoparticles (AuNPs) are increasingly being explored as integral components of nano-robotic systems engineered for guided navigation toward tumor sites, with emerging designs incorporating magnetic or optical control mechanisms to enable highly precise, site-specific therapeutic delivery.

Bioelectronics

Emerging hybrid systems integrate gold nanoparticles (AuNPs) with wearable or implantable biosensors, creating platforms capable of continuous health monitoring and responsive therapeutic action. These technologies offer the potential for real-time disease tracking and on-demand activation of treatment, marking a significant step toward fully responsive, patient-centered nanomedicine.

COMPARATIVE PERSPECTIVE OF NANOCARRIERS

S.No	Feature	Physicochemical Properties	Drug/Gene Delivery	Imaging/ Diagnostics	Therapeutic Functions	Unique Advantages
1	Gold Nanoparticles (AuNPs	Tunable size/shape, strong surface plasmon resonance (SPR), high stability	Surface conjugation of drugs, peptides, siRNA, DNA, antibodies	Intrinsic optical/electronic properties; strong contrast in CT, photoacoustic imaging, SERS	Active role: Photothermal therapy (PTT), photodynamic therapy (PDT), radiosensitizers	Dual theranostic role (diagnosis + therapy), multimodality
2	Liposomes	Biocompatible can carry both hydrophilic and hydrophobic drugs, prone to leakage/fusion	Encapsulation of drugs (e.g.,Doxil®), limited Targeting without Modification	Require external contrast agents	Passive carriers; depend on loaded drug	Clinically mature, Biocompatible, widely
3	Polymeric Nanoparticles	Versatile chemistry, Biodegradable, controlled release possible	Good for hydrophobic drugs, sustained release	Require external contrast agents	Passive carriers; depend on loaded drug	Controlled drug release, diverse polymers
4	Lipid Nanoparticles (LNPs)	Excellent carriers for nucleic acids, require optimized stability	Efficient for mRNA/siRNA delivery, widely used in vaccines	Require external contrast agents	Passive carriers; mainly for gene delivery	Highly efficient for nucleic acids, rapid clinical

Figure No.1: Conceptual overview of nanotechnology in medicine

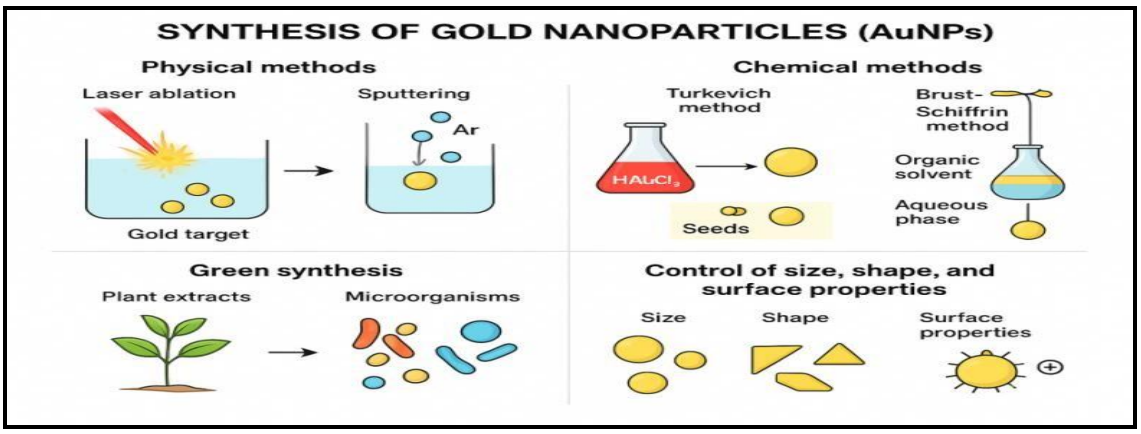

Figure No.2: Schematic overview of physical, chemical and green synthesis routes of gold nanoparticles, and factors influencing their properties

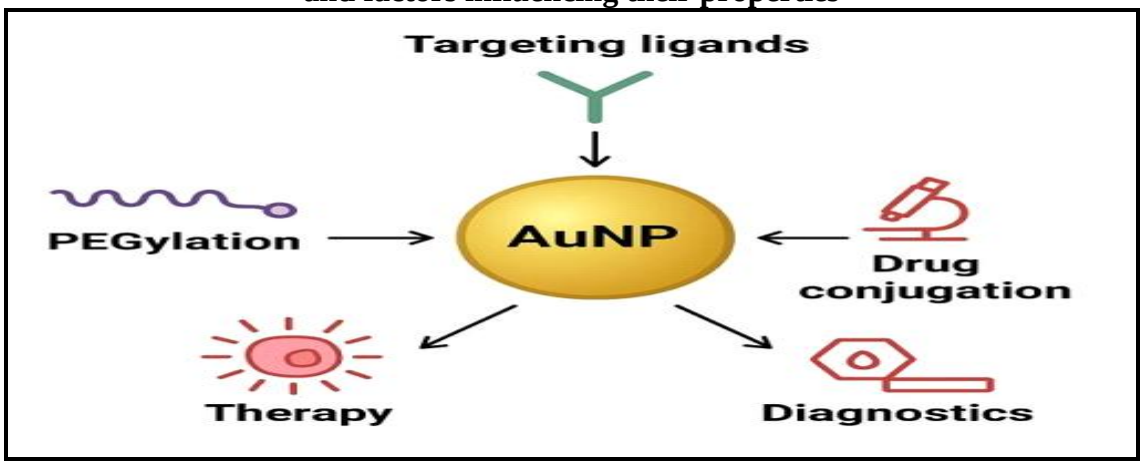

Figure No.3: Functionalization strategies for gold nanoparticles, including PEGylation for stability, targeting ligands (antibodies, peptides, folate, aptamers) for specificity and conjugation of drugs or nucleic acids for therapeutic applications

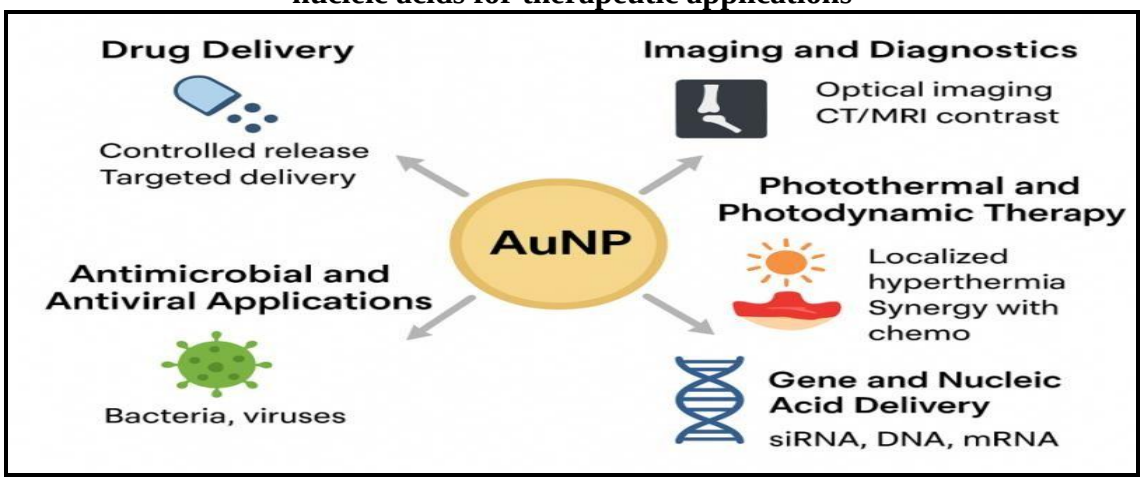

Figure No.4: Biomedical applications of gold nanoparticles (AuNPs), including drug delivery, imaging and diagnostics, photothermal and photodynamic therapy (PTT/PDT), gene and nucleic acid delivery and antimicrobial/antiviral applications

CONCLUSION

Gold nanoparticles represent a distinctive class of nanomaterials that bridge the gap between diagnostics and therapeutics. Unlike conventional nanocarriers such as liposomes, polymeric nanoparticles and lipid nanoparticles, AuNPs serve not only as drug or gene delivery vehicles but also as active agents in imaging, photothermal therapy, photodynamic therapy and radiosensitization. This dual capability firmly establishes them as true theranostic platforms.

Over the past decade, advances in synthesis, functionalization and biomedical applications have highlighted the immense potential of AuNPs in precision oncology and personalized nanomedicine. Their surface versatility allows for targeted delivery, while their unique optical and electronic properties enable real-time monitoring of therapeutic response. Furthermore, the development of stimuli-responsive AuNPs and their integration with AI, nanorobotics, and bioelectronics signal a future where cancer therapy is smarter, more adaptive and patient-specific.

Nonetheless, challenges remain. Concerns about long-term toxicity, biodistribution, clearance, and regulatory approval must be addressed to ensure safe and effective clinical translation. Large-scale reproducibility and standardized protocols are also essential to move AuNPs from bench to bedside.

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ABBREVIATIONS

AuNPs: Gold Nanoparticles; LSPR: Localized Surface Plasmon Resonance; SERS: Surface-Enhanced Raman Scattering; PLAL: Pulsed Laser Ablation in Liquid; TOAB: Tetra Octyl Ammonium Bromide; CTAB: Cetyl Trimethyl Ammonium Bromide; PEG: Poly Ethylene Glycol; SPR: Surface Plasmon Resonance; DLS: Dynamic Light Scattering; TEM: Transmission Electron Microscopy; SEM: Scanning Electron Microscopy; XRD:X-Ray Diffraction; FTIR: Fourier Transform Infrared Spectroscopy; RGD: arginine-glycine-aspartic acid; PTT/PDT: Photothermal and Photodynamic Therapy; CRISPR: Clustered regularly interspaced short palindromic repeats; SARS Cov2: Severe acute respiratory syndrome coronavirus 2; siRNA/miRNA: Small interfering RNA/microRNA.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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