An In-Depth Review of Gold Nanoparticle Applications in Healthcare and Environmental Sustainability

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Abstract:

Nanotechnology has achieved significant progress through the creation of functional, engineered nanoparticles within the nanoscale range of 1-100 nm. These minuscule particles are transforming various fields, such as medicine and electronics, by providing innovative solutions to complex problems. In nanomedicine, the use of nanomaterials has shown considerable advantages in treatment procedures, offering new curative effects and perspectives for tackling various diseases. The swift advancement of nanoscale delivery systems has facilitated their application in diagnosis and targeted drug delivery with controlled and monitored precision. Gold nanoparticles (AuNPs) are particularly well-suited for biomedical applications due to their ease of synthesis, stability, customizability, low toxicity, and ease of detection. These characteristics make AuNPs a promising tool for early disease detection, diagnosis, and treatment, especially in medical imaging, drug delivery, and cancer therapy. This article examines recent research on the use of gold nanoparticles as drug delivery systems in medicine and targeted drug delivery

Keywords: Gold Nanoparticles, Drug Delivery, Nanomedicine, Biomedical Applications, Environmental Sustainability.

Introduction:

Nanotechnology is a rapidly growing field that employs nanoscale materials for various therapeutic and diagnostic applications. "Nanoparticle" refers to particles sized between 1 and 1000 nm. It's important to note that the natural world includes a wide variety of chemicals and species at the nano meter scale. Gold nanomaterials come in several forms, including nanoparticles, nanocages, nanorods (AuNRs), nano stars, nanoshells, and nanoplates[1].

Gold exhibits unique optical properties at the nanoscale, causing it to turn purple due to size-related changes. Gold nanoparticles have remarkable attributes, including ease of synthesis, controlled size, specific surface plasmon resonance, and excellent biocompatibility, making them highly promising for treating various diseases. Targeted drug delivery is a precise

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system that directs drugs to specific areas of the body, such as organs, cellular, or subcellular levels of particular tissues.

This system mitigates the non-specific toxic effects of traditional drug delivery methods, thereby reducing the required dosage for therapeutic effectiveness. These systems enable targeted, controlled, and sustained drug delivery to meet precise therapeutic needs. Nanotechnology-based drug delivery systems can achieve targeted delivery to tumors, marking a significant advancement [2]. They offer controlled drug release, allowing sufficient time for the drugs to act with enhanced therapeutic effects and respond to specific stimuli like pH, light, heat, or enzymes. Recently, gold nanoparticles (AuNPs) have been revolutionizing drug delivery systems by providing efficient transport and release of pharmaceuticals across various cell types.

Characteristics of Gold Nanoparticles

- Gold nanoparticles are chemically inert, meaning they do not readily undergo chemical reactions or get affected by external environmental factors.
- Additionally, gold nanoparticles exhibit superior biological compatibility compared to other metallic nanoparticles. This makes them particularly suitable for various biomedical applications, such as drug delivery and medical imaging.
- Gold nanoparticles have unique optical properties, such as plasmon resonance, making them highly attractive for applications in sensing, imaging, and cancer therapy.
- Gold nanoparticles are highly versatile because they can easily be functionalized with thiol linkages, enhancing their effectiveness in biological applications.
- Gold nanoparticles accumulate in cancer cells and demonstrate cytotoxic effects, making them a promising candidate for cancer therapy.
- The photophysical properties of gold nanoparticles enable drug release at distant sites, positioning them as a promising option for targeted drug delivery applications.

Types of Gold nanoparticles

Gold nanoparticles can be classified into various subtypes based on their size, shape, and physical characteristics

Gold Nanospheres: These were among the first gold nanoparticles to be extensively studied. While not perfectly spherical, they exhibit a vibrant red color due to their interaction with visible light. The surface plasmon resonance (SPR) phenomenon causes them to absorb blue-green light (~450 nm) and reflect red light (~700 nm), especially noticeable in small, monodisperse gold nanoparticles (around 30 nm in size). As the particle size increases, the SPR wavelength shifts towards longer, redder wavelengths, resulting in varying colors [3].

Gold Nanorods: These elongated nanoparticles possess anisotropic shapes. Their surface plasmon resonance (SPR) properties can be adjusted by varying their aspect ratio, allowing them to absorb and reflect different wavelengths of light. Nanorods are widely utilized in biomedical applications and imaging.

Gold Nano cubes: These are gold nanoparticles shaped like cubes. Their surface plasmon resonance (SPR) properties are influenced by the edge length of the cube, allowing for customized optical characteristics.

Gold Nanoshells: Nanoshells consist of a core-shell structure, featuring a dielectric core enveloped by a thin layer of gold. Their surface plasmon resonance (SPR) properties can be tailored by adjusting both the size of the core and the thickness of the gold shell.

Gold Nanowires: These elongated nanoparticles resemble wires and exhibit intriguing electronic and optical properties. They find applications in various fields, including sensors and photodetectors [4].

Gold Nanocages: Nanocages feature hollow interiors and a structure resembling a cage. They are employed in drug delivery and imaging applications owing to their substantial surface area.

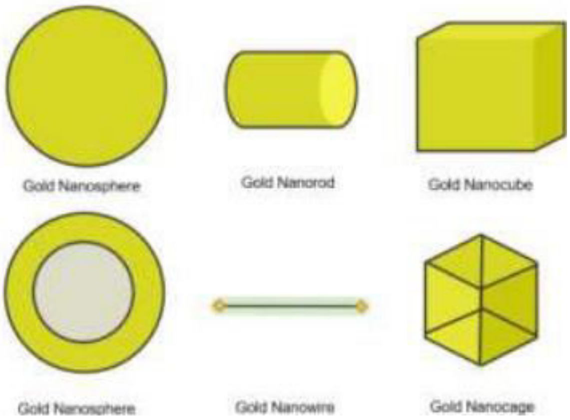

Figure 1: Various Shapes of Gold Nanoparticles

Methods for Gold Nanoparticle Synthesis

Chemical Methods: The Turkevich method is a straightforward and efficient approach for producing monodisperse spherical AuNPs suspended in water. Typically yielding nanoparticles with diameters around 10-20 nm, this method involves the reduction of hydro chloroauric acid (HAuCl4) in the presence of a stabilizing agent. The process includes rapidly agitating the solution and adding a reducing agent after HAuCl4 dissolves, converting Au3+ ions to neutral gold atoms [5].

In contrast, the Brust method synthesizes AuNPs in organic solvents that are typically immiscible with water, such as toluene. This method is particularly advantageous when AuNPs are needed to be dispersed in an organic solvent rather than in water for specific applications [6].

Seeded Growth Method: The seeded growth method is widely favoured for producing AuNPs in various nanostructures such as rods, cubes, and tubes.

Physical Methods: The γ-irradiation method has been identified as optimal for synthesizing AuNPs with controllable size and high purity. This method is utilized to produce AuNPs ranging in size from 2 to 40 nm. The γ-irradiation process is highly effective for creating AuNPs with precise control over their size and maintaining high purity [7].

Biological Methods: To expand the biological applications of AuNPs, it is essential to develop environmentally-friendly technologies. Microbial biosynthesis of AuNPs is regarded as a safe, clean, non-toxic, and environmentally sustainable approach, often referred to as 'green chemistry.

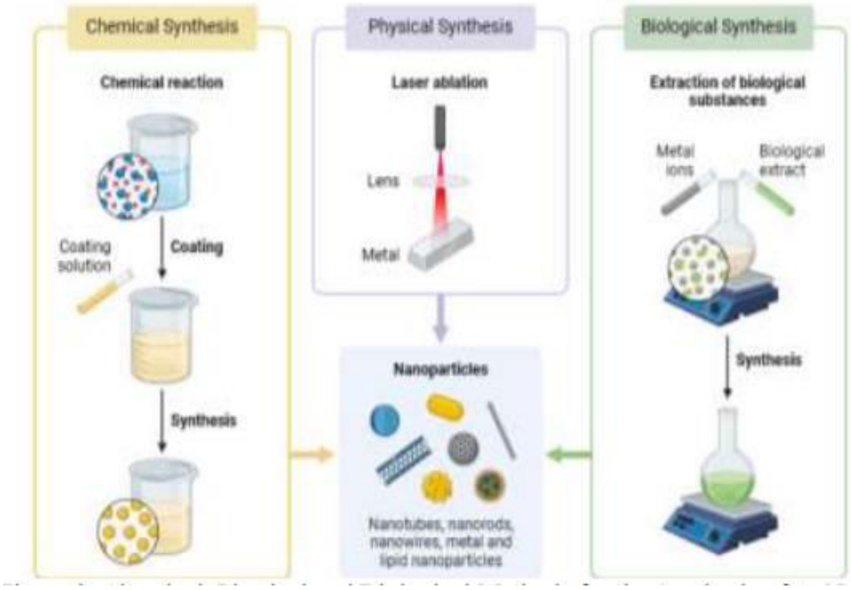

Figure 2: Methods for Synthesizing AuNPs - Chemical, Physical, and Biological Approaches

Applications of Gold Nanoparticles

The Use of Gold Nanoparticles in Oncology

Gold nanoparticles have emerged as crucial tools in oncology owing to their distinctive physical and chemical properties. Their localized surface plasmon resonance (LSPR) is particularly advantageous for numerous applications. AuNPs are investigated as carriers for drugs, enhancing the precision of therapies [8]. They provide stability and surface versatility, essential for targeted drug delivery. Additionally, they are employed to augment the immune system's capability to identify and eradicate cancer cells. AuNPs contribute to overcoming challenges such as dosage limitations and adverse immune responses.

The Use of Environmentally Friendly Gold Nanoparticles in Cancer Therapy and Diagnosis

The adoption of biologically derived precursors in AuNP synthesis has introduced promising avenues for sustainable and environmentally friendly production methods. Green synthesis involves utilizing natural sources like plants, microorganisms, or algae to produce AuNPs, thereby avoiding the use of hazardous chemicals. Plants such as Medicago sativa (alfalfa), Olax scandens, H. ambavilla, and H. lanceolatum have been successfully employed in the synthesis of AuNPs. These plant-based precursors offer a sustainable and plentiful source of raw materials [9].

Gold Nanotechnology and Its Applications in Renewable Energy

Gold nanoparticles exhibit efficient absorption of visible and infrared light owing to their localized surface plasmon resonance (LSPR) [10]. This characteristic enables them to catalyze reactions in conjunction with titanium dioxide (TiO2), facilitating electron transfer upon light absorption. The process is outlined as follows:

- Light Absorption: AuNPs absorb light, causing electrons to transition to higher energy states.
- Electron Transfer: These energized electrons can then transfer to TiO2, a semiconductor material.
- Hydrogen Production: The electrons within TiO2 participate in chemical reactions that split water molecules (H2O) into hydrogen (H2) and oxygen (O2), a process known as photocatalytic water splitting.

The research conducted by Ramesh Asapu et al. focuses on coating AuNPs with TiO2 and subjecting the composite material to different light sources. This pioneering method has demonstrated the generation of electrons capable of producing hydrogen from water, highlighting its potential as a clean fuel alternative

Gold Nanoparticles as Biosensors for Detecting Cancer Biomarkers

Gold nanoparticles (AuNPs) have been employed in detecting single-nucleotide polymorphisms (SNPs), the most prevalent type of genetic variation among individuals. Each SNP signifies a change in a single DNA nucleotide, such as replacing cytosine with thymine within a DNA segment. These variations can lead to persistent activation of specific genes and potentially result in mutations.

Two main methods used for genome variation detection are Resonant light scattering (SERS) and single-strand DNA-AuNP hybridization. In SERS, AuNPs enhance the Raman signal of nearby molecules when close to a surface, enabling sensitive detection. Alternatively, AuNPs functionalized with single-stranded DNA can hybridize with complementary sequences, facilitating the identification of specific genetic variations.

For instance, the MutS protein, which recognizes mutations in the KRAS gene critical for cell division regulation, can be combined with MutS-AuNPs (MutS protein-bound gold nanoparticles) and sequence hybridization. This sophisticated approach utilizes microcantilever resonator technology to detect DNA sequence mismatches, leveraging the MutS protein's high affinity for these variations.

AuNPs serve as a robust platform for SNP detection, and their integration with MutS protein and sequence hybridization holds significant promise for advancing personalized medicine and cancer diagnostics.

Biomedical Applications of Gold Nanoparticles in Lung Cancer Treatment

Lung cancer is the most prevalent cancer worldwide and the leading cause of cancer-related deaths. Conventional therapies for lung cancer suffer from drawbacks such as low bioavailability and non-specific drug release, leading to various side effects. Gold nanoparticles (AuNPs) play a significant role in addressing these challenges in lung cancer treatment. Their unique properties, including tunable nano size, enhanced drug bioavailability and site-specific delivery, high biocompatibility, stability against oxidation in vivo, and interaction with visible light, make them ideal carriers for biomedical applications in lung cancer. AuNPs enable improved early-stage tumor detection and offer advantages over conventional techniques by combining multiple imaging modalities. Their exceptional optical properties enhance the clarity of complex images.

Hyaluronic acid (HA) is a key component of the extracellular matrix found in various tissues. Its biocompatibility, biodegradability, and non-toxic nature make it highly suitable for drug delivery systems. HA can target tumor cells by binding to the CD44 receptor, which is often overexpressed in cancer cells. This targeted approach helps distinguish between healthy and malignant tissues, thereby minimizing off-target effects.

Gold nanoparticles (GNPs) encapsulated with HA can function as active targeting drug delivery nanocarriers. The unique optical properties and chemical stability of GNPs make them ideal for modification and use in drug delivery applications. HA-modified GNPs are particularly beneficial for treating breast cancer. Research by Chao-Ping Fu et al. has demonstrated that HA encapsulated in gold nanoparticles serves effectively as an active targeting drug delivery system for breast cancer treatment. This approach has the potential to enhance treatment outcomes by providing more efficient and targeted therapy with reduced side effects.

Gold Nanoparticles: Design for Drug Delivery and Application in Cancer Immunotherapy

Cancer immunotherapy aims to enhance the body's immune response against cancer cells. Gold nanoparticles (AuNPs) offer an effective means to deliver immunotherapeutic drugs due to their low toxicity, high stability, efficient cellular uptake, and excellent optical properties. AuNPs can accumulate in tumor tissues via the Enhanced Permeability and Retention (EPR) effect, which enables larger particles to penetrate the leaky vasculature of tumors. Drugs can bind directly to the surfaces of AuNPs through covalent or non-covalent interactions. Additionally, the surface of AuNPs can be modified with various molecules to optimize drug delivery and enhance therapeutic efficacy.

Modifiers such as antibodies, aptamers, carbohydrates, and other ligands are used for targeted delivery, specifically recognizing signals associated with tumors. This ensures that drugs are delivered directly to cancer cells, minimizing impacts on healthy cells. Research has underscored the design of AuNPs for drug delivery and their application in cancer immunotherapy, highlighting their role in enhancing precision therapies.

Applications of nanoporous gold in drug delivery

Nanoporous gold (np-Au), synthesized through dealloying, shows considerable potential for drug delivery applications. Its porous structure offers a high surface-to-volume ratio, enabling greater loading capacity for therapeutic agents. The material's ability to easily adjust shape and size, along with its compatibility for modification by organic molecules including drugs, underscores its promising characteristics. Moreover, np-Au nanostructures can generate a photothermal effect, which can be utilized to locally destroy cancer cells through heat or for controlled release of therapeutically important drugs.

Porous structures like np-Au are highly effective in pharmaceutical applications for drug delivery and release due to their significant surface-to-volume ratio. Biomedical device coatings made from np-Au have demonstrated promising results in delivering therapeutics, leveraging the porous structure of np-Au to enhance the loading capacity of small-molecule drugs and proteins with sustained release kinetics.

Gold Nanoparticles for Vaccine Delivery

Vaccination is a critical global health measure that has effectively prevented diseases such as smallpox, polio, and measles, saving numerous lives worldwide. While traditional vaccines have proven highly effective, challenges in production and distribution can limit accessibility to certain populations. Gold nanoparticles (Au NPs) have emerged as promising platforms for vaccines due to their unique properties. They offer potential advantages over traditional methods, opening new avenues for research and development in vaccination.

Joseph D. Comber has reviewed the use of Au NPs in vaccine delivery, highlighting recent advancements in Au-NP vaccine formulations. Nanoparticles of varying shapes and sizes are being tailored to target specific internal compartments within antigen-presenting cells. This targeted approach aims to enhance vaccine efficacy by precisely delivering antigens and their epitopes to these compartments.

This innovative strategy represents a multifaceted solution to vaccine design, revolutionizing the field by offering a more effective and targeted delivery method.

Challenges and Prospects

While green synthesis presents advantages, challenges persist, including the need to optimize synthesis conditions, ensure reproducibility, and address variations stemming from plant species and growth conditions. Ongoing research in this area aims to enhance the stability, specificity, and clinical applicability of gold nanoparticles (AuNPs) for cancer diagnosis and therapy. The absorption, metabolism, distribution, and excretion of these nanomaterials are influenced by their physical and chemical properties, underscoring the importance of meticulous control during synthesis. Researchers are exploring methods to improve the stability, scalability, and reproducibility of biogenic synthesis approaches.

Conclusion and Future Perspectives

The concept of drug targeting traces back to histochemical staining in the late 19th century. Paul Ehrlich's 1911 publication on "Chemotherapy Theory and Practice" marked the inception of targeted drug delivery, famously termed the "Magic bullet." Over time, drug targeting has advanced to encompass onco-protein-specific and onco-targeted drugs, integrating anticancer agents with antibodies, culminating in the current era of nanoparticle-based targeted drug delivery. Gold nanomaterials have been a subject of intensive study for more than two decades, prized for their versatile applications in biology, optics, magnetism, electronics, and catalysis. Their facile synthesis and ability to tailor size and shape have spurred numerous innovations in nanotechnology and nanoscience. Looking ahead, it's crucial to address environmental concerns associated with these particles, ensuring that their benefits outweigh any potential drawbacks. This field holds immense promise for future breakthroughs and innovations.

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