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Review Article

Overview on Gold Nanoparticles

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ABSTRACT

Due to their versatility and distinctive qualities, gold nanoparticles (AuNPs) have a variety of biomedical uses in the diagnosis and treatment of disease, including targeted chemotherapy and pharmaceutical drug delivery. Due to their simplicity in synthesis, stability, and functionalization, low toxicity, and simplicity in detection, gold nanoparticles (AuNPs) are a natural choice for biomedical applications. The synthesis of AuNPs has been carried out using a variety of chemical techniques over the past few decades, but more recently, emphasis has been drawn to more contemporary environmentally friendly green technologies. GNPs have drawn interest for a variety of uses, mostly in therapy and diagnosis. They are effective and a reliable biological platform due to their simplicity in synthesis and compatibility with different functionalizing ligands. GNPs have been widely employed as antiviral, antibacterial, and anticancer medicines because of their versatility in synthesis and functionalization. We present the advancing trends in the use of monodisperse AuNPs for diagnostic and therapeutic applications in this review, with an emphasis on the research successes and future potential in this area. All of the physiological processes in the human body can be conjugated using AuNPs. Given the complexity of cancer cells and the lack of proper dispersion of chemotherapeutics in the usual drug administration method, many nanomaterials tactics have been employed to boost tumour selectivity, therapeutic index, and anticancer activity. Recent research has shown that AuNPs are easily changed to enable direct drug delivery to the target region.

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INTRODUCTION

Innovative research in the field of nanotechnology has made it possible to significantly advance diagnostic and therapeutic medicine. It has been investigated how organic nanomaterials like liposomes and extracellular vesicles can be used, as well as inorganic nanoparticles like gold and silver. Medical nanotools offer a precise, adaptable, flexible, and economical solution to a variety of medical applications. Following the identification of the extraordinary features that made gold nanoparticles (GNPs) preferable to other nanoforms, a particular interest in these particles arose. In comparison to other nanomaterial, gold has a number of benefits, such as simplicity of production, customizable size/shape, biocompatibility, low toxicity, and surface modifiability [1].

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The preferred material for fans of Nano science has been gold. Importantly, these alterations may be investigated using the most basic techniques found in every laboratory that conducted GNP research all over the world. Applications of GNPs have captured the interest of researchers in the information age [2], much as gold has fascinated knowledge-seekers from prehistoric times.

In recent years, there has been significant advancement in the creation and study of nanomaterial with a focus on biological and biomedical applications. Man has been looking for miraculous treatments for ailments and injuries for generations. Numerous scholars think that using nanotechnology in medicine may be the first "giant step" humanity takes in that direction. The study of incredibly small structures, ranging in size from 0.1 to 100nm, is known as nanotechnology. "Nano" refers to an extremely small or miniature size. By manipulating individual atoms, molecules, or compounds into structures, nanotechnology

creates materials and gadgets with unique qualities. The design and study of nanomaterial for use in biomedical applications such as diagnosis, treatment, surgery, and other disorders has advanced significantly in recent years [2, 3].

Biomedical

In China, gold was used to treat conditions like measles, skin ulcers, and smallpox. In Japan, adding tiny gold foils to food, sake, and tea was thought to be good for your health. Traditional ayurvedic remedies are still widely utilised in Bangladesh, Pakistan, and India, with gold being consumed annually as a "rejuvenator" by millions of people.

Medicine

The potential of microscopic gold nanoparticles to concentrate particularly in a cancerous tumour by passing through the naturally leaky blood arteries linked to a tumour has lately been exploited by new technologies. There is a way to deliver a potent anticancer chemical coupled to a gold nanoparticle precisely and directly to a tumour while avoiding healthy tissues around it when it is injected into a patient. A significant advancement in the treatment of cancer, reducing side effects including lowered immunity and hair loss, is thought to have been made by the development of such an efficient drug delivery system with low toxicity [3].

The three valence states of gold are Au0, Au+, and Au3+, and it was the first metal element to be analysed. Au0, or natural gold, is the most prevalent type of gold in the world. As a result, a variety of fields have made extensive use of both gold blocks and gold nanoparticles. In line with the qualities of gold, gold nanoparticles are likewise among the most stable substances. The stability and low resistivity of gold, as well as the good conductivity and thermal conductivity of silver, have drawn attention in the field of noble metal nanomaterial. Michael Faraday proposed the Faraday-Tindall effect in 1857, which states that gold particles can deflect light. They each have unique properties when it comes to creating different nanostructures, researching the behaviour of solitary particles, examining associated electrical, optical, and magnetic properties (the quantum size effect), and using them in biology and catalysis. Therefore, there has been a lot of interest in doing in-depth research on the production, assembly, characteristics, and applications of gold nanoparticles. The domains of biosensor, bio-imaging, medical diagnosis, and treatment have successfully utilised the superior biocompatibility, low toxicity, and tunable stability. For the photo-thermal therapy of cancer, even nanoparticles functionalized with polyethylene glycol have been employed [4].

Characteristics of Gold Nanopartecles

Technically, the top down technique and bottom up approach are employed to synthesize nanoparticles. The top-down strategy focuses on particle size reduction through physical and chemical processes to create nanoparticles. Throughout the procedure, the size, shape, general physiochemical characteristics, and surface structure are treated. Atomic and molecular level engineering is covered by the bottom-up method. Numerous methods are used to characterize nanoparticles of various sizes, shapes, and surface areas, including ultraviolet-visible spectroscopy (UV-vis), powder X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR), gas chromatography mass spectrometry (GC-MS), high performance liquid chromatography (HPLC), energy dispersive spectroscopy (EDS), dynamic light scattering (DLS), Zeta potential.

Many optical and physical techniques can be used to describe functionalized GNPs. The unique size, shape, morphology, and colloidal stability of GNPs are primarily responsible for their distinctive optical and physical features. Therefore, thorough characterization using a variety of methodologies is crucial for maintaining the quality of the synthesized nanoparticles [5].

Ultraviolet-Visible Spectroscopy

One of the quite popular techniques for characterizing the localised surface plasmon resonance (LSPR), which is the phenomenon of resonant oscillation of conduction electrons on a metal surface brought on by incident light, is ultraviolet-visible (UV-VIS) spectroscopy.

Dynamic Light Scattering

An easy and nondestructive method for figuring out the hydrodynamic size distribution of GNPs as well as for describing GNP aggregation or agglomeration is dynamic light scattering (DLS).

Other Methods

For the investigation of the hydrodynamic radius and diffusion coefficient of biopharmaceuticals (such as therapeutic antibodies, peptides, and

proteins), Taylor dispersion analysis (TDA) is thought to be a useful technique. To characterize gold nanoparticles, TDA has been used to estimate the hydrodynamic diameter and diffusion coefficient of the nanoparticles with little sample preparation [6].

Classification and Type of Gold Nanoparticles

A] Classification of Nanomaterials Based On Material- Based Categories

Carbon-Based Nanomaterials

These NMs typically have carbon content and can take the form of spheres, ellipses, or hollow tubes. The group of carbon-based NMs consists of fullerenes (C60), carbon nanotubes (CNTs), carbon nanofibers, carbon black, graphene (Gr), and carbon onions. With the exception of carbon black, the main production techniques for these carbon-based compounds include laser ablation, arc discharge, and chemical vapour deposition (CVD).

Inorganic-Based Nanomaterials

Metal and metal oxide NPs and NSMs are among these NMs. These NMs can be synthesized into ceramics, metal oxides, semiconductors, such as silicon, and metal NPs, such as Au or Ag.

Organic-Based Nanomaterials

These include NMs that are mostly composed of organic material, as opposed to carbon- or inorganic-based NMs. The self-assembly and design of molecules with the aid of noncovalent (weak) interactions enables the transformation of organic NMs into desirable structures including dendrimers, micelles, liposomes, and polymer NPs.

Composite-Based Nanomaterials

Composite NMs are multiphase NPs and NSMs having one phase on the nanoscale dimension. They can either combine NPs with other NPs or NPs with larger or bulkier materials (for example, hybrid nanofibers) or more complex structures, like metalorganic frameworks. Any combination of carbon-, metal-, or organic-based NMs and bulk materials made of metal, ceramic, or polymer may be used to create the composites. NMs can be created using a variety of morphologies.

B] Classification of Nanomaterials Based On Their Origin

NPs and NSMs can be divided into natural and synthetic categories in addition to classifications based on dimension and material.

Natural

Nanomaterials are created naturally by biological species or as a result of human activity. Natural resources can easily be used to create artificial surfaces with unique micro- and nanoscale templates and features for technological applications. Unaffected by human activity, naturally occurring NMs exist in all of the Earth's spheres (including the hydrosphere, atmosphere, lithosphere, and even the biosphere). The NMs that make up Earth's spheres include the hydrosphere, which is made up of oceans, lakes, rivers, groundwater, and hydrothermal vents, the lithosphere, which is made up of rocks, soils, magma, or lava at specific stages of evolution, and the biosphere, which includes lower organisms like microbes and higher organisms like humans.

Synthetic

Nanomaterials are created mechanically through grinding, through smoke and exhaust from engines, or through physical, chemical, biological, or hybrid techniques of synthesis. The use of engineered NMs in consumer goods and industrial applications, as well as their growing manufacturing and subsequent release, has raised the issue of risk assessment methodologies recently. The behavior and outcome of manufactured NMs in various environmental media can be predicted with great accuracy using these risk assessment methodologies [7].

SYNTHESIS OF GOLD NANOPARTICLE

Gold Nanoparticles Synthesis

A 200 mL Erlenmeyer flask containing 100 mL of sterile DD water and 10g of properly washed Ennab leaves was used to create the plant extract needed to convert Au3+ ions to Au0. The mixture was then boiled for five minutes. In a typical experiment, 45mL of a 1mM aqueous HAuCl4 solution were mixed with 5mL of the plant extract. By observing the UV-vis absorption spectrum as a function of time, the reduction of AuCl4 was observed [8].

Generally, the following methods have been followed forthe synthesis of gold nanoparticles (GNPs):

Chemical Methods

The kind of chemical process most frequently employed to create GNPs is the well-known Turkevich method, which is also one of the more promising approaches when compared to others.

In this method, citrate, ascorbic acid, and tannic acid are used as mild reducing agents to decrease Au+3 ions. The Turkevich approach is used to create the biocompatible and tiny GNPs as illustrated in the examples below. For the synthesis of GNPs during this process, it is vital to manage the factors such as pH, temperature, and concentration. Brust and Schiffrin introduced the Brust-Schiffrin technique in 1944. The thermally stable and air-stable GNPs with regulated and low dispersion can be easily synthesized using this approach. This procedure involved transferring AuCl4 from an aqueous phase to toluene utilizing tetraoctylammonium bromide (TOAB) as a phase-transfer agent and reducing it with NaBH4 in the presence of dodecanethiol. The organic phase turns from orange to deep brown when reducing agents are used.

Biological Methods

Chemical methods are the most common techniques used for the synthesis of metallic nanoparticles. The cost of reducing agents and stabilizing agents limits their applications. Furthermore, the prepared nanoparticles by chemical methods may have toxic consequences in biomedical applications. So, there is a requirement to develop easy and cost-effective procedures for the synthesis of nanoparticles that do not consume any toxic chemicals. The synthesis of nanoparticles by biological methods in current years has become the center of attention as green and eco-friendly methods. In biological methods, the synthesis of nanoparticles usually carried out by microorganisms, plants or plant extracts and enzymes. In recent times, the use of plants for the synthesis of nanoparticles is of less toxic, cost-effective and eco-friendly. The biosynthesis of nanoparticles in recent years by means of plants such as Azadirachta indica, Aloe Vera, Medicago sativa, Cinnamomum camphora, Coriandrum sativum, Pelargonium graveolens, Terminalia catappa, and lemongrass have been used [9, 10].

Green Synthesis of Gold Nanoparticles

GNPs can be produced in a manner that is not harmful to the environment by using bacteria, fungi, or plants. In solutions containing monovalent or trivalent gold ions, such as gold thiosulphate and gold chloride, microbes can produce GNPs. To the best of our knowledge, Beveridge and Murray's 1980 investigation on the synthesis and storage of GNPs by microorganisms was the first. They discovered that Bacillus subtilis cell walls' amine and carboxyl groups serve as gold deposition sites, and that teichoic acid is responsible for the uptake of gold chloride. Other Gram-positive bacteria and fungi may also use this method of gold reduction and deposition. There are occasionally deposits in prokaryotes, such as gold, sulphides, and phosphorites, since prokaryotes aid in the development of some geologic deposits. In order to find gold-producing bacteria, gold-enriched soil should be examined. The gold mine-isolated fungus Epicoccum nigrum is capable of producing GNPs in spherical and rod shapes. However, bacteria that reduce gold produce colloidal gold that is blended with phosphorus and sulphur. By means of diagenesis, this colloidal gold will change into spherical pseudocysts or octahedral gold crystals. Therefore, to avoid contaminating the GNP synthesis, deposits like sulphides and phosphorites should be removed [11, 12].

Role of Gold Nanoparticles

Recently, gold nanoparticles have been used as a great candidate for delivering many carpets to their intended locations. These payloads include everything from tiny medicinal molecules to larger macromolecules including proteins, RNA, and DNA. Effective discharge of these payloads must be taken into account for effective therapy [13].

GNP for Diagnosis in Ophthalmology

With the use of biosensing paper strips functionalized with GNP, early identification of infected keratoconjunctivitis was achieved. A diagnostic tool based on the surface-enhanced Raman scattering (SERS) effect was developed using 89 GNPs that were decreased on the strips and their surface plasmon resonance. Raman spectroscopy is an effective method for identifying particular compounds. Here, the GNP's localised surface plasmon resonance causes the SERS effect, which significantly boosts the Raman signal [14].

GNP for Wound Healing

Hydrocolloid membrane coated with phytochemically stabilised gold nanoparticles has a considerable impact on the healing of cutaneous wounds. Through the use of photobiomodulation therapy, gold nanoparticles have a beneficial effect on the healing of wound infections. Gold nanoparticles' antibacterial and antioxidant properties demonstrated great

promise for wound healing and collagen tissue regeneration. The release of proteins by gold nanoparticles makes them excellent candidates for wound healing due to their antiangiogenic and anti-inflammatory properties [15].

Skin Disorders

Inflammation, proliferation, and remodelling are all part of the intricate pathophysiological process that underlies wound healing. One of the main causes of the development of chronic wounds is bacterial infection brought on by inadequate management of acute wounds.

Killing germs is a crucial component of initial wound care since they can lead to inflammation. Inflammation can be reduced and a chronic wound prevented from (re)occurring with the use of quantized gold (QG), which also causes the wound bed to move from the inflammation phase to the proliferation phase. Such a gold nanocomposite might be further developed as dual function quantized gold (QG), which would bind to LPSs without interfering with the inner core's catalytic activity. Small-sized nanogold is more effective than large-sized catalysts at catalysing the breakdown of H_2O_2 into water and oxygen.

After hemostasis, infection can impede wound repair, therefore platelet-like particles (PLP) and antimicrobial gold can be mixed to create nanogold composites (NGC), which can speed up wound healing. These NGC PLPs are intriguing compounds for avoiding post-traumatic blood loss and infection because they imitate the platelet shape, cause clot shrinking, and exhibit some antibacterial potential [16].

Lung Cancer

AuNPs have been used in a number of recent studies to diagnose and treat lung cancer. An ultrasensitive electrochemical cytosensing platform was used by Zhang et al. to create AuNP-coated carbon nanospheres that contain an anti-carcinoembryonic antigen (CEA) antibody for the diagnosis of non-small-cell lung cancer (NSCLC).

Breast Cancer

In the US, breast cancer is the second most common cancer that kills women. It has been demonstrated that AuNPs could be used to treat breast cancer due to their ability to localize in tumours, which lowers systemic side effects and boosts efficacy [17].

Future Perspective

Applications of gold nanoparticles often increase the ELISA, PCR, and immuno-PCR assays' sensitivity, specificity, assay time, and reproducibility. GNPs are multifunctional nanomaterials that can perform the following tasks for ELISA-based immunoassays: they can act as three-dimensional antibody carriers to increase the sensitivity of the assay; they can take the place of conventional enzymes to produce ultra-sensitive and highly stable immunological assays; and they can offer a quick, visually observable point of care system for clinical applications [18].

Proteins, enzymes, and other biomolecules in large amounts are required for the synthesis and stabilisation of nanoparticles. Understanding the biochemical mechanisms/pathways underlying plant heavy metal detoxification, accumulation, and resistance will lead to improved nanoparticle production. Future plans involve genetic modification to increase the productivity of these organisms in the production of nanoparticles [19].

The use of iron oxide, gold, and quantum dot nanoparticles in diagnostic and therapeutic procedures has considerable potential. Recent distribution studies imply that a trade-off between therapeutic or imaging efficacy and the undesired dissemination of the particle must be taken into account in nanoparticle design. The addition of coating and targeting moieties may improve circulation and treatment—tumor targeting, for example—but it also may increase the size of the particles to the point where they cannot be excreted by the kidneys. Identifying the immune cells impacted and characterizing the immunological response, if any, to the nanoparticles should also be included in distribution studies [20].

These systems are extremely desirable options for delivery applications due to the high degree of tenability inherent in NP monolayer. Although there has been significant progress, there are still numerous obstacles to be addressed. Fluorophore-Conjugation AuNps will be used in a systematic evaluation of the drug delivery features, such as uptake, release rate, and toxicity, to shed light on how to further optimise the application *in vivo*. Equally significant, these researches will offer fundamental understanding of how NPs are taken up by cells. Last but not least, the development of targeted delivery offers

a way to improve the treatment of acute illnesses including cancer and HIV [21].

REFERENCES

[1] Yao L, Bojic D, Liu M. Applications and safety of gold nanoparticles as therapeutic devices in clinical trials. Journal of Pharmaceutical Analysis. 2023.

[2] Faheem SM, Banu H. Gold Nanoparticles in Cancer Diagnosis and Treatment: A Review. Austin J BiotechnolBioeng. 2014; 1(6): 5.

[3] Giasuddin ASM. Gold Nanoparticles Are Medically More Precious Than Pretty Gold**,** Glob J Endocrinol Metab.2018; 1(3):1-2.

[4] Fan J, Cheng Y, Sun M. Functionalized Gold Nanoparticles: Synthesis, Properties and Biomedical Applications. Chem. Rec.2020; 20, 1–32.

[5] Santhoshkumar J, Rajeshkumar S, Kumar SV. Phyto-assisted synthesis, characterization and applications of gold nanoparticles – A review, Biochemistry and Biophysics Reports. 2017; 11: 46–57.

[6] Liu S, Lammerhofer M. Functionalized gold nanoparticles for sample preparation: A review, Electrophoresis. 2019:1–24.

[7] Jaison J, Ahmed B, Yen SC, Dufresne A, Michael K. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations, Beilstein J. Nanotechnol. 2018; 9: 1050–1074.

[8] Alaa AAA, Yazan A, Zoubi MS. Synthesis of Gold Nanoparticles Using Leaf Extract of Ziziphuszizyphus and their Antimicrobial Activity, Nanomaterials. 2018; 8: 174-185.

[9] Hussain S, Amjad M. A Review on Gold Nanoparticles (GNPs) and their Advancement in Cancer Therapy. Int J NanomaterNanotechnolNanomed. 2021; 7(1): 019-025.

[10] Guven ZP, Silva PH, Luo Z. Synthesis and Characterization of Amphiphilic Gold Nanoparticles. J. Vis. Exp. 2019; (149): 1-11.

[11] Cai F, Li S, Huang H, Iqbal J, Wang C, Jiang X. Green synthesis of gold nanoparticles for immune response regulation: Mechanisms, applications, and perspectives. J Biomed Mater Res. 2021; 1–19.

[12] Harish KK, Nagasamy V, Himangshu B, Anuttam K, Metallic Nanoparticle: A Review. Biomed J Sci&Tech Res. 2018; 4(2): 3765-3775.

[13] Amina SJ, Guo B. A Review on the Synthesis and Functionalization of Gold Nanoparticles as a Drug Delivery Vehicle. International Journal of Nanomedicine, 2020: 9823-9857.

[14] Masse F, Ouellette M, Lamoureux G, Boisselier E. Gold nanoparticles in ophthalmology, Med Res Rev, 2019;39:302-327.

[15] Ovais M, Ahmad I, AT Khalil. Wound healing applications of biogenic colloidal silver and gold nanoparticles: recent trends and future prospects. ApplMicrobiolBiotechnol, 2018.

[16] Ko WC, Wang SJ, Hsiao CY. Pharmacological Role of Functionalized Gold Nanoparticles in Disease Applications. Molecules, 2022; 27: 1551.

[17] Liu XY, Wang JQ, Ashby CR, Zeng L, Fan YF, Chen Z. Gold nanoparticles: synthesis, physiochemical properties and therapeutic applications in cancer. Drug Discovery Today. 2021; 26 1284-1292.

[18] Tabatabaei MS, Islam R, Ahmed M. Applications of gold nanoparticles in ELISA, PCR, and immuno-PCR assays: A review, AnalyticaChimicaActa. 2020.

[19] Ojha S, Green synthesis of metallic nanoparticles: Advancements and future perspectives, Biological Sciences. 2022; 2(3): 262-268.

[20] Almeida J, Chen A, Foster A, Drezek R. *In-vivo*biodistribution of nanoparticles, Nanomedicine (2011); 6(5): 815–835.

[21] Han G, Ghosh P, Rotello V. Functionalized Gold Nanoparticle for Drug Delivery, Nanomedicine, 2007; 2(1):113-123.