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Review Article

Therapeutic and Diagnostic Potential of Metallic Nanoparticles: A Comprehensive Review

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ABSTRACT

Metallic nanoparticles (MNPs) are among the most widely investigated nanomaterials due to their unique physicochemical and biological properties. With particle sizes ranging from 1–100 nm, MNPs such as gold, silver, copper, zinc, and iron exhibit high surface-to- volume ratios, plasmon resonance, and enhanced reactivity compared to their bulk counterparts. These properties make them attractive candidates for biomedical applications, particularly in targeted drug delivery, imaging, antimicrobial therapies, and cancer treatment. Synthesis approaches are broadly classified into top-down and bottom-up methods, with growing emphasis on green synthesis for sustainable and biocompatible production. Gold and silver nanoparticles have demonstrated significant roles in photothermal therapy, radiotherapy enhancement, rheumatoid arthritis treatment, and tumor inhibition. Despite these promising applications, limitations related to toxicity, stability, and large-scale reproducibility must be addressed for successful clinical translation. This review discusses the synthesis strategies, key properties, and therapeutic potential of MNPs, highlighting their role as an emerging platform for nanomedicine and biomedical innovation.

INTRODUCTION

Nanotechnology has been established since the turn of the century. Given that “nanotechnology” was through the Latin names meaning very much, the prefix nano is derived from the ancient Greek Vavoc That Nobel laureate Richard P. Feyn-Man delivered in his renowned 1959 talk “Feynman, 1960” states that “There’s Plenty of Room at the Bottom.” Various groundbreaking discoveries in the realm of nanotechnology Technology that works with things the size of nanometres is made possible by nanotechnology. It is anticipated that nanotechnology will advance on multiple fronts, starting with materials. Systems and gadgets. The

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level of nanomaterials is the most advanced currently in terms of both commercial uses and scientific knowledge. Ten years previously, nanoparticles were examined due to their size-dependent chemical and attributes. They are now in the commercial investigation phase Science and engineering applied to the nanoscale is called nanotechnology. The development and synthesis of materials, devices, and systems at the nanoscale is known as nanotechnology as much as 1-100 nm. High surface volume ratios are found in nano formulations. The creation of tiny objects, such as electronic devices, catalysts, sensors, etc., is the focus of nanotechnology. One of the most significant and fascinating areas of research in physics, chemistry, biology, medicine, engineering, and technology in recent years is nanomaterials. Design, development, and use of materials at the atomic, molecular, and macromolecular range are represented by nanotechnology. Creation and use of materials at the molecular, macromolecular, and atomic level services, and systems at the nanoscale is known as nanotechnology.1 Nanoparticles (NPs) can vary largely in size. Generally, they can be zero-dimensional, meaning that their length, thickness and height are all determined by a single point, as in the case of nano dots; one-dimensional, meaning that they only present a single parameter, as in the case of nanotubes; two-dimensional, such as graphene; and three-dimensional, such as metal NPs (silver, gold, copper, etc.). NPs can also have a wide range of structures and shapes (e.g., spherical, cylindrical, tubular, conical, helical), while some can be flat or even irregular. NPs can be aerated or compact, amorphous or crystalline, with one or more solid crystals.2 Metallic nanoparticles or metal nanoparticles(MNPs), area newly emerged form of nanoparticles MNPs have gained significant recognition in many research areas, as they have been suggested as a promising alternative tool for targeted-site, sustained, and controlled drug delivery attributed to the novel size dependent behaviour and related properties Furthermore, MNPs may be produced using a straightforward laboratory technique in a variety of size ranges with a low dispersity index. They are also biocompatible, non-toxic, and inert. Because of their straightforward structure and ease of synthesis, MNPs offer straightforward and flexible surface functionalization. Because of these characteristics , MNPs offer a promising platform for the binding of targeting ligands on the surface at low core diameter sizes ,making them ideal for use in drug delivery systems.3 MNPs have various reaction response mechanisms and can easily penetrate the target organs and cross biological membrane barriers. MNPs can alter cellular function by binding with cellular protein sand nucleic acids and expressing enhanced biological activity due to their smaller particle size and correspondingly high surface Gold and silver have obtained more attention than other MNPs For instance ,gold is widely used in medicines, and its nanoparticles are used in different drug delivery and diagnostic cases The wide application and recognition of MNPs as targeted drug delivery vehicles are mainly attributed to their high degree of drug- carrying capacity with the least toxic it and fewer side effects despite the high loading of drugs with various coatings like polymers, SiO_2, inorganic metals, etc. They are used to modify the surface of MNPs to make them appropriate for drug delivery.4

Types of different metal-based NPs

Metal NPs are purely made of metal precursors. Due to well-known localized surface plasmon resonance (LSPR) characteristics, these NPs possess unique optoelectrical properties. NPs of the alkali and noble metals, i.e., Cu, Ag, and Au, have a broad absorption band in the visible zone of the solar electromagnetic spectrum. The facet, size, and shape-controlled synthesis of metal NPs are essential in present-day cutting-edge materials.5

Silver nanoparticles (Ag NPs)

Ag NPs are particles with a size range of 1–100 nano meters made of silver. They have unique physical and chemical properties due to their small size, high surface area-to-volume ratio, and ability to absorb and scatter light in the visible and near-infrared range. Because of their relatively small size and high surface-to-volume ratios, which cause chemical and physical differences in their properties compared to their bulk counter parts, silver nanoparticles may exhibit additional antimicrobial capabilities not exerted by ionic silver.6

Zinc nanoparticles (ZnO NPs)

Zinc nanoparticles (ZnO NPs) are particles with a size range of 1–100 nm made of zinc. Zinc oxide (ZnO) NPs are a wide band gap semiconductor with a room temperature energy gap of 3.37 eV. Its catalytic, electrical, optoelectronic, and photochemical capabilities have made it widely worthwhile ZnO nanostructures are ideal for catalytic reaction processes Laser ablation, hydrothermal methods, electrochemical depositions, sol-gel method, chemical vapor deposition, thermal decomposition, combustion methods, ultrasound, microwave-assisted combustion method, two-step mechanochemical-thermal synthesis, anodization, co- precipitation, electrophoretic deposition, and precipitation processes are some methods for producing ZnO nanoparticles.7

Copper nanoparticles (CuNPs)

Copper nanoparticles (CuNPs) comprise a size range of 1 100 nm of copper-based particles Cu and Au metal fluorescence have long been known to exist. For excitation at 488 nm, a fluorescence peak centering on the metals' interbond absorption edge has been noted. Additionally, it was noted that the fluorescence peaked at the same energy at two distinct excitation wavelengths (457.9–514.5 and 300–400 nm), and the high-energy tail somewhat grows with increased photon energy pumping. A unique, physical, top-down EEW approach has been used to create Cu nanoparticles. The EEW method involves sending a current of 1,010 A/m2 (1,010 A/m2) across a thin Cu wire, which explodes on a Cu plate for a duration of 10–6 s.8

Gold nanoparticles (AuNPs)

Gold nanoparticles (AuNPs) are nano meters made of gold. They have unique physical and chemical properties and can absorb and scatter light in the visible and near-infrared range Scientists around the turn of the 20th century discovered anisotropic AuNPs. Zsigmond said that gold particles "are not always spherical when their size is 40nmorlower" in his book, released in 1909. Additionally, he found anisotropic gold particles of various colors. Zsigmondy won the Nobel Prize in 1925 for "his demonstration of the heterogeneous character of colloidal solutions and the methods he utilized" and for developing the ultramicroscope, which allowed him to see the forms of Au particles. He noticed that gold frequently crystallized into a six sided leaf shape AuNPs are the topic of extensive investigation due to their optical, electrical, and molecular-recognition capabilities, with numerous prospective or promised uses in a wide range of fields, including electron microscopy, electronics, nanotechnology, materials science, and biomedicine.9

Aluminum nanoparticles (AlNPs)

Aluminum nanoparticles (AlNPs) are nanoparticles made of aluminum. Aluminum nanoparticles' strong reactivity makes them promising for application in high-energy compositions, hydrogen generation in water processes, and the synthesis of alumina 2D and 3Dstructures.10

Iron nanoparticles (FeNPs)

Iron nanoparticles (FeNPs) are particles with a size range of 1 100 nano meters (Khan et al., 2019) made of iron. FeNPs have several potential applications, including their use as catalysts, drug delivery systems, sensors, and energy storage and conversion. They have also been investigated for use in photovoltaic and solar cells and water purification and environmental remediation. FeNPs can also be used in magnetic resonance imaging (MRI) as contrast agents to improve the visibility of tissues and organs. They can also be used in magnetic recording media, such as hard disk drives.11

Comparison of common imaging techniques along with the nanoparticles currently used or under clinical trials

Technique	Advantages	Disadvantages	Nanoparticles used
Ultrasound	Easy to perform	Resolution of images is often limited	Fe_2O_3, Gd_2O_3
	Non-invasive	Reflected very strongly on passing from tissue to gas, or vice versa	
	No radiation hazard because it has	Does not pass well through bone	
	nonionizing radiation being emitted	Attenuation can reduce the resolution of the image	
	Relatively inexpensive as compared to		
	other imaging modalities currently available		
	Wide field of view		
PET	Can image biochemical and physiological phenomena	Cost	Radioactive ^{64}Cu, ^{68}Cu, ^{82}Rb, and ^{18}F, with particles tagged or conjugated with any organic moiety containing ^{18}F being with the first choice
		Some tumors show poor FDG affinity	
		FDG uptake is not limited to the tumor cells and is prevalent in other benign cells	
		Motion artifact is the serious problem	
		Resolution of images is lower as compared to CT or MRI. This results in poor localization of lesions	
		Interpretation is very challenging	
		Most expensive technique	
MRI	Higher resolution	Expensive to use	Iron oxide nanoparticles are most commonly used, but

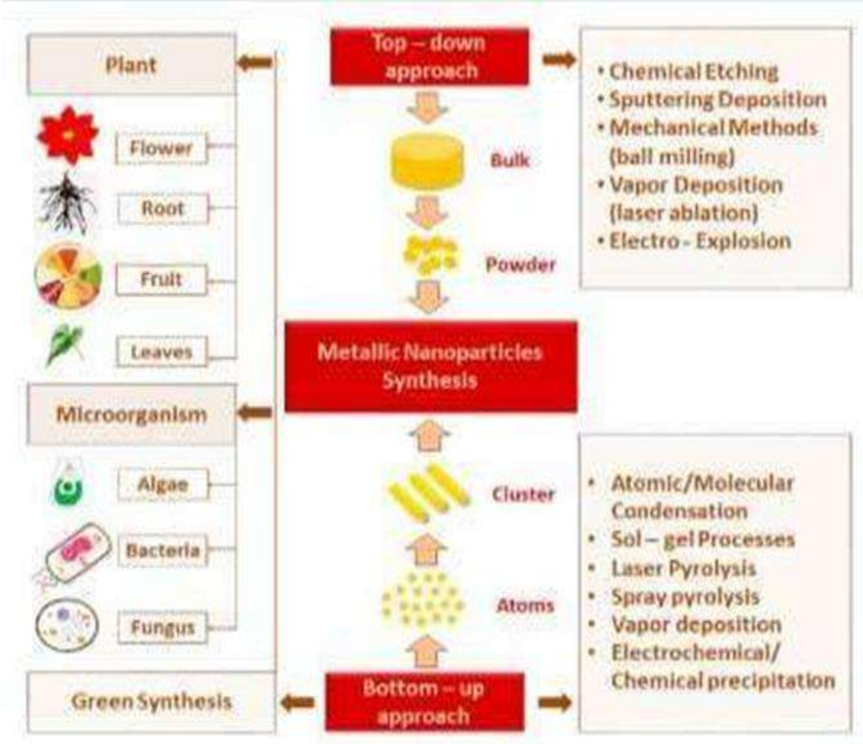
			newer generation multimodal imaging agents are also considered for clinical trials
	Can show the anatomical details	Cannot be used in patients with metallic devices, like pacemakers	
	Does not use any ionizing radiation		

Characteristics of Metallic Nanoparticles

a) Large surface energies
b) As compared to bulk they have large surface area to volume ratio
c) Quantum confinement
d) Plasmon excitation
e) Increased number of kinks.13

Methods of synthesizing MNPs

The two most commonly investigated approaches to acquiring nanomaterials of desired features are the top-down method (dispersion) and bottom-up (condensation) method. The top-down method is a destructive approach that utilizes the concept of decreasing the size of starting bulk metals l mm to a nanosized range using various physical and chemical treatments This approach includes mechanical methods (ball milling), sputtering deposition, and vapor methods. In the ball-milling method, bulk powder is subjected to high-energy hitting impact from the rotating solid balls in a series of parallel layers. The balls may roll down on the surface of the chamber containing bulk material The mechanochemical method combines the mechanical and chemical characteristics of a metal at its molecular level, and nanoparticles can be obtained by applying the mechanical aspects of a ball mill operating at low temperatures and with the use of a size-reducing agent to perform the chemical reaction Vapor deposition requires high temperature or pulse irradiation and contains laser ablation and gas evaporation. Laser ablation depends on laser irradiation. The bulk target material is exposed to a pulsed laser and heated to its boiling point. This leads to the fragmentation of the target, which condenses to produce MNPs Bimetallic nanoparticles (BMNPs) such as Mf-AI and ZnoAl are produced. MNPs can be synthesized by the combination of two metals (bimetallic), three metals (trimetallic), or more than three metals. Magnesium nanoparticles are preferred over monometallic particles due to their satisfactory stability, catalytic, and selectivity activity. They are widely used in various fields, with a particular focus on protein conjugation and modified drug delivery reported that the metal changed its state from its molten state into a chamber charged with inert gas following the gas evaporation technique. MNPs are formed by the condensation of the gaseous metals. The purity and type of the inert gas atmosphere influence the properties of the produced nanoparticles. In the bottom-up technique, nanoparticles are formed by joining smaller atoms and molecules, so this method is also called the building-up method. Laser pyrolysis, spray pyrolysis, and green synthesis are examples of this method. The laser pyrolysis method involves the application of laser energy to form nanoparticles. The precursor absorbs laser energy, such as infrared CO2 lasers, to incite homogeneous nucleation reactions In the spray pyrolysis technique, nanoparticle precursors in a vapor state are directly carried by a nebulizer into the hot reactor. Metals such as nitrate, acetate, and chloride are often used as metal precursors In general, physical and chemical approaches require high energy consumption, are expensive, and use poisonous and risky chemical agents that are responsible for many hazards to the environment Against those limitations, "green synthesis" techniques are gaining attention in contemporary research into the development of nanoparticles. Green synthesis avoids the production of undesirable or dangerous by-products through the build-up of dependable, eco-friendly, and sustainable synthesis procedures. Additionally, green synthesis is cost-effective and does not involve the use of high energy, temperature, pressure, and toxic chemicals Microorganisms and various plants can synthesize MNPs by utilizing microbial enzymes, polysaccharides, vitamins, and other biological and biodegradable substrates The synthesized nanoparticles from these microorganisms have found applications in different fields and have less toxicity. These properties make MNPs an appropriate option for developing drug delivery systems and as carrier material for sensors in diagnostic devices Biogenic MNP scan becreated in two less time-consuming ways: either by combining the metal salt with intra- and extracellular extracts of microorganisms at ambient temperature or by reducing metallic ions to their stable forms where enzymes act as reducing agents Bacterial species are used extensively in commercial biotechnological applications such as genetic engineering, bioleaching, and bioremediation Bacteria can reduce metal ions, and due to their low energy consumption and process controllability, they are a favourable source of synthesizing MNPs Among the bacterial species, Actinomycetes and Prokaryotic bacteria have been widely explored for making metal or metal oxide nanoparticles. A single bacteria can alter the toxicity of metal ions into non-toxic, safe NPs. Another important species of microorganisms is fungus. Compared to all other microorganism species, fungus has shown higher productivity and tolerability to metals Syntheses that use fungi and yeast can be done via intracellular and extracellular approaches. The expression of mycelia provides a high surface area, which supports the fungus in secreting more proteins than bacteria, which consequently results in a tremendous increase in MNP production. Various types of algae have also been found to be capable of holding heavy metals and, therefore, can also be used to synthesize MNPs of heavy metals such as gold and silver Plants biomolecules, such as proteins, carbohydrates, and coenzymes, may have the potential to reduce metal salt into nanoparticles The MNPs from plant extract can be prepared simply by mixing the metal salt solution with the extract of the plant of interest The size, surface morphology, and quality aspects of MNPs prepared from plant extract depend on the mixing ratio of plant extract and metal salt and the reaction temperature Details of some MNPs synthesized by microorganisms and plants, their characteristics.14

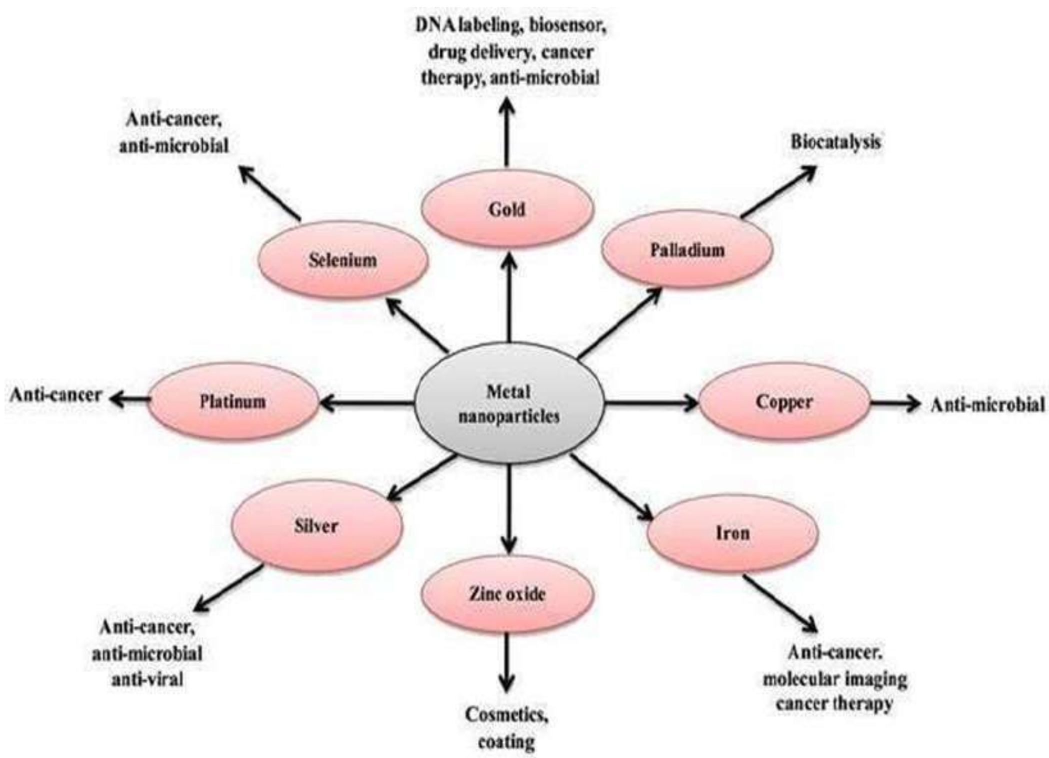


Therapeutic Applications of Metallic Nanoparticles

In Rheumatoid Arthritis Scientists from the University of Wollongong (Australia) have built a new class of anti-arthritic drug which could be used by gold nanoparticles and it has fewer side effects. Rheumatoid arthritis is an autoimmune disease that occurs when the immune system not function properly and attacks a patient's joints. New research has shown that gold particles can invade macrophages, and stop them from producing inflammation without killing them. Journal of inorganic biochemistry it has been published that by reducing the size of gold into smaller nanoparticles (50nm) was able to cause more gold to immune cells with lesser toxicity. As anti-Angiogenic It is well known that angiogenesis is the development of new blood vessels and occurs during normal development and in some disease states. It plays a main role in number of diseases such as cancer, rheumatoid arthritis. In normal conditions, angiogenesis is tightly regulated between various pro-angiogenic growth factors (VEGF, PDGF, and TGF- B) and anti-angiogenic factors (platelet factor 4, TSP-1). Under diseased conditions, angiogenic is turned on. Some reviews have reported that these agents have serious toxicities such as fatal haemorrhage, thrombosis, and hypertension. It may be overcome if these nanoparticles alone can be efficacious as an anti-angiogenic agent. In Leukemia B-chronic Lymphocytic Leukemia (CLL) is an incurable disease predominantly characterized by apoptosis resistance, by co-culture with an anti-VEGF antibody, found induction of more apoptosis in CCL B cells. In CLL therapy, gold nanoparticles were used to increase the efficacy of these agents. Gold nanoparticles were chosen based on their biocompatibility, very high surface area, surface functionalization and ease of characterization. To the gold nanoparticles, VEGF antibodies were attached and determined their ability to kill CLL B cells. In Photo Thermal Therapy Gold nanoparticles absorb light strongly as they convert photon energy into heat quickly and efficiently. Photo-thermal therapy (PTT) is an invasive therapy in which photon energy is converted into heat to kill cancer. In Radiotherapy Tumours loaded with gold, this absorbs more X-rays as gold is an excellent absorber of X-rays. Thus deposition of more beam energy and results in a local dose which increase specifically to tumour cells. Gold nanoparticles have been more useful to treat cancer. In Tumour Therapy It has been studied that naked gold nanoparticles inhibited the activity of heparin-binding proteins such as VEGF165 and bFGF in vitro and VEGF induced angiogenesis in vivo. Further work in this area has been reported that onto the surface of AuNPs heparin binding proteins are absorbed and were subsequently denatured.The researchers also showed that surface size plays a main role in the therapeutic effect of AuNPs. Mukherjee and colleagues also experimented the effect of gold nanoparticles on VEGF mediated angiogenesis using a mouse ear model injected with an adrenoviral vector of VEGF (Ad-VEGF- mimics the resulting angiogenic response found in tumours). A week later, the Ad VEGF administration, mice treated with AuNPs developed lesser edema than the same treated mice. Eom and Colleagues revealed the anti-tumour effects of 50nm AgNps In vitro and In vivo.15

Applications of Nanoparticles.[16-20]

Metal Nanoparticle	Application
Silver	Anti-microbial, anti-cancer, anti-protozoal, anti- fungal
Gold	Anti-microbial
Palladium	Anti-bacterial
Copper	Anti-microbial, anti-cancer
Selenium	Anti-cancer



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