PLANT SCIENCE TODAY
ISSN 2348-1900 (online)
Vol 10(sp2): 260–268
https://doi.org/10.14719/pst.2417

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MINI REVIEW ARTICLE

Biogenesis and Green Synthesis of Metal Nanoparticles and Their Pharmacological Applications

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OPEN ACCESS

ARTICLE HISTORY
Received: 09 February 2023
Accepted: 29 October 2023
Available online
Version 1.0 : 23 November 2023
Version 2.0 : 21 December 2023

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

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Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS,UGC Care etc. See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

CITE THIS ARTICLE
Ghosh A, Pappuswamy M, Chaudhary A, Meyyazhagan A, Arumugam V A, Balasubramanian B, Meganathan G. Biogenesis and Green Synthesis of Metal Nanoparticles and Their Pharmacological Applications. Plant Science Today. 2023; 10 (sp2): 260-268.
https://doi.org/10.14719/pst.2417

Abstract

Nanomaterial innovation is the primary catalyst of advancement in nanotechnology. Although there are many known chemical processes for creating nanoparticles that use harmful substances, it is now more important than ever to use processes that are safer, greener, and more environmentally friendly. The goal of research in this field is to use diverse life forms as "nanoparticle factories." Phytochemicals can convert salt into the appropriate nanoparticles thanks to their regular biosynthetic routes. In recent years, green chemistry methods for the synthesis of metallic nanoparticles have emerged as a fresh and exciting area of study. Metal nanoparticles, including gold (Au), silver (Ag), iron (Fe), and cadmium (Cd) along with certain oxides, can be synthesized using a variety of chemical and physical techniques as well as biological techniques carried out using plants. It has been discovered that methods involving plant-mediated synthesis are a more efficient and cost-effective way to create these metal nanoparticles. The plant-mediated nanoparticles are used as potential pharmaceutical agents for many diseases, including hepatitis, cancer, malaria, and HIV. Due to the higher efficacy and fewer side effects of nanodrugs compared to other commercial cancer drugs, the synthesis of nanoparticles targeting biological pathways has gained tremendous popularity. This review paper aims to cover the different green methods for the biogenesis of these nanoparticles, the different compounds and salts used, and the metals obtained. Ultimately, the significance and prospects of these metal nanoparticles especially in the fields of medicine, pharmacology, drug designing, and drug delivery engineering will also be commented on.

Keywords

Biotechnology; Green synthesis; Pharmacological; Phytochemicals; Nanoparticles

Introduction

Nanotechnology is the area of science and engineering that focuses on materials with dimensions of less than one-hundredth of a nanometer (1). Despite being new, diction has been extensively used to produce more effective technology. Due to its uses in the fields of electronic storage systems, biotechnology (2), magnetic separation and preconcentration of target analytes (3), targeted drug administration (4), and vehicles for gene and drug delivery (5), nanotechnology has recently gained the support of various industrial sectors. Consequently, these particles have the potential to have a substantial impact on society given the wide range of applications(6) (Fig.1)

The biosynthetic approach often involves simple scaling without high temperatures, pressures, or harmful chemicals and utilizes resources that are both cost- and environmentally friendly (7). It has been claimed that a variety of biofactories, including plants, algae, and diverse microorganisms like bacteria, actinomycetes, fungi, viruses, and yeast, have the special ability (8) to create metallic nanoparticles. In general, bioreduction and biosorption, which enable the metal-peptide interaction (cell wall), are the two biogenic production strategies to create metal nanoparticles (9). These processes reduce metallic ions into a biologically stable form. The advantages of cost-effective biogenic methods over other stated traditional methods include the need for a room with the proper temperature and atmosphere, as well as environmentally friendly technology and non-toxic solvent (10). The goal of green nanoparticle synthesis is to reduce waste production and promote sustainability (5).

The majority of nanoparticles used in biotechnology have particle diameters between 10 and 500 nm, seldom exceeding 700 nm. Because of their small size, these particles can interact with biomolecules both inside and outside of cells in several ways that can be interpreted and linked to various biochemical and physiochemical properties of these cells. Similar to how it would have several advantages over conventional pharmacological agents if used in noninvasive imaging and drug delivery systems (6). In comparison to conventional drug delivery methods, nanoparticles have advantages. The capacity to be tailored to varied sizes, shapes, and functions is the first and most obvious benefit of nanoparticles. They can be altered with targeting molecules or loaded with different medications to deliver therapeutic agents simultaneously and on target. Primarily, the production of gold nanoparticles that target tumors to detect in vivo Raman scattering was invented(10). This review provides a basic overview of nanoparticles, their synthesis, and the factors that can influence the production of various nanoparticles. It also discusses the effectiveness of nanoparticles in the pharmaceutical field. It helps to optimize one's choice of method of synthesis according to the function, efficiency, and appropriation.

Nanoparticles

Nanoparticles are tiny particles with dimensions typically ranging from 1 to 100 nanometres (nm). They can be synthesized from a wide range of materials, including metals, metal oxides, polymers, and carbon-based substances, among others. Nanoparticles exhibit unique physical and chemical properties due to their small size and high surface area-to-volume ratio, setting them apart from their bulk counterparts (11).

Physical Properties of Nanoparticles include (i) Size-Dependent Properties (Nanoparticles often display size-dependent properties. As their size decreases, their properties can change dramatically. For example, the colour of gold nanoparticles can shift from red to blue as their size decreases.), (ii) Large Surface Area (Nanoparticles have an exceptionally large surface area compared to their volume, making them highly reactive. This property is advantageous in applications like catalysis, where a greater surface area enhances catalytic activity.), (iii) Quantum Effects (In semiconductor nanoparticles (quantum dots), quantum effects become significant at the nanoscale (12). These effects can tune the absorption and emission of light, making them valuable in applications such as displays and photovoltaics). Chemical Properties

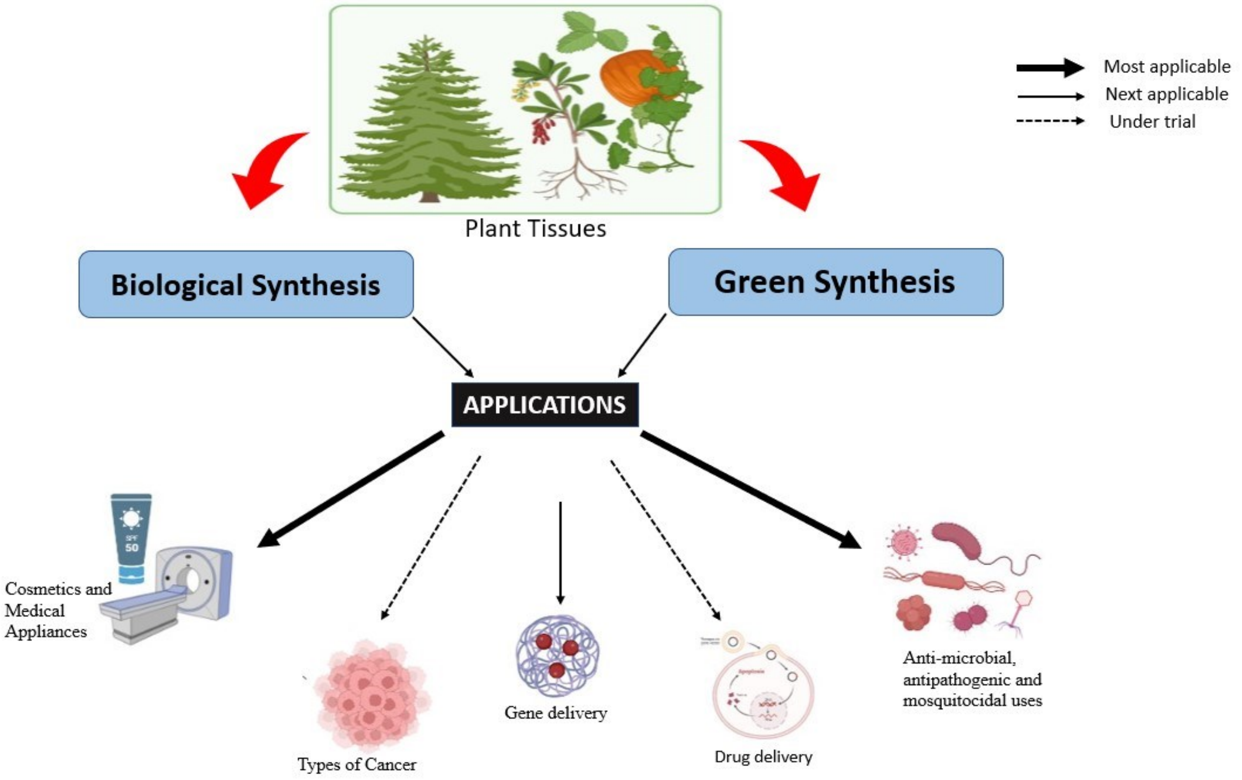

Figure 1. Diagrammatic Representation of Applications of Biological and Green Synthesis of Nanoparticles

of Nanoparticles include (i) Enhanced Reactivity (Due to their high surface area, nanoparticles can interact more readily with surrounding molecules, leading to increased reactivity. This is exploited in catalysis and drug delivery, where nanoparticles can carry and release specific chemicals.), (ii) Surface Modification (Nanoparticle surfaces can be chemically modified with ligands or functional groups to tailor their chemical behavior. This modification can enhance stability, solubility, and targeting capabilities.), (iii) Magnetism (Some nanoparticles, like iron oxide nanoparticles, exhibit unique magnetic properties. These magnetic nanoparticles find applications in medical imaging (e.g., MRI contrast agents) and targeted drug delivery.), and (iv) Plasmonic Properties (Certain metal nanoparticles, such as gold and silver, exhibit plasmonic behavior. They can resonate with light, leading to localized surface plasmon resonance (LSPR). LSPR is used in biosensing and imaging techniques.). Lastly, some unique features of Nanoparticles include (i) Size-Tuneable Properties (The ability to control nanoparticle size precisely allows researchers to tailor their properties for specific applications.), (ii) Drug Delivery (Nanoparticles can be engineered to encapsulate drugs and release them at a controlled rate, enhancing drug delivery efficiency and minimizing side effects.), (iii) Diagnostic Tools (Nanoparticles are used in diagnostic assays and imaging techniques, improving sensitivity and accuracy.), (iv) Environmental Remediation (Nanoparticles are employed in the removal of pollutants from water and air due to their high reactivity and adsorption capabilities and (v) Materials Reinforcement (Incorporating nanoparticles into materials like composites can improve mechanical strength, thermal conductivity, and electrical conductivity) (13).

Materials and Method

Biological Synthesis of Metal Nanoparticles

Although it has been discovered that the microbial-based synthesis process is easily scalable, environmentally friendly, and consistent with the use of the product for pharmaceutical applications, microorganism-based production is frequently more expensive than plant-based manufacturing (14). The primary advantage of plant-based synthesis approaches over traditional chemical and physical methods is that they are more environmentally friendly, less expensive, and easier to scale up for the large-scale synthesis of nanoparticles (15). They also do not require the use of toxic chemicals or high temperatures or pressures. The biological manufacture of metal nanoparticles employing microbes like bacteria, fungi, algae, and plants has been the subject of numerous research studies (16). This is because of their reducing or antioxidant characteristics, which, accordingly, cause metal nanoparticles to be reduced (17). Additionally, it is discovered that microbe-mediated synthesis is not appropriate for large-scale production because it necessitates strict aseptic conditions and special maintenance (18). As a result, using plants to synthesize nanoparticles is preferable to using microorganisms because it is simpler to scale up and does not necessitate maintaining cell culture. The use of plant extract boosts the practicability of nanoparticle production by microorganisms while decreasing the additional requirements of microbe isolation and culture medium preparation. While bacteria over time may lose their capacity to produce nanoparticles due to mutation (19), plant-mediated synthesis is a one-step process.

Green Synthesis of Metal Nanoparticles

The general processes and methods for the environmentally friendly synthesis of different nanoscale metals can be summed up as follows: obtain plant extract, combine extract with the metal salt solution under specific conditions, reduce the metal particles, perform filtration, and other processes to obtain the desired nanoscale metal.

Factors Affecting Genesis of Nanoparticles

The production of green nanoparticles depends on several environmental parameters, including temperature, pH, the concentration of reducing agents, the concentration of metal ions, and the method of synthesis (intracellular vs. extracellular) (20). In addition, factors such as contact time, pressure, and the type of microbe used in the growth medium are crucial in the synthesis of nanoparticles, notably in determining their form, size, texture, and quantity (21). For instance, changing the pH of the medium can affect the size and shape of Nanoparticles, with big Nanoparticles forming when the pH is acidic. It was found that smaller-sized gold Nanoparticles at pH 3.0 and 4.0 during the production of Au Nanoparticles using oat (*Avena sativa*) biomass compared to the produced Nanoparticles at pH 2.0 (22) This is because there are more functional groups available at higher pH ranges than at lower pH ranges, making them more accessible for nucleation. The concentration of biomolecules in the extract, in addition to pH, influences the size and form of produced Nanoparticles (15). Due to the presence of carbonyl compounds in the aloe vera extract, larger concentrations of spherical gold nanoparticles rather than triangular ones were produced when aloe vera leaf extract concentrations were increased (23). By adjusting the extract content in the solution, the size of the nanoparticles was also controlled between 50 and 350 nm. A quick change in the color of the reaction mixture is the primary indicator that the reaction's time is important in the reduction of nanoparticles and their size. This time frame can be anything from a few minutes to a few days (16).

Applications in Medicine

Nanoparticles have revolutionized the field of medicine through their unique properties and applications. These minuscule structures, typically measuring between 1 and 100 nm in size, offer a wide range of opportunities for improving diagnostics, treatment, and drug delivery in the medical field. One of the most significant applications of nanoparticles in medicine is drug delivery. Nanoparticles can serve as carriers for various drugs, improving their bioavailability and targeting specific tissues or cells (24). Nano-sized drug carriers, such as liposomes, micelles, and polymer nanoparticles, can encapsulate drugs, protecting them from degradation and delivering them to the desired site of action (25). Targeted nanoparticles can be guided by ligands or antibodies that recognize specific markers on the surface of diseased cells, such as cancer cells (26). Nanoparticles are used in medical imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET). They enhance contrast and improve the sensitivity of these imaging modalities (27). Nanoparticles can be used in biosensors for the rapid and sensitive detection of various diseases, including cancer, infectious diseases, (28), and diabetes. Functionalized nanoparticles can bind to specific biomarkers or pathogens, enabling early and accurate diagnosis. Nanoparticles play a role in regenerative medicine by assisting in tissue engineering and regeneration. They can deliver growth factors, genes, or stem cells to damaged tissues (29). Metallic nanoparticles, like silver or gold, can also be used as components of scaffolds for tissue engineering (30). The applications of nanoparticles in medicine are vast and continue to expand with ongoing research and technological advancements. However, it is essential to ensure the safety and biocompatibility of nanoparticles, understand their pharmacokinetics, and address potential toxicity concerns when developing medical applications. The field of nanomedicine offers the potential for more effective treatments and improved patient outcomes. (Table 1)

Nanoparticles have become pivotal players across an astonishing array of scientific disciplines, industries, and technological landscapes (38). These minute structures, endowed with unique and often fascinating properties, have transcended their size to yield transformative applications with profound implications for our world. At the pinnacle of this exploration of the vast and dynamic realm of nanoparticle applications, it is important to recognize the substantial impact they exert in shaping our present and future (39). From pioneering strides in medicine (40), where they are revolutionizing diagnostics and drug delivery (41), to their indispensable role in electronics (42), catalyzing innovation in displays

Table 1. The Medical Applications of the Different Nanoparticles.

Sl.No	Name of the metallic nanoparticles	Name of the drug tagged to it or coated to (if any)	Disease used or action against microbes/virus	Pharmacological action	References
1	Gold (AuNPs)	Doxorubicin	Chemotherapy drug	Can be absorbed and circulated in the bloodstream. They accumulate in organs like the liver, spleen, and kidneys. Drug delivery and imaging in cancer therapy. Some concerns about potential toxicity at high doses.	(1)
2	Silver (AgNPs)	Silver sulfadiazine	Wound Healing and Anti-microbial	Can be absorbed in the gastrointestinal tract and are distributed throughout the body. Used as antimicrobial agents in wound care and medical devices. Concerns about potential toxicity, especially with prolonged exposure.	(2)
3	Iron Oxide (Fe_3O_4)	Ferumoxytol	NMR imaging and Detection Instrumentation in Medicine.	Iron oxide nanoparticles can be taken up by cells, especially in the liver, spleen, and bone marrow. Primarily used as contrast agents in MRI and for targeted drug delivery.	(3)
4	Copper (CuNPs)	Self	Antimicrobial in wound dressings.	Incorporated into wound dressings and coatings for medical devices to prevent bacterial growth Concerns about potential toxicity, particularly with systemic exposure.	(4)
5	Titanium Dioxide (TiO_2NPs)	Paclitaxel	Chemotherapy drug	carriers for photodynamic therapy in cancer treatment. They may be absorbed through the skin, inhaled, or ingested. Safety concerns related to potential skin penetration and long-term exposure.	(5)
6	Zinc Oxide (ZnONPs)	Insulin	Diabetes 1 and 2, alternative forms of Oral drugs	drug delivery wound healing UV blockers in sunscreens Micronutrient Oral bioavailability	(6)
7	Platinum (PtNPs)	Cisplatin	Chemotherapy drug	cancer therapy delivery of platinum-based anticancer drugs. May accumulate in the liver and spleen.	(7)

and sensors, nanoparticles are enablers of groundbreaking progress (43). Notably, they are indispensable assets in energy technologies, contributing to advancements in solar cells and fuel cells (44). Moreover, their exceptional adsorption and catalytic capabilities are at the forefront of environmental remediation efforts (45). As the journey through the realm of nanoparticles, each step will reveal a multitude of remarkable applications, with scientific studies and technological innovations underpinning every assertion.

Medicine stands as one of the most dynamic and transformative fields for nanoparticle applications. Consider gold nanoparticles, whose mesmerizing optical properties are being harnessed to revolutionize diagnostic techniques (46). Gold nanoparticles functionalized with specific biomolecules can serve as sensitive and selective probes in diagnostic assays, detecting biomarkers associated with various diseases, including cancer and infectious agents, with remarkable accuracy and speed (47). In the realm of imaging, iron oxide nanoparticles emerge as unsung heroes. Coated with biocompatible materials, they function as potent contrast agents in magnetic resonance imaging (MRI) and computed tomography (CT) scans, facilitating the precise visualization of tissues and lesions, thus enhancing diagnostic capabilities (48).

However, it is in the domain of drug delivery that nanoparticles wield their greatest transformative power. Their diminutive size and inherent versatility allow for the efficient encapsulation of drugs, offering a lifeline to patients across the globe. Lipid-based nanoparticles, such as liposomes, stand out as prime examples. These microscopic carriers can encapsulate chemotherapeutic drugs, protecting them from degradation while facilitating controlled drug release within the body. This targeted delivery system not only enhances the efficacy of treatment but also minimizes side effects and collateral damage to healthy tissues, heralding a new era of personalized medicine.

Electronics is yet another arena significantly influenced by the exceptional properties of nanoparticles. The rise of quantum dots, and semiconductor nanoparticles, has spurred a revolution in display technology. By precisely tuning the size of these nanocrystals, scientists can control the colours of light they emit. This capability lies at the heart of quantum-dot displays, found in today's high-resolution screens, from televisions to smartphones. Furthermore, nanoparticles have opened doors to cutting-edge electronic components. Silver nanoparticles are utilized in conductive inks for printing flexible electronic circuits, (49) while carbon nanotubes serve as the bedrock of advanced sensors, ranging from environmental monitoring devices to medical diagnostics.

As we journey into the domain of energy production, nanoparticles demonstrate their prowess in harnessing sunlight. Quantum dots reappear, offering enhanced solar cell efficiency through their ability to capture a broader spectrum of light. (50) This innovation holds the promise of more efficient and affordable solar energy, paving the way for a sustainable energy future. Additionally, nanoparticles serve as critical catalysts in energy conversion processes, such as the hydrogen evolution reaction in fuel cells. Precious metal nanoparticles, including platinum and palladium, excel in these catalytic roles, facilitating the conversion of hydrogen into electrical energy with unprecedented efficiency.

Environmental concerns have galvanized scientists and engineers to seek sustainable solutions, and here again, nanoparticles play a pivotal role. Their extraordinary adsorption properties make them effective agents in pollutant removal from air and water. Activated carbon nanoparticles, for example, excel in adsorbing a wide range of contaminants, purifying both air and water resources. Nanoparticles can also be engineered to facilitate the breakdown of harmful compounds (51). Titanium dioxide nanoparticles, activated by ultraviolet light, catalyze the degradation of organic pollutants, offering promise in advanced water purification systems and air purifiers, thus mitigating environmental hazards.

These profound applications are merely the tip of the iceberg. Nanoparticles have extended their influence into diverse arenas, from the food industry—where they enhance food texture, appearance, and shelf life by encapsulating flavours or nutrients—to the world of cosmetics, where they contribute to skin care products, improving their performance and sensory attributes. The domain of materials science benefits significantly from nanoparticles, as they are integrated into composites to bolster mechanical strength, thermal conductivity, and electrical properties, resulting in advanced materials used in aerospace, automotive, and construction industries. Furthermore, nanoparticles feature prominently in the realm of energy storage, enhancing the electrical conductivity and storage capacity of electrode materials in lithium-ion batteries (52). These advancements power electric vehicles and portable electronics, providing longer-lasting and more efficient energy.

Despite their immense potential, it is imperative to recognize that the rise of nanoparticles is accompanied by safety, environmental, and ethical concerns. Questions about their long-term impact on human health and ecosystems necessitate rigorous research and regulatory oversight to ensure their responsible and sustainable deployment.

In conclusion, nanoparticles, although diminutive in size, represent monumental advancements in science, technology, and industry. Their unique properties and versatility make them indispensable across diverse fields, from medicine and electronics to energy production and environmental remediation. As we unlock the vast potential of nanoparticles, it is our collective responsibility to harness their transformative power responsibly, fostering a future that leverages their incredible capabilities for the betterment of society.

Recently, promising antibacterial and antiviral characteristics of nanotechnology-based techniques have drawn attention (53). These might include antiviral facemasks, clothing, and other coatings that, when in touch with a surface, could potentially destroy the virus (54). Numerous studies have confirmed that nanoparticles are also promising agents for enhancing cellular immunity and extending the impact of antigens. (55) Due to their multiple targeted mechanisms of action, silver nanoparticles, in particular, synthesized utilizing plant extracts, are a promising contender for novel antiviral medicines. (56) These nanoparticles are antiviral against viruses like HIV (57), hepatitis B (58), type 1 herpes simplex (59), Chikungunya virus, and influenza virus (60). Recent years have seen a remarkable advancement in nanomedicine, which has provided fresh perspectives on cancer immunotherapy (18) These gold nanoparticles were coated with a thiol-modified PEG coat after being encoded with a Raman reporter. The pegylated gold nanoparticles were next coupled with an antibody against the epidermal growth factor receptor, which is occasionally overexpressed in particular kinds of cancer cells, to more precisely target tumour cells (61). Then, using SERS, the customized particles' Raman increase was seen with electronic transitions at 633 or 785 nm. (62) Ag nanoparticles exhibited antiviral effects against the yellow mosaic virus (BYMV) (31), potato virus Y (PVY) (63), sun hemp rosette virus (SHRV) (64), and tomato mosaic virus (65), according to several researchers (ToMV). They suggested that by attaching to the virus particle, Ag nanoparticles limit viral nucleic acid replication in plant cells. They also noticed an increase in the generation of reactive oxygen species (ROS) and the induction of system-acquired resistance (SAR).

Conclusion and Future Perspective

This paper delivers a brief synopsis of some of the basic nanoparticles currently being fabricated for application in medicine. The need for nanotechnology to examine outside of cell walls has become more pertinent as the study of nanoscience has evolved over the last 20 years. Although nanoparticles have been successfully employed to treat a variety of ailments, biomedical imaging breakthroughs are mostly dependent on the size, shape, and target selectivity of the nanoparticles.

Out of all the nanoparticles mentioned and identified in the literature, bio-inspired noble metals have garnered the greatest attention from scientists. This is due to their antiviral and antibacterial activities on various antigens. Continued study requires effort to create nanoparticles that can be employed in nanomachines to tackle a specific group of viruses. Furthermore, due to the tendency of germs to acquire resistance over time, these nanoparticles may not operate against some strains of these pathogens. As a result, further research is imperative for allowing the nanoparticles to target multiple illness kinds. Future studies should concentrate on the biocompatibility and safety of the nanoparticles, particularly their long-term toxicity. Improved human and animal clinical studies are requisite to support their use, particularly in biomedical imaging employing MRI, CT, ultrasound, PET, SERS, and optical imaging (Table 2).

Table 2. The varied nanoparticle synthesis and their applications

Sr No.	Nanoparticle synthesized	Plant system utilized	Morphology and application	References
1	Gold	*Coriandrum sativum* (coriander)	Spherical, triangular. Cancer hyperthermia, optical coatings	(8)
2	Gold and silver	*Aloe barbadensis* Miller (Aloe vera)	Spherical. Antibacterial activity against water-borne pathogens	(9)
3	Gold	*Terminalia catappa* (almond)	Spherical Biomedical field	(10)
4	Gold and silver	*Tanacetum vulgare* (tansy fruit)	Triangular, spherical Antibacterial, sensors	(11)
5	Zinc oxide	*Sedum alfredii* Hance	Hexagonal wurtzite and pseudo-spherical Nanoelectronics	(12)
6	Gold	*Psidium guajava* (guava)	Mostly spherical Catalysis, biosensing	(13)
7	Gold	*Pelargonium roseum* (rose geranium)	Crystalline, hexagonal, triangular, and spherical Biolabeling, biosensor	(14)
8	Silver	*Ocimum sanctum* (tulsi; leaf extract)	Spherical Catalytic reduction	(15)
9	Silver	*Mentha piperita* (peppermint)	Spherical, triangular, truncated triangular, decahedral Larvicidal activity against malaria and filariasis vectors	(16)
10	Gold	*Syzygium aromaticum* (clove buds)	Crystalline Cancer hyperthermia, drug delivery	(17)

Acknowledgements

The authors would like to use this occasion to express their gratitude to the institution for all of its support, which offered guidance, critical assessments, software tools, and, on top of that, creative thoughts whenever they were sought.

Authors' contributions

AG conceived the paper, conducted a literature search, authored the manuscript, and presented the data in a tabular format. The paper was edited by MP and AC in collaboration with BB, AM, GM, and VAA. MP conceived of the study and helped to develop and coordinate it. The paper has been reviewed and approved by all authors.

Compliance with ethical standards

Conflict of interest: The authors affirm that they have no personal or financial affiliations that might be seen as jeopardizing the submitted study's findings.

Ethical issues: None.

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