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From Nature to Nanoparticles: Biogenic Synthesis of Gold Nanoparticles and their Applications

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Abstract

In recent few years, studies have already reported that nanoparticles are a promising alternative option against to antibacterial reagents because of their exhibited antibacterial activities in several biomedical, electrical , thermal , optical fields , like molecules, drugs and genes delivery, tissue engineering . Nanomaterial research are helps to know the possible relationship between the morphology characters of a nanomaterial and its deliver toxicity. Recent advances and updated in the synthesis of metal nanoparticles (MeNPs), and more especially gold nanoparticles (AuNPs), have led to mark their tremendous expansion in different fields. Nanotechnology has become one of the emerging topics and receiving universal attention and also playing an important role in agriculture, environment and pharmacology. In various techniques are employed for nanoparticle synthesis like laser ablation, mechanical milling, spinning and chemical deposition. This is not possible to continuing the whole process cause usage of hazardous chemicals and expensiveness it is unsuitable for environment and also industries. Just because of its necessity of sustainable, economic and environment friendly it is approach for increased development in recent years. Microbial synthesis of nanoparticles is connected with microbiology and nanotechnology is one of the green techniques employed for sustainable production. Gold and other nanoparticles are biosynthesis by bacteria, fungi, yeast and algae have been reported already. On the basis of microbial rich community, some microbes have been explored for the production of nanoparticles. Nanoparticles are also involved in environmental remediation processes such as pollutant removal and detection of contaminants. This review discussed about the synthesis of gold nanoparticles and their role in biomedical , agriculture and others field.

Keywords: *Antibacterial activity, pharmaceutical application, Toxicity, Synthesis, Nanomaterials, Genes delivery.*

1. Introduction

Gold nanoparticles (AuNPs) is an extensively studied nanoparticles (NPs) and are known to have profound applications in medicine. The researcher made continuous efforts for the environmental-friendly and economical methods, such as biogenic methods known as green synthesis. There are many strategies for separating and applying gold (Au) and silver (Ag) nanoparticles, of which biological routes have emerged as efficient, low-cost, and environmentally friendly techniques (Saha & Dutta Gupta., 2018). This focuses on recent developments of green synthesized AuNPs and AgNPs using biogenic sources such as algae, animals, plants, microbes, bacteria, fungi, and so on. Hence, it discusses their numerous biomedical applications and separating Au and Ag nanoparticles from plants, bacteria, fungi, and algae (Dutta Gupta et al., 2020).

Nanotechnology explains the use of materials at the nanometer level, which starts with the synthesis and ends with its application. Nanoparticles, whose dimension is defined between 1 and 100 nm , have created a historical revolution in the industrial sectors due to their exceptional surface activity and electrical, magnetic, and optical properties. This is achieved by modifying materials to different conformations by changing the structure. Since Faraday reported on gold nano-sized form in 1856 , significant contributions in this field have been observed in the late twentieth century with the advancement in technology for the analysis in the nanometer range (1–100 nm). Scanning tunneling microscope (STM) was the beginning of the technology for a better understanding of materials. Many applications have been proposed in nanotechnology. However, the opportunities of nanotechnologies are yet to be explored for potential applications (Soliman et al., 2023). Due to improved surface properties, there is a tremendous deviation in the properties of materials in the nanometer range compared to their bulk. The quantum confinement in nanoparticles leads to quantized energy levels in valence and conduction bands; hence, enhanced electronic and optical properties are exhibited by nanomaterials.

Although chemically synthesized nanostructures have been used during various stages of civilization, nature has its own processes for synthesizing nanomaterials. The idea of biosynthesis of nanoparticles has evolved from the need for the synthesis of nanoparticle processes and the knowledge of metal bioremediation . Total potential should be investigated to assess against either physical techniques or concoction strategies for various applications. In liquid suspensions, the strength of nanoparticles is significantly improved within sight of biomolecules . Notably, the biosynthesis of nanoparticles has attracted attention due to their reliable and eco-friendly nature. Biosynthesis of nanoparticles offers controlled size and morphology due to the slow rate of formation of nanoparticles and its stabilization due to dilution with medium and steric hindrance due to attached molecules (Patil et al., 2023).

The application of nanotechnology in biological fields is known as nanobiotechnology. It is a multidisciplinary field that currently recruits approaches, technology, and facility available in conventional and advanced avenues of engineering, physics, chemistry, and biology . Medicinal nanotechnology applications include molecular imaging, cancer detection, and therapeutic application, in vivo sensors, X-ray absorbers, and so on, which have been explored further. Other important nanotechnology applications are for the cultivation, processing, and packaging of food due to its antimicrobial property . The utilization of nanotechnology is noticeable in each circle of life . Two metallic nanoparticles, namely silver and gold, have been reported widely in the literature for various applications.

Silver is one of the most studied nanometals . It shows antimicrobial properties similar to silver ions and also exhibits antibacterial activity. Silver-based compounds as a source of silver ions have been used in antimicrobial applications. This phenomenon is called the oligodynamic effect. The growth of a wide range of microorganisms is hindered in the silver and silver compounds. Thus, the enormous importance of silver as new antibacterial material has been observed. Gold nanoparticles also demonstrate antimicrobial, antibacterial, and anticancer properties similar to gold ions . The growth of a wide range of microorganisms is hindered in the gold and gold compounds-thus, the enormous importance of gold nanoparticles as new antibacterial material has been observed (Saha and Dutta Gupta., 2016). It has been reported that reductases might cause the reduction of silver (and gold) ions to elemental silver (and gold) in the plant, bacteria, algae, and fungi systems . The high surface area to volume ratio of silver/gold nanoparticles leads to a high number of silver/gold atoms exposed to the environment. This causes effective interaction of nanoparticles on the surface of other particles and, in turn, in contact with microorganisms. The small nanoparticles (1–10 nm) may be transported through the cell membrane to reach within the cell and disrupt the cell .

The silver and gold nanoparticles show antimicrobial properties against different species of fungus and bacterium .The size and morphology of the nanoparticles affect antimicrobial activity. The silver nanoparticles enhance the antimicrobial property of the antibiotics . A possible health hazard in humans is probably due to the accumulation of silver nanoparticles.

The accumulation of nanoparticles in the tissue has been observed that can be hazardous . The influence of nanoparticles as a catalyst in reactions, especially in the anaerobic decomposition process, can be extended to industrial processes. The anticipated impact of silver nanoparticles on well-being recommends considering the use of silver nanoparticles for the constituent of the ink .

Very few studies have been conducted for silver-gold bimetallic nanoparticles. In a competitive process involving both silver and gold ions, the reduction of gold ions is accelerated and is an important feature. Silver particles are relatively small and do not form a uniform layer around the gold nanoparticles; otherwise, this would have led to considerable damping of the gold surface plasmon band. Silver-gold bimetallic nanoparticles are effectively shown to be a catalyst for many reactions (Sinha et al., 2023). Large bimetallic Au-Ag particles of 50–500 nm was formed with some cubic structure, possibly due to interactions between the bioorganic capping molecules bound to the gold and silver nanoparticles, while pure Ag particles were smaller with 15–90 nm and predominantly spherical. Core-shell bimetallic nanoparticle formation is also possible. The biosynthesis of silver nanoparticles, like any inorganic nanoparticles, requires three important steps, namely, the reduction of silver ions, crystal nucleation, and crystal growth . The first step is the bioreduction of silver ions may be due to either enzymatic reactions or the effect of some reducing compounds or a combination of both. Controlled growth of the crystals to nanoparticles and stabilization of nanoparticles are the other two key steps in the synthesis. The biological environment, especially, proteins may be effective in the stabilization of nanoparticles.

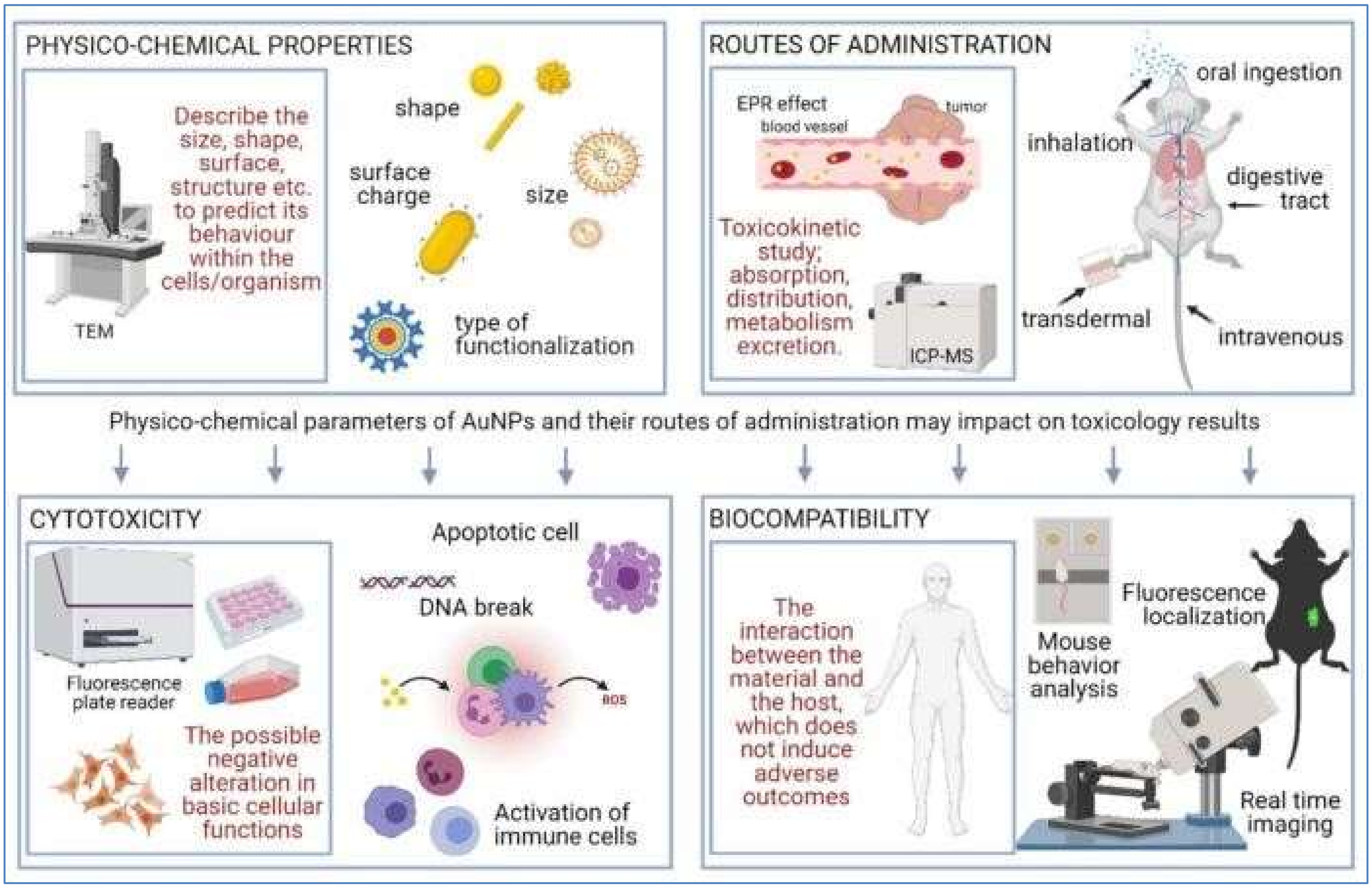

Figure 1 Schematic presentation of the various aspects of AuNPs (Int. J. Mol. Sci. 2021, 22(20), 10952)

The size, shape, and route by which AuNps are administered into the body (e.g., oral, transdermal,etc.) strongly dominance toxicity and caused by unfavourable (apoptosis, behavioural abnormalities, etc.). This particular part of features can be measured at the cell or organism level. EPR, Enhanced Permeability and Retention effect; TEM, transmission electron microscope; ICP- MS, inductively coupled plasma mass spectrometry (Wang et al., 2023).

Indeed, it has been shown that cytotoxicity and biocompatibility are governed by some factors, which include the inherent physicochemical properties of the AuNPs and how they are distributed into the body (Figure 1). For instance, a higher toxicity of the AuNPs was found when oral and intraperitoneal administration was performed as compared to an intravenous injection Nanoparticle cytotoxicity is also strongly related to physicochemical characteristics such as size, shape, surface charge, and aggregation state. Generally, all these highlight that nanoparticle biocompatibility depends closely on various factors, which span from the intrinsic properties of particles, formulation, biological target and even the methodology employed to evaluate their toxicity.

2. Microorganisms' size and particles

The size of AuNPs considerably modulates their uptake by cells and their cytotoxicity. AuNPs penetrate cells mainly via clathrin-mediated endocytosis, and exit cells via exocytosis. The trend for increased uptake of smaller particles may be explained by assuming that smaller particles require less energy to be internalised and must interact with a lower number of cell surface receptors compared with larger particles, and thus, this may impact their toxicity. Generally, the smaller the size of nanoparticles, the higher the cytotoxic effect. A size-dependent cytotoxicity study of polyethyleneglycol (PEG)-coated AuNPs in mice has been reported . Particles with sizesranging between 10 and 60 nm exhibited an adverse effect, such as alteration in cell shape, inhibition of their proliferation, or mutation in DNA, while those with sizes ranging between 5 and 30 nm had no toxicity. Nanoparticle shape is a structural feature that can also modulate their cytotoxicity. AuNPs with various shapes (spherical, rods, triangle, star, octahedron, plate, and prisms shapes) have been synthesised and assessed for their cytotoxicity. Steckiewicz et al. investigated the cytotoxicity of rods, stars, and spherical AuNPs on human fetal osteoblast hFOB 1.19 and pancreatic duct cell hTERT-HPNE cell lines. AuNP rods were the most toxic to human cells, while AuNP spheres appeared to be the safest. Wang et al. reported that AuNPs nanorods were highly toxic in comparison to AuNP hexapods. This highlighted that the cytotoxicity of AuNPs was shape-dependent. According to the different shape, the distribution of the surface atoms in AuNPs may have changed. Thus, some explanation may be offered by considering the geometry of a sphere in relation to the stars or rods. More atoms at angles and edges may cause stronger interactions with biomolecules. Therefore, the rods and stars (featuring a larger amount of edges and corners) showed toxicity, which is often not observed for spherical nanoparticles.

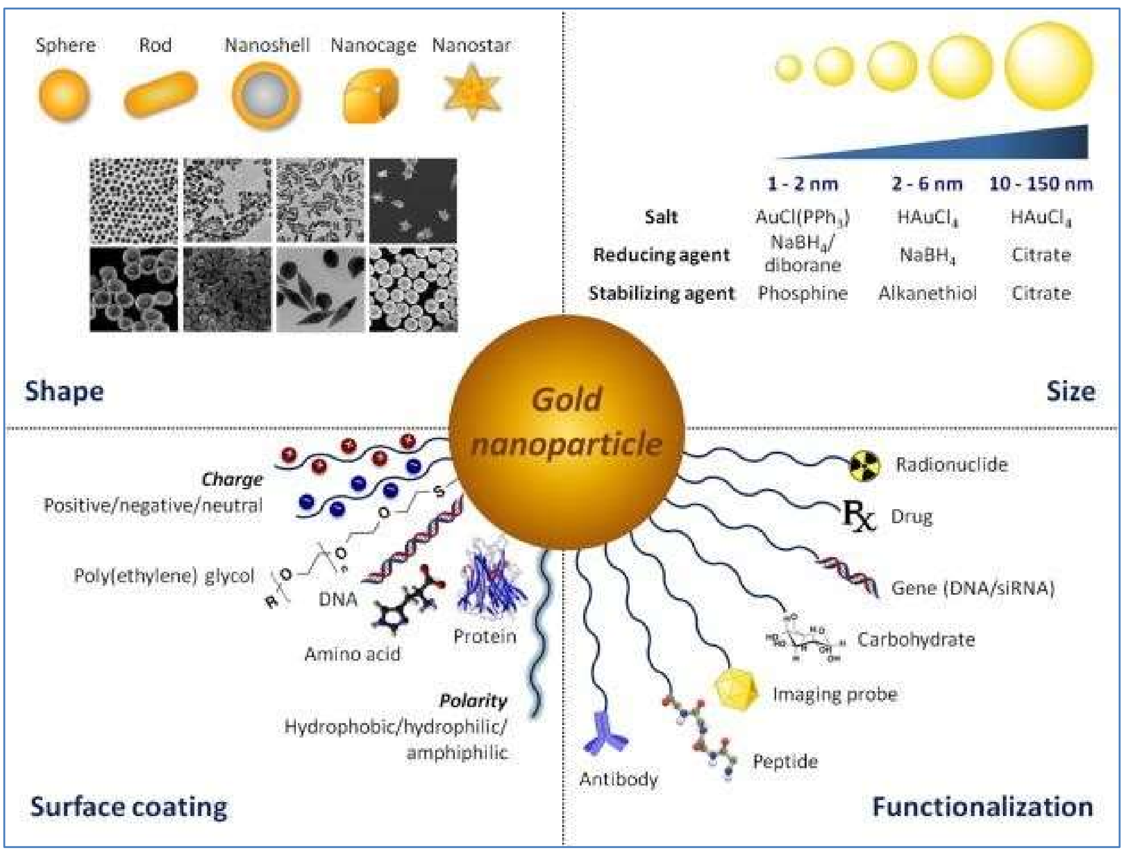

Figure 2 Gold Nanoparticles for applications in cancer radiotherapy: Mechanisms and recent advancements

Species	Size and shape	Bioactivity
Nuts extracts	13.7 nm, spherical	Catalytic and antioxidant
M. calabura fruits	27 nm, spherical	No activity reported
Mangifera indica seed	46.8 nm, spherical	Antibacterial and antiangiogenic
A. bettzickiana	80–120 nm, spherical	Antibacterial and cytotoxic
A. nigra leaves	21.52 nm, spherical	Antibacterial and antioxidant
Coleous forskohlii	35.5 nm, spherical	Antimicrobial and antioxidant
Elettaria cardamomum	15.2 nm, spherical	Antioxidant and antibacterial
Rhazya stricta	30–60 nm	Antibacteria
Crescentia cujete L. Leaf	32.9 nm, spherical, triangular, hexagonal	Anticancer
Paederia foetida Linn.	10–50 nm, irregular	Antimicrobial
Cannonball fruit	25 ± 6 nm, spherical	Antioxidant
Mimosa pudica	12.5 nm, spherical	Anticancer
Coleus aromaticus	28 nm, spheroid	Antibacterial and antiradical
Areca catechu nut	13.7 nm, spherical	Antibacterial and antioxidant

Table 1 Gold Nanoparticles from different plants having different size and its activity (Donga et al., 2020)

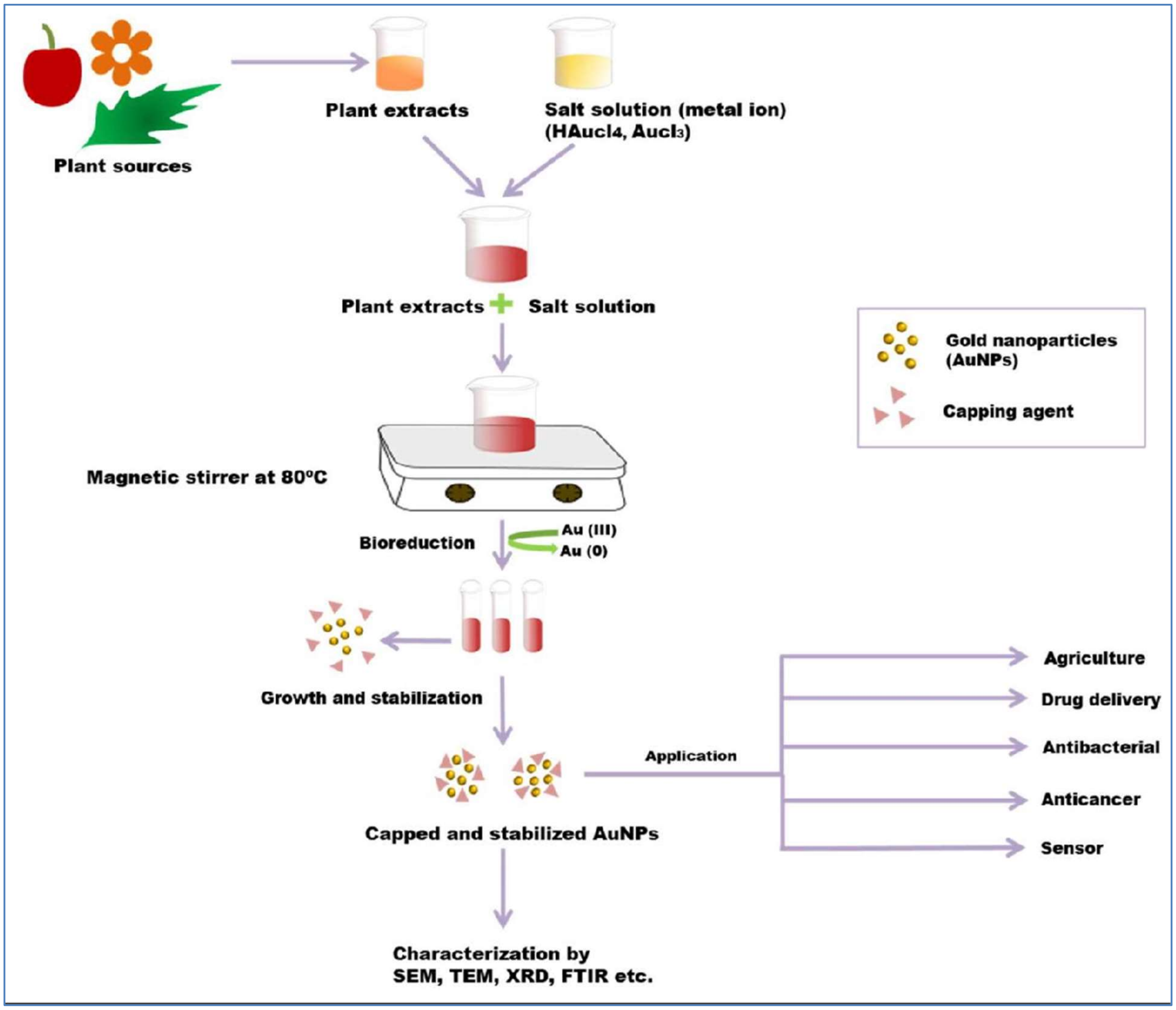

Figure 3 Green synthesis of AuNPs from a plant

3. Application of gold nanoparticles

Gold nanoparticles, for example, may be used in air cleaning, including the removal of odours and harmful carbon monoxide from rooms, emission management, water purification, power cells, and critical medical applications. Because of their small scale, these particles can enter tissues and attack immune cells, like lymphoid tissues, rendering them potentially useful in immunotherapy. Even though a broad number of medicinal nanoparticles are in (pre-clinical) usage for diagnostic and therapeutic applications, their role on the immune system in terms of particle properties are still poorly known. Researchers worked on vital medical technologies (Fernández et al., 2015) which will be addressed later.

- **Anticancer therapy**

Cancer becomes greatest critical soundness problems, the most reason of death in the globe. Significant developments in nanomedicine have given rise to cancer detection and treatment. Due to low toxicity of AgNPs compared to other metal nanoparticles, it showed a predominant preference in medical applications, especially due to low toxicity. Gold nanoparticles also shown outstanding diagnostic and therapeutic uses, including biosensors, targeted distribution of anticancer medications, and enzyme-linked immunosorbent assays. Gold nanoparticles (AuNPs) with increased absorption and scattering properties, optical tenability, and specific tumour targeting competence (Anticancer Activity) for cancer care. Through the advent of chemical synthesis technologies, AuNPs of diverse shapes and sizes with desired properties that can obtain multimodal cancer therapy with extended anti-tumour activity can be synthesized. AuNPs are classified into five main types: gold nanorods, gold nanotubes, gold nanospheres, nanostars, and gold nanocages of different sizes for various applications. The example uses nano-shells to combat cancerous tumours. Gold-shells are tiny balls that are coated with a thin film of nanogold. Nano-shells and nanogold are injected inside the body and aggregated into the tumour, then an infrared ray is applied to the tumour region so that these rays move through healthy tissues safely, however heat the nanoscale shells of gold, so that their temperature rises and the tumour is killed without sacrificing healthy cells. Successful treatment, with minimal side effects. The potential role of AuNPs in scientifically validated cancer therapies such as Chemo-Radio-Therapy (CRT), Thermo-Chemo-Therapy (TCT), Thermo-Radio-Therapy (TRT), Thermo-Chemo-Radio-Therapy (TCRT), and Gene Therapy (GT). Each counselling has a specific purpose in the recovery and has a distinct disadvantage or benefit (Deymehkar et al., 2018). AuNPs are used/1in ultra- sensors and imaging-based methods for the treatment of severe diseases because of their significant optical properties sensitive.

- **Drug delivery**

Precise delivery of nano-vehicles to diseased tissues, monitoring the rate and area of release of drugs, enhancing drug bioavailability at the goal site, improving drug solubility and stability are few of the attractive features of medication by the use of nanoparticles that reduced mortality. Liposomes, polymers, dendrimers, and metallic nanoparticles have all been used in medicine, but AuNPs have exceptional properties that make them the ideal drug delivery scaffold. AuNPs have easy preparation, are bioinert, and are non-toxic, making them suitable for nano carrier building. The manufacturing tenability of AuNPs allows for the development of particles of varying core diameters and complete power over size dispersion. For example, after chemical therapy, cancer cells become insensible as effect of repeated drug administration, nanoparticles are capable to raise the accumulation of intracellular drugs due to their power to target and distribute more specific drugs. Doxorubicin (DOX)-linked AuNP scans help with medication aggregation and retention in (multi-drug-resistant MCF-7 / ADR cancer). As a consequence, enhanced intracellular DOX concentration results in superior cytotoxicity in cells when opposed to free doxorubicin (Beik et al., 2019).

- **Nano-sensor and biomarker**

It is important to calculate the ionizing radiation level of therapeutic radiation, which depends on precise and fast radiation measurements. A new and highly sensitive nano-sensor for Gamma detection is created, with single-stranded DNA fragments serving as "radiation-sensitive data" and gold nanoparticles serving as "signal reporter." Under optimal conditions, the radiation nano-sensor has outstanding linearity in the 0–100 Gy dose scale. A quick and effective approach that provides a different path for the Gamma-radiation "dosimeter," which is aninstrument used to calculate the absorbed dose of ionizing radiation and could have implications for radiation-induced biological consequences, such as the Chernobyl catastrophe

.MicroRNAs (miRNAs) are small non-coding regulatory RNA molecules that have 19 to 22 nucleotides. It can be used as a biological marker because of its excellent early disease detection features, and it can be detected in a variety of bodily secretions and samples collected. For example, studying the expression of renal microRNAs may help in the early detection of a major cause of kidney failure (diabetic nephropathy) .There is no role was documented either in obesity or type 2 diabetes-mellitus . However, due to their unique characteristics or low quantities, they are highly challenging to identify. The use of positively charged gold nanoparticles significantly improves the performance of miRNA biosensors(Gauglitz, 2020, Nossier et al., 2020).

- **Antimicrobial agents**

It is possible that the use of gold nanoparticles as new antibacterial agents may provide a viable alternative to the current methods of limiting or inhibiting the growth of many pathogenic species. The gold nanoparticles synthesized with the help of *Solanumnigrum* leaf extract were expected to have free radical scavenging action as well as antibacterial static agents, which they achieved. The DPPH radical and hydroxyl radical scavenging abilities of these nanoparticles were demonstrated. These nanoparticles also/ 1 greatly/ 1 suppressed/ 1 the/ 1 growth/ 1 of pathogenic *Staphylococcus saprophyticus* and *Bacillus subtilis* (Gram-positive bacteria), as well as *Escherichia coli* and *Pseudomonas aeruginosa* (gram-negative bacteria) . An investigation of the antibacterial efficacy of *Hibiscus cannabinus* stem extract mediated gold nanoparticles against *P. aeruginosa* and Staphylococcus aureus was undertaken. The antibacterial impact was stronger in the case of *P. aeruginosa*, which could be owing to electrostatic interaction between positively charged nanoparticles and negatively charged microbe cell surfaces .The antibacterial activity of green synthesised gold nanoparticles derived from the leaf extract of *Euphorbia hirta* against bacterial strains of *Escherchia coli*; *Pseudomonas aeroginosa,* and *Klebsiella pneumonia* was investigated using the minimal inhibitory concentration (MIC) method, and it was discovered that they were extremely effective against these bacteria .

- **Colorimetric sensing**

Colorimetric usage of AuNPs in sensing is one of the most promising analytical approaches for recognizing analytes and detecting biomolecules such as amino acids, peptides and proteins, nucleic acids, inorganic ions, and enzymes. The key mechanism is that while the lengths between the antiparticles are smaller than the average diameter of the AuNPs, the colour changes from red to blue, which is readily detectable through the naked eye. The track added to the sensors can be divided into two strategies: red change and blue shift in absorption, which result in AuNP aggregation and disaggregation. The UV–vis spectrophotometer may be used to record the results(Qin et al., 2018) .

- **Applications of nanoparticles into plants**

AuNPs have been recommended for use in a variety of agricultural crops, as well as in the germination of seeds from endangered plant species . The effect of AuNPs synthesized utilizing Terminalia arjuna fruit extract on the germination of Gloriosasuperba seeds and the growth of the plant's leaves has been investigated. AuNPs were found to have a beneficial effect on seed germination, node elongation, and vegetative growth of plants. Gloriosasuperba seed germination and vegetative growth were shown to be strongly correlated with the concentration of AuNPs in the environment. Moreover, it has been observed that spraying AuNPs at concentrations of 10 and 25 mg/L on Brassica juncea plants can increase the quantity of chlorophyll (Arora et al., 2012) . Finally, we can conclude that AuNPs have favourable impacts on plant growth and development.

References

1. Ahmad, A., Wei, Y., Ullah, S., Synthesis of phytochemicals-stabilized gold nanoparticles and their biological activities against bacteria and Leishmania, Microbial Pathogenesis., 2017, 110, 304–312.

2 . Ai J., Biazar E., Jafarpour M., Montazeri M., Majdi A., Aminifard S., Zafari M., Akbari H.R., Rad H.G. Nanotoxicology and nanoparticle safety in biomedical designs. Int. J. Nanomed., 2011, 6, 1117–1127.

3. Ali, M., Nelson, A.R., Lopez, A.L. & Sack, D.A., 2015. Updated global burden of cholera in endemic countries. PLoS neglected tropical diseases., 2015, 9(6).

4. Banerjee K., Das S., Choudhury P., Ghosh S., Baral R., Choudhuri S.K. A Novel Approach of Synthesizing and Evaluating the Anticancer Potential of Silver Oxide Nanoparticles in vitro. Chemotherapy., 2017, 62, 279–289.

5. Bantz, C., Koshkina, O., Lang, T., Galla, H. J., Kirkpatrick, C. J., Stauber, R. H., & Maskos, M.. The surface properties of nanoparticles determine the agglomeration state and the size of the particles under physiological conditions. Beilstein journal of nanotechnology, 2014, 5(1), 1774-1786.

6. Baruah, D., Goswami, M., Yadav, R. N. S., Yadav, A., & Das, A. M. Biogenic synthesis of gold nanoparticles and their application in photocatalytic degradation of toxic dyes. Journal of Photochemistry and Photobiology B: Biology., 2018, 186, 51-58.

7. Bhuyan, B., Paul, A., Paul, B., Dhar, S. S., & Dutta, P. *Paederia foetida* Linn. promoted biogenic gold and silver nanoparticles: synthesis, characterization, photocatalytic and in vitro efficacy against clinically isolated pathogens. Journal of Photochemistry and Photobiology B: Biology., 2017, 173, 210-215.

8. Carnovale C., Bryant G., Shukla R., Bansal V. Identifying Trends in Gold Nanoparticle Toxicity and Uptake: Size,/1Shape,/1Capping/1Ligand,/1and/1Biological/1 Corona. ACS Omega., 2019. 4, 242–256.

9. Daniel, M. C., & Astruc, D. Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology. Chemical reviews, 2004, 104 (1), 293-346.

10. Desai, M. P., Sangaokar, G. M., & Pawar, K. D. Kokum fruit mediated biogenic gold nanoparticles with photoluminescent, photocatalytic and antioxidant activities. Process biochemistry, 2018, 70, 188-197.

11. Donga, S., Bhadu, G. R., & Chanda, S. Antimicrobial, antioxidant and anticancer activities of gold nanoparticles green synthesized using Mangifera indica seed aqueous extract. Artificial Cells, Nanomedicine, and Biotechnology, 2020, *48*(1), 1315-1325.

12. Dutta Gupta, S., N. Saha, A. Agarwal, and V. Venkatesh. "Silver nanoparticles (AgNPs) induced impairment of in vitro pollen performance of

Peltophorum pterocarpum (DC.) K. Heyne." *Ecotoxicology*, 2020, 29, 75-85.

13. Gialanella, S., & Lutterotti., Nanocrystalline metallic materials. In Nanoclusters and nanocrystals, American Scientific Publisher., 2003, 1-52.

14. Huang Y.-W., Cambre M., Lee H.-J. The Toxicity of Nanoparticles Depends on Multiple Molecular and Physicochemical Mechanisms. Int. J. Mol. Sci., 2017, 18, 2702.

15. Jeevanandam, J., Barhoum, A., Chan, Y. S., Dufresne, A., & Danquah, M. K. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein journal of nanotechnology., 2018, 9(1), 1050-1074.

16. Kohane D.S., Langer R. Biocompatibility and drug delivery systems. Chem. Sci., 20101 441–44.

17. KS, Uma Suganya, K. Govindaraju, D. Prabhu, C. Arulvasu, V. Karthick, and Niranjan Changmai. Anti-proliferative effect of biogenic gold nanoparticles against breast cancer cell lines (MDA-MB-231 & MCF-7). Applied Surface Science., 2016, 371, 415-424.

18. Kus-Liśkiewicz, M., Fickers, P. & Ben Tahar, I. Biocompatibility and cytotoxicity of gold nanoparticles: recent advances in methodologies and regulations. International journal of molecular sciences., 2021. 22(20) 10952-10954.

19. Mohanpuria, P., N. K. Rana, and S. K. Yadav, “Biosynthesis of nanoparticles: technological concepts and future applications,” Journal of Nanoparticle Research, 2008, 10(3), 507–517.

20. Mohapatra, D. P., F. Gassara, & S. K. Brar. "Nanoparticles—Production and Role in Biotransformation." Journal of Nanoscience and Nanotechnology., 2011, 11 (2), 899-918.

21. Naahidi S., Jafari M., Edalat F., Raymond K., Khademhosseini A., Chen P. Biocompatibility of engineered nanoparticles for drug delivery. J. Control. Release., 2013, 166, 182–194.

22. Nagalingam, M., V. Nagarajan Kalpana, & A. Panneerselvam. Biosynthesis, characterization, and evaluation of bioactivities of leaf extract-mediated biocompatible gold nanoparticles from *Alternanthera bettzickiana*. Biotechnology Reports., 2018. 19.

23. Ng C.T., Tang F.M.A., Li J.J.e., Ong C., Yung L.L.Y., Bay B.H. Clathrin-Mediated Endocytosis/1of/1Gold/1Nanoparticles/1In/1Vitro. Anat. Rec., 2015, 298, 418–427.

24. Patil, T., Gambhir, R., Vibhute, A., & Tiwari, A. P. Gold nanoparticles: Synthesis methods, functionalization and biological applications. Journal of Cluster Science., 2023, 34(2), 705-725.

25. Pradeep, T. Nano: the essentials: understanding nanoscience and nanotechnology. McGraw-Hill Education, 2007.

26. Rajan, A., Rajan, A. R., & Philip, D. *Elettaria cardamomum* seed mediated rapid synthesis of gold nanoparticles and its biological activities. OpenNano, 2017, 2, 1-8.

27. Rajan, A., Vilas, V., & Philip, D., Studies on catalytic, antioxidant, antibacterial and anticancer activities of biogenic gold nanoparticles. Journal of Molecular Liquids, 2015, 212, 331-339.

28. Saha, N., & Gupta, S. D. (2016). Biogenic synthesis and structural characterization of polyshaped gold nanoparticles using leaf extract of Swertia chirata along with process optimization by response surface methodology (RSM). Journal of Cluster Science, 27, 1419-1437.

29. Saha, N., Astray, G., & Dutta Gupta, S./1Modelling and optimization of biogenic synthesis of gold nanoparticles from leaf extract of Swertia chirata using artificial neural network. Journal of Cluster Science, 2018, *29*, 1151-1159.

30. Saravanan A, Kumar PS, Karishma S, Vo DN, Jeevanantham S, Yaashikaa PR, George CS. A review on biosynthesis of metal nanoparticles and its

environmental applications. Chemosphere., 2021, 264, 128580.

31. Sathishkumar, G., Jha, P. K., Vignesh, V., Rajkuberan, C., Jeyaraj, M., Selvakumar, M., & Sivaramakrishnan, S. Cannonball fruit (*Couroupita guianensis*, Aubl.) extract mediated synthesis of gold nanoparticles and evaluation of its antioxidant activity. Journal of Molecular Liquids., 2016, 215, 229-236.

32. Seetharaman, P., Chandrasekaran, R., Gnanasekar, S., Mani, I., & Sivaperumal, S. Biogenic gold nanoparticles synthesized using *Crescentia cujete* L. and evaluation of their different biological activities. Biocatalysis and agricultural biotechnology., 2017, 11, 75-82.

33. Sinha, R., Das, S. K., Ghosh, M., & Chowdhury, J. Self-assembled gold nanoparticles on the serpentine networks of Calf Thymus-DNA Langmuir-Blodgett films as efficient SERS sensing platform: Fabrication and its application in thiram detection. *Materials Chemistry and Physics*, 2023. *295*, 127140.

34. Soliman, Mohamed KY, Salem S. Salem, Mohammed Abu-Elghait, and Mohamed Salah Azab. Biosynthesis of silver and gold nanoparticles and their efficacy towards antibacterial, antibiofilm, cytotoxicity, and antioxidant activities." *Applied Biochemistry and Biotechnology* 2023, 195 (2) 1158-1183.

35. /1Sridharan, K., Jang, E., Park, J. H., Kim, J. H., Lee, J. H., & Park, T. J. Silver Quantum Cluster (Ag9)-Grafted Graphitic Carbon Nitride Nanosheets for Photocatalytic Hydrogen Generation and Dye Degradation. Chemistry–A European Journal, 2015, 21(25), 9126-9132.

36. Stark, W. J., Stoessel, P. R., Wohlleben, W., & Hafner, A. J. C. S. R. Industrial applications of nanoparticles. Chemical Society Reviews, 2015, 44(16), 5793-5805.

37. Stark, W.J., P. R. Stoessel, W. Wohlleben, & A. Hafner, "Industrial applications of nanoparticles," Chemical Society Reviews, 2015, 44 (16), 5793–5805.

38. Steckiewicz K.P., Barcinska E., Malankowska A., Zauszkiewicz-Pawlak A., Nowaczyk G., Zaleska-Medynska A., Inkielewicz-Stepniak I. Impact of gold nanoparticles shape on their cytotoxicity against human osteoblast and osteosarcoma in in vitro model. Evaluation of the safety/1of/1use/1and/1anti-cancer/1potential. J./1Mater./1Sci./1Mater./1Med., 2019, 30:22.

39. Sukhanova A., Bozrova S., Sokolov P., Berestovoy M., Karaulov A., Nabiev I. Dependence of Nanoparticle Toxicity on Their Physical and Chemical Properties. Nanoscale Res. Lett., 2018, 13:44.

40. Vilas, V., Philip, D., & Mathew, J. Biosynthesis of Au and Au/Ag alloy nanoparticles using *Coleus aromaticus* essential oil and evaluation of their catalytic, antibacterial and antiradical activities. Journal of Molecular Liquids, 2016, 221, 179-189.

41. Villiers C., Freitas H., Couderc R., Villiers M.-B., Marche P. Analysis of the toxicity of gold nano particles on the immune system: Effect on dendritic cell functions. J. Nanopart. Res., 2010, (12), 55–60.

42. Vimalraj, S., Ashokkumar, T., & Saravanan, S. Biogenic gold nanoparticles synthesis mediated by Mangifera indica seed aqueous extracts exhibits antibacterial, anticancer and anti-angiogenic properties. Biomedicine & Pharmacotherapy., 2018 105, 440-448.

43. Vimbela GV, Ngo SM, Fraze C, Yang L, Stout DA. Antibacterial properties and toxicity from metallic nanomaterials. Int J Nanomedicine., 2017, 12, 3941-3965.

44. Wang S., Lu W., Tovmachenko O., Rai U.S., Yu H., Ray P.C. Challenge in Understanding Size and Shape Dependent Toxicity of Gold Nanomaterials in Human Skin Keratinocytes. Chem. Phys. Lett.. 2008, 463,145–149.

45. Wang, L., Ge, S., Gao, C., Yan, H., Wang, J., Jia, J., & Wu, Q.. One-pot synthesis of gold-copper nanoparticles mediated by silk fibroin peptides: Peroxidase-like properties and its application in antioxidant detection. 2023, *Microchemical Journal, 185*, 108250.

46. Xie X., Liao J., Shao X., Li Q., Lin Y. The Effect of shape on Cellular Uptake of Gold Nanoparticles in the forms of Stars, Rods, and Triangles. Sci. Rep., 2017, 7. 3827.

47. Zhang X.-D., Wu D., Shen X., Liu P.-X., Yang N., Zhao B., Zhang H., Sun Y.-M., Zhang L.-A., Fan F.-Y. Size-dependent in vivo toxicity of PEG-coated gold nanoparticles. *Int. J. Nanomed.* 2011, 6, 2071–2081.

48. Zhang X.D., Wu H.Y., Wu D., Wang Y.Y., Chang J.H., Zhai Z.B., Meng A.M., Liu P.X., Zhang L.A., Fan F.Y. Toxicologic effects of gold nanoparticles in vivo by different administration routes. *Int. J. Nanomed.* 2010, (5) 771–781.