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Advance Research on Phytosynthesis of Gold Nano Particles and its Biomedical Application -A Review

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ABSTRACT

Nanoscience and Nanotechnology are attracting a lot of interest nowadays due to their unique characteristics and wide range of applications. Plant materials are especially interesting in the synthesis and production of gold nanoparticles (AuNPs). Various plants have been highlighted in this article for the green synthesis of AuNPs in faster and more efficient manner than using conventional methods. A number of reaction variables, including concentration of gold precursor and plant extract, is found to affect the synthesis, characterization, and uses of AuNPs. The morphological characteristics of synthesised AuNPs need to be assessed in order to determine their potential in biomedical applications. With a focus on research from the last five years, the purpose of this study is to review and highlight the utilisation of green synthesis techniques mainly from various medicinal plant extract for the production of AuNPs. Current research of plant mediated AuNPs having potential of antimicrobial, antitoxic and anticancer activities has also been explored.

Key Words:Green synthesis, plantextract, goldnanoparticles, biocompatibility, applications

INTRODUCTION

Recently, a global assessment of recent breakthroughs reveals a great deal of interest in the subject of nanotechnology(Elahi *et al.*, 2018).Nano research has become a very significant area(Hughes*et al.*,2015) of study due to the hunt for a permanent solution to enhance human health condition(Nithin*et al.*,2023)through illness diagnostics and the creation of revolutionary medicines(Patil*et al.*, 2023).Numerous unusual physical and

chemical characteristics of materials at the nanoscale level have sparked the interest like high surface-to-volume ratio and an increase in surface activity in relation to their bulk components when using the same compounds(Suslick*et al.*,1988).The quantized energy levels in the conduction and valence bands caused by nanoparticle quantum confinement povide nanomaterials their improved electronic and optical characteristics(Assatsea*et al.*,2019).

On one side, the physical and chemical processes used in nanotechnology result in nanoparticles with regulated morphologies and distinctive features, in contrast, such procedures are expensive(Saha*et al.*,2012)and hazardous to the environment(Xu*et al.*,2018).To deal with these problems,biological nanoparticle synthesis has grown in popularity(Lee*et al.*,2020) and considered a green and environmentally beneficial strategy in recent years(Kalimuthu*et al.*,2020).Research investigations currently being conducted in this field are concentrating on the nanoparticle bio-fabrications (Barabadi*et al.*,2017).Many ways have been developed to make an impact in this field by utilising green technologies, such as the synthesis of nanoparticles (NPs) from plant extract(Vaid*et al.*,2020).

Despite the fact that the chemical production of metallic nanoparticles is a common technique, the expense and adverse effects of stabilising and reducing agents limit their utilisation(Herizchi*et al*,2016.)These methods rely on the conventionally costly reducing and stabilising substances like sodium citrate, sodium dodecyl sulphate, and sodium borohydrate to reduce metal ions. Additionally, the use of these materials poses a danger to environment as well as human health(Noruzi*et al.*,2015).

As opposed to conventionally manufactured NPs using physicochemical synthetic pathways, the use of natural resources in NP synthesis is chosen to create eco-friendly and sustainable products(Saravanan*et al.*,2020). In comparison to other biological processes, the production of NPs by plants is more advantageous because the cell culture is preserved and maintained without disruption. In contrast to microbes, plant-mediated synthesis is a simple,

one-step process with no risk of mutation(Veerasamy*et al.*,2011).Moreover there is little to no possibility of contamination, and they take less time to produce(Singh*et al.*,2016).Nanomaterials, particularly noble metals, have piqued the interest of researchers because to their little stature and potential applications in a variety of fields that advance mankind(Muddapur*et al.*,2022).For the unique qualities, which include the size and large surface area (Habibullah*et al.*,2021)noble metal NPs, like gold (Au), have most recently been the focus of much investigation(Abid*et al.*,2022).Since ancient times, gold has been employed in medicine, particularly in China and India where it was believed to encourage life span and fertility. Still now it is utilised in various Indian ayurvedic remedies(Yafout*et al.*,2021).Gold (Au) belongs to block-d transition metal having higher atomic number. The gold nanoparticles exhibit significant dispersion as a result of their tiny size and substantial surface area. It is a good choice for biological applications due to its resistance to aerial oxidation, moisture, and mild acids as well as biocompatibility especially in the fields of drug delivery, cell targeting, tumour detection(Zheng*et al.*,2016)biomolecular imaging, cancer treatment, antibacterial, biological and chemical sensing(Barai*et al.*,2018).

This review summarises current research on the phytosynthesis of gold nanoparticles with exploring some of their biomedical applications like antimicrobial, antioxidant, and anticancer potentials of these nanoparticles.

General Procedure for Nanoparticle Synthesis

Plant Extraction: The standard preparation method for plant-AuNPs comprises collecting various plant components washing in water to get rid of dust and contaminants, solvent extraction, fine-mesh filtration, dryingor powdering, followed by synthesis.Certain fundamental criteria must be considered while executing an extraction procedure because they influence the effectiveness of an extract. The extraction of the relevant components is highly reliant on the selected section of both the plant material and solvents, which must be evaporable and incapable of chemically modifying the solutes(Pandey*et al.*,2014).

Choosing an extraction method necessitates consideration of the extraction length, solvent pH, temperature, solvent-to-sample ratio and raw material particle size. These variables can cause changes in the metabolic composition of the extracts(Belokurov *et al.,*2019) .

Extracts can be derived from a variety of plant parts fresh or dry including leaves, stem, bark, roots, twigs, peels, fruits, pulp(Yallappa *et al.,*2015)seeds, flowers, latex, essential oils, or whole part(Filip *et al.,*2015).

Synthesis of AuNPs: There are many methods to synthesise Au Nps from plant extract but here we only focus on the simple,rapid one pot hydrothermal method.Usually, diverse morphologies of plant-AuNPs have been created by combining metal salt ($HAuCl_4$) with plant extracts. Generally two processes are involved in one-pot hydrothermal chemical reduction techniques for producing plant-AuNPs: reduction of metal salt using reducing agents, followed by stabilisation with capping agents.In general, the reaction occurs within few minutes or several hours(Zarzuela*et al.,* 2018).Scaling up of the reaction is possible by altering the reaction parameters, particularly the pH and temperature as well as the concentration of $HAuCl_4$ and plant extracts(Qiao*et al.,* 2021).

Plant secondary metabolites function as a reducing and stabilising agent.Plant extract phytochemicals include active substances like phenolic compounds, flavonoids, alkaloids,(Yu*et al.,* 2019)terpenoids,polysaccharides, reducing sugars, amino acids, tannins, saponins, steroids, vitamins, proteins, ketones, and functional groups(Zhang *et al.,* 2020) such as hydroxyls carboxyls, and aldehydes which plays an important role in reduction of Au^{3+} to $Au^0$to form plant-AuNPs(Sun*et al.,*2018).To produce plant-AuNPs, several plant components of various medicinal plants are being utilised.

Characterization: Different Analytical and spectral approaches were utilised to determine the shape, size, crystalline structure, elemental composition and surface plasmon resonance peak. Initially, scanning electron microscopy (SEM), field-emission scanning electron

microscopy (FESEM), transmission electron microscopy (TEM), and high-resolution transmission electron microscopy (HRTEM), Atomic Force Microscopy (AFM) were employed to evaluate the morphology of the generated gold nanoparticles. TEM does not only offers direct images of nanoparticles it equally gives an accurate estimation of their homogeneity(Mourdikoudis*et al.,*2018).SEM gives information about the chemical composition, external morphology, orientation and crystalline structure of AuNPs(Devi*et al.,* 2012).The difference between AFM technique and SEM/TEM is the production of three-dimensional images(Pal *et al.,* 2011)which enable the evaluation of the particle volume and height(Folorunso*et al.,* 2020).

Surface plasmon resonance is a crucial property of gold nanoparticles. The surface plasmon resonance peak of the synthesised gold nanoparticles in the wavelength range of 200-800 nm was observed using a UV-Visible spectrophotometer (UV-Vis). For AuNps particles, surface plasmon resonance occurs in the 510-560 nm region(Patra*et al.,* 2014**).**

A mixture of techniques, including selected area electron diffraction (SAED) and an energy-dispersive X-Ray spectrometer (EDX), were used to determine the elemental composition(Mata*et al.,* 2016).Dynamic light scattering (DLS) and a particle size analyzer (PSA) were utilised to determine the size and dispersive nature of the generated nanoparticles. DLS study analyses the size distribution and measures the surface charges of nanoparticles(Muhamma*et al.,* 2017). In addition to these parameters, the surface charge of the synthesised gold nanoparticles was evaluated using a zeta potential analyzer or zeta sizer (ZP)(Clogston*et al.,*2011). The crystalline nature and structure of gold nanoparticles synthesised utilising plant extracts were investigated using X-ray diffraction (XRD), crystallography, or X-ray photoelectron spectroscopy (XPS)(Mustafa*et al.,* 2017).Raman spectroscopy/surface-enhanced Raman spectroscopy (SERS) technique has been reported to display a remarkable advantages of rapid identification of NPs from their dissolved ions and bulk counterparts over other techniques(Huiyuan*et al.,* 2017).The existence of functional

groups and chemical composition were investigated using Fourier transform infrared spectroscopy (FTIR) at 400-4000 cm^{-1}. The surface residues and functional groups such as flavonoid, phenol, and hydroxyls that adhere to the surface of nanoparticles during their production for effective reduction and stabilisation are identified by FTIR Spectroscopy(Rabeea*et al.,* 2020).

Plant Extract Mediated Synthesis of AuNP: The gold nanoparticles synthesised from plant extracts are very convenient and simplest way owing to the rapid synthesis of gold nanoparticles(Gour*et al.,* 2019).Plant extracts are preferred for the creation of NPs due to the possibility of expansive production, diversity in nanoparticle shape, and size(Javed*et al.,* 2020).Generally the significant shift in pressure and temperature is not necessary in this procedure(Mikhailova*et al.,* 2021).Several types of medicinal plant species are involved in Au NPs green synthesis.Leaf extract of *Piperbetle*was added to $HAuCl_4$ aqueous solution in boiling condition while the colour changed to red from yellow and then purple within five minutes confirming the synthesis of AuNPs.The NP exhibit variety of colours based on their size and shape. The concentration of the gold precursor was shown to be a significant determinant of particle dimension, monodispersity, and uniformity. The reason for this was that lots of nucleation sites occur at high concentrations of precursor, and further growth results in a rise in size of particles(Patra *et al.,* 2020).The phennomenon of surface plasmon resonance (SPR) was also studied by acquiring the distinctive peak in the 500-600nm range(Aromal*et al.,* 2012).

Pure dry *Crocus sativus* (saffron) flower stigmas were able to synthesise mostly spherical AuNPs in the size range of 25–35 nm. The results showed that as synthesised nanoparticles from saffron stigma extract are encircled by functional metabolites like carboxylic acid, alcohols, amines, ketones, and aldehydes. Polyphenols existing in stigma extract leads to the reduction and stabilisation of AuNPs. The pH level of the AuNPs solution was varied from 1 to14 at room temperature, and the impact was observed by UV-Visible spectra, in

order to better understand how pH affects the stability of AuNPs. The outcomes demonstrated that AuNPs were more enduring at pH values ranging from 3 to 12.But with increasing acidity and basicity, less stability had been observed owing to the stabiliser (plant extract's) removal from the surface of the gold. In addition, neutral AuNPs were reoxidized by extremely low pH(Alhumaydhi*et al.,* 2021).

TEM images revealed that the green synthesis of AuNpsutilising*Glycyrrhzia glabra* commonly known as licorice, root extract yielded spherical non-aggregated, and homogeneous AuNps. Another major factor that influences the shape and size of nanoparticles is pH. The UV-VIS spectrophotometer was used to measure the absorption spectra of synthesized AuNPs at different pH levels (pH1 to pH6). The results indicated that the most uniform AuNPs were synthesised at pH 5 which was also confirmed by TEM images(Al-Radadi*et al.,* 2021).The majority of the nanoparticles acquire a spherical form and do not aggregate at pH 5. Simple and low-cost one-pot green synthesis of AuNPs were done by Black lemon fruit extracts. The XRD pattern of Au-NPs exhibited a face-centered cubic (fcc) structure. SEM analysis reported the cubic and spherical forms of Au-NPs having different sizes(Mahdi *et al.,*2019)To synthesize *Pistacia chinensis* seed extract nanoparticles the extract was combined with gold salt ($HAuCl_4$) solution in various ratios.After that, the solution was constantly stirred for five hours to optimize the environment for nanoparticle creation. Metallic nanoparticle production may be facilitated by sugars found in plant extract.Twoneoflavone dimers (4-arylcomarin) with outstanding estrogen-like characteristics have been identified from Pistacia chinensis. Plant extract proteins with functionalized amino groups ($-NH_2$) can take part in the metal ion reduction. In order to stabilise and restrict the growth of nanoparticles, capping ligands have a significant function. For reduction of Au^{+3} to Au^0, various concentrations of the extract solution were mixed with a constant concentration of the salt solution. Due to the varied sizes of the generated AuNPs, there was a variable absorbance.The peaks intensity demonstrated the homogeneity of

AuNPs. The maximum absorbance was exhibited by the concentration of salt solution and extract (1: 4), indicating the existence of a higher quantity of AuNPs. It can be concluded that formation of AuNps were concentration dependent(Alhumaydhi*et al.,* 2022).

The eco-friendly production of gold nanoparticles was carried out employing *Ceiba pentandra* bark extract.For varied time intervals, the reduction procedure was incubated.UV-visible absorption spectroscopy was used to monitor the samples for 30days.Maximum absorbance at 535nm was observed after 30days which suggest the completion of bioreduction process.This highlights the fact that the creation of steady plasmonic peaks is caused by a longer reaction period between the biological reductant and gold ions(Brian*et al.,*2020).It was claimed that aqueous fruit peel extract stimulates the synthesis of AuNPs via its reducing enzymes and capping agents such as secondary metabolites from $HAuCl_4$ salt solution. The colour shift from green to ruby red of *Benincasa hispida* peel extract confirmed the development of AuNPs. The synthesised AuNPs have a zeta potential of -26 mV, demonstrating good particle stability. There were no indications of agglomeration in the aquatic dispersion of AuNPs at room temperature during storage, apparently because the electrostatic repulsive forces among the nanoparticles prevent them from approaching one another.(Al Saqr*et al.,*2021).Other than the plant components mentioned above AuNPs have also been created using certain unusual parts of the plant such as essential oils, gall, calus,pulpand latex.Table 1 lists the specific components of various plants employed in the creation of Au NPs.

Mechanism Involved in Plant Mediated Synthesis of AuNPs: In the case of biogenesis (AuNP), many phytochemicals contained in the plant extract, such as phenolic, alkaloid, flavonoid, enzymes, proteins, etc., provide the first step in reducing Au^{3+} to Au^{0}.Additionally, they serve as a stabilising agent for the created nanoparticles(Santhosh*et al.,*,2022).These phytochemicals are responsible for gold precursors reduction as they possess hydroxyl (-OH) functional groups which may transfer electrons to gold ions.Plant

extracts containing hydroxyl functional groups had an improved ability to interact with Au^{3+} ions to produce gold complexes. According to published research, tautomeric conversions of flavonoids from their enol to their keto forms can release reactive hydrogen atoms that can reduce metal ions to produce nanoparticles(Makarov*et al.*, 2014).

The following reactions were suggested as a potential mechanism for the reduction of gold salt in synthesis of AuNPs(Santhosh*et al.*,,2022).

Gold salt Dissociation: $HAuCl_4 = H^+ + Au^{3+} + 4Cl^-$

Oxidation process: $4Cl^- = 2Cl_2 + 4e^-$

Reduction process: $Au^{3+} + 4e^- = Au^0 + e^-$

There are still unanswered concerns regarding the mechanism for the AuNP bioreduction and its stabilisation. In order to describe the mechanism of AuNP synthesis and its impact on the

Plant Name	Part used	Phytoconstituents involved in the reduction	Shape and Size nm	Reaction time	Colour produced	SPR peak (nm)	Reference
Lobelia nicotianifolia	Leaf	OH groups-	Hexagonal and Trinangular 50 -100	6hrs	Red wine	532	(Lava *et al.*, 2020)
Platycodon grandiflorum	Leaf	Flavonoids,saponins, alkaloids, amino acids, proteins, andcarbohydrates	Spherical 15	30min	Brownish red	545	(Anbu *et al.*, 2020)
Eclipta alba	Whole	Phenols	Spherical 26	20 min	Wine red	536	(Vijayakumar *et al.*, 2020)
Cassytha filiformis	Whole	Phenolic -OH	Spherical12	4hrs	Purple	530	Singh *et al.*, 2020)
Polianthes tuberosa	Flower	Amines, phenol, alcohol, ester linkages, and carboxylic acidfunctional groups	Spherical, triangles, pentagons, hexagons, and rods 38.76	60 min	Purple-red	543	((Alghuthaymi *et al.*, 2021)
Piper nigrum	Seed	Carboxylic ketonic group phenols	Spherical and oval 40–60	4hrs	Wine red	550	(Bawazeer *et al.*, 2022)
Linumusitatissimum	Seed	Flavonoids, phenolicacids, and lignans	Spherical and triangle 3.4 - 6.9	6hrs	Ruby red	540	(Al-Radadi *et al.*, 2021)
Cinnamon	Bark	Terpenoids,carbohydrates, flavones, and proteins	Spherical35	30min	Purple red	566	(lMitwalli et al., 2020)
Terminalia	Fruit	Polyphenols	Spherical25	5 min	Ruby red	524	(Nirmala et al., 2021)
chebula Terminalia belerica Phyllanthus emblica							

Ananas comosus and Passiflora edulis	Fruit peel	Phenolic compound, ferulic acid, andvitamin carotenoids and flavonoids	Spherical 20.71 ± 7.44 and18.68 ± 5.55	1hr	Reddish brown dark purple	545	(Pechyen et al., 2021)
Garcinia kola	Pulp	Terpenoids, steroids isoflavonoids, and neoflavonoids	Spherical18 -38	5hrs	Violet	568	(Akintelu *et al.*, 2021)
Allium sativa	Bulb	Organosulfur compounds, saponins, phenolic compounds, and polysaccharides	Spherical6	20 min	Red	537	(M.Villanueva *et al.*, 2019)
Tussilago farfara	Flower bud	Sesquiterpenoids	Spherical18 .20± 4.11	2hrs	Violet	538	(Lee et al., 2019)
Momordica dioica	Root	Alkaloids, triterpenoids, flavonoids, protein, and sugars	Spherical9. 4	10 min	Pink	540	(Naik et al., 2020)
Zingiber officinale	Rhizome	Terpenes, lipids, phenolic compounds,polysaccharides, organic acids, and volatile oils	spherical 15.11 ± 8.5	60min	Purple	530	(Fouda et al., 2022)

shape and size of AuNPs the NP for a variety of applications, more investigation and analysis are suggested.

Table 1: Plant-mediated synthesis of gold nanoparticles with their synthetic parameters

Application of Plant Mediated AuNPs

Antimicrobial Application: Plant mediated AuNPs have recently been widely employed as antimicrobial agents against a variety of microbes.The benefits of AuNP include its great impact, affordability, biocompatibility, and ease of synthesis(Parveen *et al.*, 2016).In this current investigation, AuNPs inhibited a wide range of bacteria, which was achieved through

various mechanisms.The activity of AuNPs have been tested on both the Gram-positive and Gram-negative bacteria though the significant antibacterial action of AuNPs against Gram-negative bacteria may be due to the thin layer of peptidoglycan in the bacterial cell wall permitting AuNPs to adhere on the cell membrane by penetrating the cell wall, as well as interact with DNA and proteins (Nishanthi *et al.*, 2019).On the other hand, the cell wall of Gram-positive bacteria have a thick layer of peptidoglycan composed of short peptides cross-link linear polysaccharide chains, making the structure more rigidpreventing AuNPs from passing through it.As a result, higher concentrations of nanoparticles are necessary for Gram-positive bacteria. According to Sharma et al, AuNPs were discovered to be efficacious against *Bacillus subtilis* bacterial strains only at high dosage rates(Sharma *et al.*, 2019).

Another way of bacterial inhibition includes the binding of AuNPs with SH moeities (thiol) of proteins, which causes oxidative phosphorylation to be disrupted and DNA replication to be hampered.Because of the electrostatic attraction between negatively charged cell membrane and positively charged gold nanoparticles, the Au NPs may bond to the cytoplasmic membrane and damage the bacterial cell.Au NPs may trigger the generation of reactive oxygen species, resulting in the degradation of DNA and proteins in bacteria cells and, eventually, cell death(Balasubramanian *et al.*, 2020). It was shown that the AuNPs developed in the investigation had an inhibitory impact on low concentrations of various gramme (+) and gramme (-) bacteria when contrasted with further research in the available literature(Keskin *et al.*, 2021).

The binding of AuNPs to the surfaces of microbes via electrostatic interactions may also contribute to their antifungal activity.Reactive oxygen species (ROS) will be produced as well as the fungal growth will be inhibited by such reaction.This is also a fact that where AuNPs demonstrated potential antimicrobial properties, in most of the cases the NPs were spherical in shape and tiny in size.

The increased membrane permeability and consequent cell damage might be attributed to the smaller size with high surface area of AuNPs(Rotimi *et al.*, 2019).Recent investigation summarises how phytoconstituents from various plant components have effected the growth of microorganisms.

Table 2: Recent progress of the antimicrobial properties of some plant mediated AuNPs

Plant Name	**Parts used**	**Shape and Size nm**	**Phytocompound present for reduction**	**Method of Assay**	**Target Pathogen**	**Zone of Inhibition (mm) / MIC**	**Reference**
Jasminum auriculatum	Leaf	Spherical 8–37	Terpenoids, flavonoids, tannins, steroids,alkaloids and polyphenols	Disc diffusion	(*Streptococcus pyogenes, Staphylococcus aureus, Escherichia coli and Klebsiella pneumonia*) and fungus (*Candidaalbicans, Aspergillus fumigatus, Lecanicilliumlecanii and Trichoderma viride).*	*Streptococcus pyogenes* 12 at conc. 30 µl Escherichia coli 12 at conc. 30 µl Trichoderma virideLecanicilliumlecanii 5 at conc. 30 µl	(Balasubramanian et al., 2020)
Artemisia absinthium	Leaf	spherical and rectangular 13.40	Aldehyde, Amide group	Microdilution	Escherichia coli Pseudomonas aeruginosa Staphylococcus aureus Streptococcus pyogenes	*Pseudomonas aeruginosa* MIC 0.033 mg/ml	(Keskin *et al.*, 2021)
Callistemoncitrinus	Seed	Spherical triangular and rectangular 37	Eucalyptol with α-terpineol and terpinen-4-ol	Agar well diffusion	*Escherichia coli, Vibroalginolyticus, Salmonella typhi, Staphylococcalenteritis, Staphylococcus aureus, Listeria Ivanoviiand Mycobacterium smegmatis*	*Staphylococcalenteritis and Staphylococcus . aureus (20.0 ± 0.5 and20.0 ± 0.4 mm) at 0.625 µl*	(Rotimi *et al.*, 2019)

Macadamia	Nut shells	Spherical50	Polyphenols,Flavonoids	Kirby-Bauer	*Staphylococcus epidermidis Escherichia coli*	*Staphylococcus epidermidis* 9mm Escherichia coli 11mm	(Dang *et al.*, 2019)
Avicennia marina	Seed	Spherical 10–15	Alkaloid,phenol, steriods and terpenoids	Micro dilution	*Escherichia coli*, *Klebsiella pneumoniae*,Staphylococcus aureus, and Pseudomonas aeruginosa	MIC 200 µg/ml	(Naidu et al.,2020)
Syzygium cumini	Leaf	Spherical 50-60	Phenol	Disc diffusion	*Escherichia coli*, *Klebsiellapneumoniae, Proteus vulgaris, Acinetobacter baumannii, Staphylococcus aureus, and Enterococcus faecalis*	MIC 200 µg/mL	(Diksha et al., 2023)
Punica granatum	Fruit	Spherical 2-12	Flavonoids, tannic acid, and ellagitannin	96well microtitre	*Staphylococcus aureus; Bacillus subtilis; Enterococcus faecalis;*	----	(Franzolinet al.,2022)
Convolvulus fruticosus	Flower	Spherical 25-60	Cuscohygrine.	Micro-broth dilution	*Enterococcus faecalis*, *Staphylococcus aureus*, Acinetobacter baumannii, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Klebsiella pneumonia	MIC of 0.075mg/ml,	(Ebrahimzadehet al., 2020)
Hybanthusenneaspermus	Flower	Spherical 22	steroid, phenol, flavoniod, saponin, terpenoid and alkaloids	Disc diffusion	*BacillussubtilisStaphylococcusaureus Salmonellaparatyphi Escherichia coli*	*Escherichia coli* 29 mm	(Kamatchiet al., 2023)

Nigella sativa	Oil	Spherical 13– 78	Thymoquinone, longifolene, carvacrol, β-pinene, *p*-cymene and γ-terpinene	Well-diffusion	*Escherichia coli,Pseduomonas aeruginosa, Staphylococcus aureus &Bascillussubstilis*	*Salmonella typhi MIC 50µg/ml 20.3mm*	(Gothainayagiet al.,2020)
Medinilla speciosa	Fruit	Spherical	Tannins, flavonoids, saponins and glycosides	Well-diffusion	*Pseudomonas aeruginosa* and *Staphylococcus aureus*	*Staphylococcusaureus7.43±0.276*	(Prihapsaraet al.,2022)
C*ynodon dactylon*	Whole plant	Spherical 22-34	Flavonoids, alkaloids, and terpenes	Well-diffusion	*Enterobacter cloacae, StaphylococusHaemolytics, Staphylococcus petrasii*subsp. *Pragensis* and *Bacillus cereus*	*Enterobacter cloacae,* 13 mm	(Vinayagamet al., 2021)

Antioxidant Application:Living cells go through metabolic processes that result in theproduction of free radicals, which damage proteins, lipids,nucleic acids and carbohydrates, resulting in a variety of health disorders in humans(Phaniendra*et al*,2015).

Propyl gallate (PG), Tertiary butyl hydroquinone (TBHQ), Butylated hydroxyanisole (BHA), and Butylated hydroxytoluene (BHT) are chemicals that are frequently used as antioxidants to prevent oxidative reactions in processed foods, drinks, juice, and other edible items. Their prolonged use can create adverse effects on the body(Khezerlou*et al.*,2022).

Although the easy availability of these conventional antioxidants, interest in developing nano-antioxidants is expanding(Dehghani*et al.*, 2022) because of their reasonable cost and absence of negative side effects.(Kasi*et al.*,2023).The 2,2-diphenyl-1-picrylhydrazyl (DPPH) technique is frequently used to evaluate the antioxidant capacity of various plant species and metallic nanoparticles(Sathishkumar*et al.*, 2016). It works by utilising antioxidants that lower the rate of absorption at 517 nmwavelength to trap the material's free radicals, known

as DPPH. When a substance that might provide hydrogen atoms is combined with DPPH solution, radical revitalization and colour reduction result. Purple colour is eliminated in the reaction whose index generating an absorption band at 517 nm(Chang*et al.,* 2021).The antioxidant activity was expressed by the percentage inhibition of DPPH computed as follows.

DPPH free radical scavenging %= Absorbance (Control)– Absorbance (Test)/ Absorbance (Control) × 100(Jalalvand*et al.*,2019).

Potency of the antioxidant is determined by the reduction percentage of the colour from dark purple to yellow(Hemmati *et al.,* 2019). The researchers have proposed that AuNPs are demonstrated to efficiently scavenge DPPH, free radicals in a shorter amount of time(Das,*et al.,* 2015) .The secondary metabolite of synthesised AuNPs, and other phenolic and flavonoid moieties present in the plant extract, may be responsible for the antioxidant action of the nanoparticles. Those compounds may function as capping agents by adhering to the surface of AuNPs helping them to act as excellent antioxidant(Patra*et al.*, 2016).

In addition to DPPH, the free radical scavenging activity of nitric oxide and 2,2'-azino-bis-3-ethylbenzotiazolin-6- sulfonic acid (ABTS) for Au Nps are also well reported. (Patra*et al.*,2015).Recently AuNPs have received a considerable amount of attention for their significant antioxidant activities due to optimization of surface area, particle dimension, and surface activity(Aji*et al.,* 2022).The capacity of aqueous extract of *Physalis minima* and as synthesized AuNPs to transport DPPH (free radicals) was assessed at different concentrations.Due to the suppression of free radicals, the ability of the extract and phyto-synthesised AuNPs, to transport DPPH free radicals, greatly enhanced with increasing concentrations and revealed 86–90% of its potential for scavenging. The functional groups present in the phytoconstituent determines the potentiality of the nanoparticles to scavenge the free radicals. The ability of the phytoconstituent to adhere on the metal nanoparticle surface may result in increased active surface areas. (Sekar *et al.,* 2022).

*Gymnosporiamontana*demonstrated considerable activity equivalent to the positive control, ascorbic acid, Additionally At greater doses, or above 800 g/ml, G. montana and AuNPs displayed significant antioxidant activity. Determined IC50 values were given as *G.montana*(1612.35 µg/ml), AuNPs (1959.39 µg/ml), and ascorbic acid (1503 µg/ml).According to the author, no studies utilising*G. montana* in the production of AuNPs have been published before(Patel *et al.*,2023).

Detailed studies of the antioxidant property of some AuNPs are shown in Table 3.

Table 3:Antioxidant property of some Plant derived AuNPs

Plant Name	**Parts used**	**Shape and Size nm**	**Phytocompound present for reduction**	**Method of Assay**	**Ref erence**
Clerodendrum inerme	Leaf	Spherical 5.82	Flavonoids, phenolics, alkaloids	DPPH	(Khan*et al.*,2020)
Moringa oleifera	Leaf	Spherical 14–30	Polyphenols, organic acids, andproteins	DPPH	(Boruahet al., 2021)
Acalypha indica	Leaf	Spherical 20	Amide, phenolic, and carbonyl	DPPH	(Boomiet al.,2020)
Centaurea behen	Leaf	Spherical 50	Acetylenic compounds flavonoids , alkaloids sesquiterpene lactones;and lignans	DPPH	(Abdoliet al., 2021)
Leucosidea sericea	Aerial parts	Spherical 6.3±2	Phenoloic compounds	ABTS	(Badeggiet al.,2020)
Carduus edelbergii	Aerial parts	Sphericall y 15.6	Phenols	DPPH and ABTS	(Jamilet al.,2022)
Elaeocarpus ganitrus	Seed	Quasi-spherical 30.34 ± 0.56	Flavonoids, carbohydrates, tannins	DPPH	(Vinayet al., 2021)
Nigella sativa	Seed	Spherical 20-30	Thymoquinone	DPPH	(Veeramaniet al., 2022)

Hylocereus polyrhizus	Fruit pulp	Spherical 24.9	Phenolic, flavonoids, carotenoids, Organic acids and glycosides	DPPH	(Al-Radadiet al., 2022)
Rosa canina	Pseudofruit	Quasi-spherical 26	Ascorbic acid, carotenoids, phenoliccompounds	DPPH	(CardosoAvilaet al.,2021)
Scutellariabaicalensis	Root	Spherical 20-40	Flavones	DPPH	(Chenet al., 2020)

Anticancer Application: A significant barrier to successful cancer therapy is the severe adverse effects associated with conventional therapies(Anwar*et al.*,2017).Extensive research in nanotechnology is being conducted to provide novel cancer treatment methods with less negative effects (Soto*et al.*,2021).and an increased survival rate.(Sargazi*et al.*, 2022). Plant mediated AuNPs have received a lot of interest in this area now a days.(Tan,*et al.*, 2023).Greenly synthesised AuNPs contain a variety of anticancer mechanisms which have been documented whereas three of the suggested processes are widely regarded.Dysfunctional mitochondria as a result of a modification in cell permeability(Bharadwaj*et al.*,2021). A high quantity of ROS is required for the ROS-induced apoptosis, which causes oxidative stress and DNA breakage in the malignant cell. Alteration of proteins/DNAchemistry.The following section summarises several studies conducted in recent years to examine the anticancer impact of different green AuNPs against various cancer cell lines(Sargazi*et al.*, 2022).The MTT assay in the breast cancer AMJ-13 cell line was used to determine the effectiveness of orchid leaf extract mediated AuNPs as an anti-cancer agent. AuNPs reduced the ability of cancer cells to proliferate and had a cytotoxic impact in a dose-dependent way. An increase in AuNP concentration led to an increase in anticancer activity. IC_{50} was recorded in the AMJ13 cell line with a value of 14.56 g/ml.(Yas,*et al.*, 2021).

Higher doses (125 and 250 mg/mL) at 24 h more clearly demonstrated the in vitro cytotoxicity of *Crassocephalumrubens* leaf mediated AuNPs against the colorectal cancer

(Caco-2). The high concentration of phytochemicals on the outer layer of synthesized AuNPs and their small size, which facilitates cell absorption, may be the cause of the heightened cytotoxic action.(Adewale*et al.*, 2020).

Hepatocellular carcinoma cell lines HepG2 and human colon carcinoma cell lines HCT-116 were tested by Heba Ibrahim et al. It was reported that AuNPs showed an excellent selective cytotoxicity towards both, with IC_{50} values of 6.27 mg/ml and 23.60 mg/ml, respectively. The cytotoxic effect may be caused by the generation of free radicals by AuNPs, followed by increase in reactive oxygen species (ROS)(El-Moaty*et al.* 2021).*Cyclopia genistoides* extracts, commonly known as honeybush (HB), and HB-AuNPs were tested against different human cell lines like breast (MCF-7), colon (Caco-2), and prostate (PC-3) cancer cells for their cytotoxicity as well as apoptotic effects both alone and combined with doxorubicin (Dox). It was observed that when Dox and HB-AuNPs were combined (at non-toxic doses), the anti-cancer effects on Caco-2 cells were dramatically increased. Also it was illustrated that HB-AuNPs caused apoptosis, which led to PC-3 cell death(Sharma*et al.*,2023). The anticancer activity on different cancer cell lines by plant extract derived AuNPs are depicted in Table 4.

Table 4: Anticancer activity of different cancer cell lines by plant extract derived AuNPs

Plant Name	**Parts used**	**Size nm and shape**	**Phytocompound present for reduction**	**Anticancer activity**	**Method of Assay**	**CycotoxicityIC50 µg/mL**	**Reference**
Commiphorawightii	Leaf	Spherical triangular and hexagonal 20.2±6.6	Terpenoids, flavonoids, steroids, carbohydrates, sterols	Human breast cancer cells (MCF7 cell line)	MTT	66.11 µg/mL	(Uzmaet al., 2020)
Tecoma capensis	Leaf	Spherical 10–35	Polyphenols, flavonoids, glycosides, terpenoids	Human breast cancer cells (MCF7 cell line)	MTT	9.6 µg/mL	(Hosnyet al.,2022)

Annona muricata	Leaf	Spherical 89.34 ± 2.76	Hydroxyl and carbonyl groups	Metastatic melanoma (MM-138) and primarymelanoma (FM-55) Human breast cancer cells (MCF7 cell)	MTT	-------	(Imranet al.,2021)
Mentha Longifolia	Leaf	Spherical 36.4	Polyphenols ,alkaloids, organic acids, terpenoids,	Breast adenocarcinoma (MCF7), breast carcinoma (Hs 578Bst), breast infiltrating ductalcell carcinoma (Hs 319.T), and breast infiltrating lobular carcinoma (UACC-3133).	MTT	264 µg/mL269 µg/mL223 µg/mL201 µg/mL	(Liet al., 2021)
Curcumae kwangsiensis	Leaf	Spherical 8–25	Terpenoids, phenolicco mpounds,flavonoids,	Ovarian cancer cell lines (PA-1, SW-626, and SK-OV-33)	MTT	153 µg/mL, 166 µg/mL, 204 µg/mL	(Chenet al.,2021)
Tasmannia lanceolata	Leaf	Spherical 7.10 ± 0.66	Terpenoids, flavonoids, and phenolicco mpounds	Human liver cancer (HepG2), melanoma cancer (MM418 C1) and breast cancer (MCF-7)		----	(Khandanlou et al., 2020)

Curcumaw enyujin	Rhizo me	Spherical 100	Polyphenols	Human breast cancer cells(MDA-MB231/HE R2)	MTT assay	10 µg/mL	(Zhanget al., 2020)
Cirsium japonicum	Aerial part	Spherical or polygona l 6 -38 nm	Cirsimarin, Cirsimaritin , flavonoids, flavones	AGS gastric cancer cells	MTT	------	(Miet al.,2022)
Vigna radiata	Seed	Spherical 4–10	Apigenin, Genistein, Vitexin, Naringin Gallic acid,	Human breast cancer cell lines (MCF-7, MDA-MB-231, MDA-MB-435S, MDA-MB-453, MDA-MB-468)	MTT and Alamar assay	------	(Singhet al., 2021)
Garcinia kola	Seed	Spherical 2–17	Kolaviron, garcinoic acid, garcinal, benzophenone and kolanone	Lungs, prostrate, human cervical and human colon cancer cells,	MTT	------	(Anadozieet al.,2023)
Tribulus terrestris	Flowe r	Spherical 10–15	Triterpenoids, sterols, saponins, tannins, flavonoids, phenols	Leukemic cell line (THP-1)	MTT	468 µg/mL	(Dhanalekshmiet al., 2021)
Phragmites australis	Root	Spherical 5–20	Polyphenolic compounds	Human lung cancer cells (A549 cell)	MTT	111.44 µg/mL	(Hosnyet al.,2021)
Ganoderma lucidum	Fruit	Spherical oval andirregular 25–29	Monoterpenes, triterpenoids and flavonoids	Colon cancer cell line (HT-29)	MTT	84.58 µg/mL	(Elumalaiet al., 2021)

Citrus aurantium	Fruit	Spherical 20–50	Phenolic, flavonoid, triterpenes	Human gastric NCI-N87, MKN45, GC1401 and GC1436 cancer cell lines	MTT	192 µg/mL	(Poorshamohammadet al., 2023)
Spondias dulcis	Peel	Spherical 36.75 ± 11.36	Phenolic compounds and flavonoids	Human breast cancer cells (MCF-7)	MTS	----	(Pechyenet al., 2022)
Juglans regia	Shell	Spherical 10-50	Polyphenols, flavonoids	Human breast cancer cells (MCF-7)	MTT	----	(Salandariet al., 2021)
Pistacia vera	Hull	Spherical 20–35	Polyphenolic compounds	AGS-3 and MCF-7,	MTT	0.58 µg/mL and1.48 µg/mL	(Ahodashtiet al., 2023)
Mentha spicata	Essential oil	Spherical 19.61	Limonene and carvone.	Human liver cancer cells (HEPG-2)		483.4 µg/mL	(Moosavy et al., 2023)

CONCLUSION AND FUTURE PROSPECTIVE:Green synthesis of nanoparticle is a novel and growing area with benefits over both chemical and physical synthesis methods due to its low investment, operational costs, less pollution, and increased biocompatibility and stability.This review thoroughly discussed the plant extract mediated one pot hydrothermal procedure for green synthesis of AuNPs. Numerous techniques were used to characterise AuNPs produced using phytosynthetic processes. The enormous prospective of the synthesised AuNPs in biomedical applications such as antimicrobial, antioxidant and anticancer activities was amply demonstrated. The extraordinary properties for these applications are responsible due the functional groups present in plant extracts and the morphological characteristics of AuNPs.Extensive research are still needed in order to clarify the effects of temperature, time, light, and various other variables on gold nanoparticle

production, in addition to the regulation of nanoparticle shape and size.As there is a lack of understanding the chemical constituents and particular mechanisms which are involved in reduction and stabilization of phytosynthesized AuNPs, researchers are facing many challenges.Because particle size monitoring and customization are simpler in laboratory scale, there is still a gap in converting lab based technologies to real-world applications.Toxicity assessment and scaling-up of these AuNPs remain the primary problems prior to their usage as therapeutic agents.Before being released, a thorough toxicity test must be performed to assess the safety and duration of NPs in human bodies.In addition, research should begin to emphasize in vivo investigations so that AuNPs can be extensively used to treat pathogens and cancerous cells in the future.This brief summary is intended to aid researchers in their investigation of the long term benefit of AuNPs created by biosynthesis.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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