International Journal of Biomedical Materials Research
2022; 10(2): 39-52
http://www.sciencepublishinggroup.com/j/ijbmr
doi: 10.11648/j.ijbmr.20221002.12
ISSN: 2330-7560 (Print); ISSN: 2330-7579 (Online)

Biogenic Synthesis of Gold Nanoparticles, Characterization and Their Biomedical Applications

Muhammd Ilyas[1, *], Muhammad Arif[1], Abbas Ahmad[2], Hikmat Ullah[3], Faisal Adnan[4], Shehryar Khan[2], Fazal Rahman[5], Irshad Khan[6], Muhammad Nadeem Khan[2], Sayed Muhammad Shafi Shah[2]

[1]Department of Biotechnology, University of Malakand, Chakdara, Pakistan
[2]Department of Biotechnology, Abdul Wali Khan University, Mardan, Pakistan
[3]Department of Microbiology, University of Science and Technology, Kohat, Pakistan
[4]Department of Botany, Abdul Wali Khan University, Mardan, Pakistan
[5]Department of Biotechnology, Quaid-i-Azam University, Islamabad, Pakistan
[6]Department of Chemistry, University of Malakand, Chakdara, Pakistan

Email address:
m.ilyasuom555@gmail.com (Muhammd Ilyas)
[*]Corresponding author

To cite this article:
Muhammd Ilyas, Muhammad Arif, Abbas Ahmad, Hikmat Ullah, Faisal Adnan, Shehryar Khan, Fazal Rahman, Irshad Khan, Muhammad Nadeem Khan, Sayed Muhammad Shafi Shah. Biogenic Synthesis of Gold Nanoparticles, Characterization and Their Biomedical Applications. *International Journal of Biomedical Materials Research*. Vol. 10, No. 2, 2022, pp. 39-52. doi: 10.11648/j.ijbmr.20221002.12

Received: July 18, 2022; **Accepted**: August 11, 2022; **Published**: August 17, 2022

Abstract: Nanotechnology is starting to the characterization, fabrication, and possible applications of numerous materials at the Nano-scale. Over the last few eras, nanomaterials provide a platform to researchers from diverse arenas due to high surface to volume ratio and other novels, and new significant belongings. Recent advances in the field of science and technology, immensely nanotechnology, have contributed to the diverse applications of metal oxide nanoparticles in various fields, especially the biomedical division. Among all the metallic nanoparticles, gold nanoparticles (AuNPs) are highly remarkable. Consequent to their significant nature, spherical and gold nanorods (Au NRs) nanoparticles attract greater attention. Gold colloids have fascinated scientists for over a century and are heavily utilized in chemistry, biology, engineering, and medicine. Gold nanoparticles have a rich history in chemistry, dating back to ancient Roman times where they were used to stain glasses for decorative purposes. Gold nanoparticles can be fabricated using different approaches such as chemical, physical, and biological methods. The green route (biological method) is an eco-friendly, cost-effective, reliable, and comfortable and simple way to synthesize gold nanoparticles compared to physical and chemical approaches. This review aims to address the popular AuNPs synthesis methods, characterization, and their antibacterial, antifungal, anticancer, and antiviral applications.

Keywords: Nanotechnology, Green Synthesis, Gold Nanoparticles, Biomedical Applications

1. Introduction

Nanotechnology is primarily the manipulation of nanoscale materials to achieve desirable physical, chemical, and biological properties for wide applications in physical, natural sciences and engineering. Nano-revolution has expanded its horizon globally with huge momentum in academia and industry [1, 2]. A nanomaterial constitutes Graphene, Carbon nanotubes (CNTs), Quantum Dots and various types of nanoparticles. In the recent decade, nanoparticles (NPs) are of particular interest due to their unique properties and vast applications like drug delivery, antimicrobial activity, catalysis etc. [3]. Due to their small size, NPs have novel physicochemical properties that offer the progress of unique functional uses [4]. Nanoparticles have various roles in different industry areas like food science and technology, health care system, medical and optical devices, tissue engineering and gene delivery, environmental and climate emissions, space industry and missiles etc. [5]. Nanoparticles are of many kinds that include polymer NPs, metallic NPs, hybrid

NPs etc. The metallic nanoparticles are considered promising in antimicrobial properties compared to other nanoparticles due to their large surface area to volume ratio [6]. While in metallic nanoparticles, the most important ones are silver (Ag), gold (Au), platinum (Pt), titanium (Ti), palladium (Pd), iron (Fe), aluminum (Al) and copper (Cu), which are intensively developed [7]. These metal nanoparticles have a major role in developing nanotechnology-based solutions. Among the aforementioned metal nanoparticles, gold nanoparticles (Au-NPs) have most promising in the medicinal application for a long time, such as in the treatment of autoimmune diseases and cancer diagnosis and treatment [8] less immunogenic properties. Au-NPs constitute enhanced surface plasmons resonance (SPR) property used in biosensing, bioimaging, photothermal and radiotherapies treatments, and surface modification, leading to a specific drug delivery [9].

The fabrication of nanoparticles involved two types of approaches, i.e., top-down and bottom-up. In the bottom-up approach, nanoparticles are synthesized by using a chemical method (reducing agents and surfactants) and biological methods (use of bacteria, viruses and plant extract etc.) in which atoms are self-assembled to form a bigger particle at the nanoscale [10]. In the top-down approach, a bigger particular is broken into smaller particles until it reaches at nanoscale level with various physical techniques, e.g., ball milling and grinding, laser sputtering, thermal/laser ablation methods, etc. The chemical and physical methods used for synthesis are hazardous for the environment, and their biocompatibility with the environment is also a question for long-term exposure. Their wastage consists of harmful chemicals, and disposal is quite expensive [11]. Eco-friendly methods are more welcoming now in chemistry and chemical technology, and nanotechnology as people are more conscious of environmental protection. So, the fabrication through green processes is emerging as a new field as green nanotechnology. Biogenic synthesis of nanoparticles has been in practice for years. Metallic nanoparticles catch interest in biogenic synthesis due to the simplicity and biocompatibility of the nanoparticles [7].

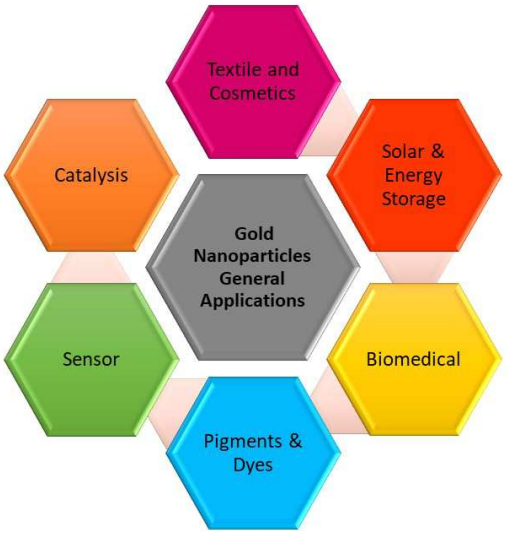

Figure 1. *General applications of Au-NPs.*

Au-NPs are intensively biogenic synthesized by various methods through plant tissues, bacteria, fungi, actinomycetes, etc. Among other biogenic syntheses of Au-NPs, extracellular synthesis has received most of the attention as it is an easy method that reduces various steps in the process. In this study we summarized the Au-NPs biological synthesis from different sources, their characterization techniques, and also we summarize their biomedical applications.

2. Characterization of Gold Nanoparticles

In recent years, numerous characterization tools have been introduced according to their inherent optical, thermal, electrical, and chemical properties, to classify noble metal nanoparticles and validate their mean particle size-specific shape, crystal structure, distribution, surface charge properties, and surface area characteristics. Whenever a synthesis process is conducted, the structure or composition of the final product must be known. Using various spectroscopic techniques, we can analyze the degree of purity, the concentration of the analyte, composition, crystal phase and structure of Au-NPs.

The characterization of gold nanoparticles begins with visual color variations that can be detected with the unaided eye since small gold nanoparticles are ruby red. Gold nanoparticles have remarkable optical properties based on their Surface plasmon resonance which can be observed by UV-vis spectrophotometer analysis. This important technique will track the production and stabilization of the gold nanoparticles. Au-NPs' absorption spectra fall within the range of 500-550 nm. Stretching of the SPR bandwidth, which demonstrates a redshift, has been suggested to measure their size, shape, and porosity. Dynamic light scattering (DLS) is a commonly used analytical technique for calculating and analyzing nanoparticle size. It is used to evaluate the particle size distribution and size in the range of a few nanometers to a few micrometers in diameter [12].

The X-ray diffraction (XRD) can confirm the purity and crystalline structure of gold nanoparticles. This indicates the size of the particle, calculated by the Debye-Scherer equation. Energy-dispersive X-ray spectroscopy (EDX) will confirm the chemical composition of Au-NPs. The interparticle distance of gold nanoparticles can be measured by Small-angle X-ray scattering (SAXS) analysis. It is used for tumor imaging applications and tissue engineering. Fourier transform infrared spectroscopy (FT-IR) can investigate the surface chemistry to identify the functional groups or biomolecules responsible for the reduction and capping attached to the surface of gold nanoparticles.

Significant progress in advanced microscopic techniques has made it possible to characterize the structure of Au-NPs better. Scanning electron microscopy (SEM), transmission electron microscopy (TEM), atomic force microscopy (AFM), and high-resolution transmission electron

microscopy (HR-TEM) are widely used to measure their surface morphology scale, shape, and size [13].

Scanning electron microscopy offers nanoscale particle information and is used to confirm the production of Au-NPs and evaluate their surface characteristics. In contrast, Transmission electron microscopy (TEM) is used to provide data on the number of layers of material and broad proof of absorption and localization, structure, tethering of polymers, and physical properties. Besides, this technique is also widely used as a quantitative tool for measuring scale, volume, particle shape distribution, the elemental composition of the Au-NPs, generating three-dimensional (3D) nanoparticles primarily in two-dimensional (2D) images. The exact size, shape, and crystalline structure can be determined by using high-resolution transmission electron microscopy. Information about the surface topography of gold nanoparticles is given by AFM, identical to scanning probe microscopy (SPM). In a liquid world, AFM seems to benefit from 3D images being obtained [14].

3. Gold Nanoparticles Synthesis

Different approaches can be employed for the synthesis of nanoparticles. These approaches are divided into two classes,' i.e., top-down approach and bottom-up approach. A top-down approach is a destructive approach in which larger molecules are decomposed into smaller ones, and these smaller molecules are then converted into suitable nanoparticles. In comparison, the bottom up is a building approach that involves the assembly of atomic size to form nano-sized particles [15]. These two approaches are further divided into different classes. However, in this review, we will only focus on the green synthesis of Au-NPs nanoparticles and their biological applications.

Green synthesis Au-NPs using plant extracts

In contrast to bacteria, algae, and fungi, plants have been extensively used to synthesize Gold nanoparticles. This is because of their abundance, safe nature, and greater stabilization and reduction of plant phytochemicals [16]. This method has been considered an alternative to complex and costly physicochemical processes due to its viability, commercial feasibility, eco-friendly, reliability, no waste generation, and simplicity [17]. Different parts of the plant, such as leaves, roots, stem, fruits, seeds, latex, inner parts of the plant, shells, and peels, have been used to synthesize Gold nanoparticles, as shown in Table 1. The plant extracts have various flavonoids, polysaccharides, amino acids, polyphenol, phenolic acids, ferulic acid, gentisic acid, terpenoids, thymol, tryptophan, and alkaloids which act as stabilizing, reducing, and chelating agent. These metabolites act as oxygen quenchers, reducing and stabilizing agents, metal chelating agents, and hydrogen donors [18]. The reduction of metal ions by these substances within the plant extracts leads to the formation of respective nanomaterials [19]. Due to a rich source of metabolites, leaf extracts have been widely used to synthesize gold nanoparticles. The metal salts have been mixed with the whole plant/ part of plant extracts, and the reaction completes in a few hours at normal lab conditions [20].

Table 1. *Gold Nanoparticles synthesized using various plant extract.*

Plant	Part of Plant	Shape	Characterization	Phytochemicals	Size	Ref
Medicago sativa	Shoot	Crystal	UV-vis spectroscopy, atomic absorption spectrometry, (SEM),, and (XRD), XAS	isopropanol, and methanol, and tetrachloroaurate ion ($AuCl_4^-$)	4-10 nm	[21]
Sesbania	Seed	Crystal	TEM, XRD and SEM	4-nitrophenol (4-NP)	6-20 nm sizes	[22]
Medicago sativa	Seeds	Crystalline	XAS, TEM, X-ray EDS and		4 nm	[23]
Cymbopogon flexuosus	Leaves	triangular	UV–VIS–NIR, SEM, AFM, XRD, TEM,		8-18 nm	[24]
Pelargonium graveolens	geranium leaves	rods, flat sheets and triangles	UV-vis, TEM, XRD, FTIR,	7-dimethyl, formate and Selinene	510–560 nm	[25]
Medicago sativa	Cone belt	Crystal	XAS, XANES, EXAFS,	flavonoids extraction		[26]
Lemongrass	Leaves	Triangular, spherical and hexagonal	UV-vis-NIR, TEM,		525 nm	[27]
azadirachta indica	Neem leaf	Crystal	UV/Vis, TEM, and EDS	total extracts	5.5 and 7.5 nm	[28]
Brassica Junsea	Seed	Spherical	UV/Vis, TEM	Oil	10-20 nm	[29]
Cacumen Platycladi	Leaf	Crystal	UV/Vis, TEM, XRD, FTIR, SAED and TG	Flavonoids and Reducing Sugars	15.3 nm	[30]
Camellia sinensis		Crystal	UV–Vis–NIR, TEM,	Phenolic compounds, Terpenoids	40 nm	[31]
Cassia tora	Leaf	Spherical	UV–Vi, FT-IR, HR-TEM and zeta sizer	anthraquinones, carbohydrates, glycosides, cardiac glycosides, amino acid, phytosterols, fixed oils and fats, phenolic compounds, tannins,	57 nm	[32]
Chenopodium album	Leaf	Quasi-spherical	TEM, XRD, EDX, FTIR	flavonoids, steroids and saponins viz. aldehyde, alkaloids, apocarotenoids and flavonoids	10–30 nm	[33]

Plant	Part of Plant	Shape	Characterization	Phytochemicals	Size	Ref
Cicer arietinum L.		Triangular prisms	UV-vis/NIR, TEM, EDS, light microscope, XRD, XPS, ATR-FTIR, and ESI-MS	protein and biomolecules from protein		[34]
Cinnamomm camphora	Leaf	spherical	UV–vis, FTIR, XRD, SEM and AFM		540 nm	[35]
Cinnamomm zeylanicum	Leaf broth	nanoprisms and spheres	UV–vis, XRD, TEM and SAED	terpenoids like eugenol, cinnamaldehyde	25 nm	[36]
Coleus amboinicus Lour	Leaf extract	spherical, triangle, truncated triangle, hexagonal and decahedra	UV–Vis spectroscopy, XRD, TEM and SAED	Carvacrol, caryophyllene, patchoulane and flavanoids	4.6 to 55.1 nm	[37]
Coriandrum sativum	Leaves	spherical, triangle, truncated triangles and decahedral	UV-Vis, XRD, EDAX, FT-IR and TEM	Whole Extract	6.75–57.91 nm	[38]
Commelina nudiflora L.	Weed	1. Spherical 2. Crystalline	UV–Vis, FESEM, TEM, XRD, EDX, FT-IR,	alkaloids, saponins, flavonoids and steroids	1. 50 and 150 nm 2. <150 nm	[39]
Cumin	Seeds	monodispersed spherical	TEM, XPS, XRD		1–10 nm	[40]
Magnolia kobus	Leaf extract	triangles, pentagons, hexagons and spherical	UV–vis, ICP, EDS, SEM, TEM, XPS, AFM,		5–300 nm	[41]
Diopyros kaki	Leaf extract	triangles, pentagons, hexagons and spherical	UV–vis, ICP, EDS, SEM, TEM, XPS, AFM		5–300 nm	[41]
Euphorbia hirta L.	Leaf extract	Crystal	TEM, XRD, EDAX, AFM, FTIR and Raman spectra	polyphenols, flavonoids, steroids, tannins, and alkaloids	530 nm	[42]
Ficus racemosa	Latex		UV-Vis, XRD and FESEM,	aspartic protease	50–120 nm	[43]
Maduca longifolia		crystalline triangular	UV–Vis, FTIR, TEM and HrTEM	tyrosine residue	525 nm	[44]
Mangifera indica	Leaf	Spherical	UV–vis, TEM, XRD, SAED, FTIR,		20 nm and 17 nm	[45]
Memecylon edule	Leaf extract	triangular, circular, and hexagonal	UV-vis, SEM, TEM, EDAX, FTIR	triterpenes, tannins, and flavonoids	20–50 nm	[46]
Momordica charantia	Fruit peel	monodisperse	UV-Vis, XRD and TEM	glutathione and Phytochelatins	10-100nm	[47]
Mentha piperita	Dried Leaves	Spherical	UV–Vis, FTIR, SEM, and EDS	alkaloids, flavones, steroids, polysaccharides, amino acids, oximes and proteins	150 nm	[48]
Morinda citrifolia L	Root extract	triangle and mostly spherical	V–vis, XRD, FTIR, FE-SEM, EDX and TEM		12.17-38.26 nm	[49]
Moringa oleifera	petals	well-dispersed triangular, hexagonal and spherical	UV–vis, SEM, EDX, XRD, TEM, DLS FTIR and H-NMR	carotenoids, vitamins, minerals, amino acids, sterols, glycosides, alkaloids, flavonoids and phenolics	5 nm	[50]
Nigella sativa	Seeds	Spherical	UV–vis, XRD, FTIR, TEM,	Phenol, Resin, Saponin, and Steroid	15.6-28.4 nm	[51]
Pelargonium graveolens	Germanium Leaves	Spherical	UV-vis, TEM, FTIR, XRD		8 to 40 nm	[52]
Pistacia integerrima	Gall extract		UV-Vis, FTIR, SEM,	monoterpenes, triterpenoids, sterols, dihydromalvalic acid and flavonoids	20-200 nm	[53]
Psidium guajava	Leaf extract	Hexagonal	UV–vis, XRD, FESEM, TEM, XRD, FITR,		30–35 nm	[54]
Punica granatum	fruit extract	triangular, pentagonal, hexagonal and spherical	HRTEM, XRD, FTIR, EDX and SAED	terpenoids, alkaloids, sterols, polyphenols, sugars, fatty acids, aromatic compounds, amino acids and tocopherols	23–36 nm	[55]
Rosa hybrida	Petals	spherical, triangular and hexagonal	UV–vis, FT-IR, XRD, DLX, EDX and TEM		10nm	[56]
Rosa rugosa	Leaf extract	triangular and hexagonal	UV–vis, TEM, XRD, FTIR, Zetasizer and EDX		11 nm	[57]
Salix alba L.	Leaves		UV-Vis, FTIR, AFM, SEM	amines, amides and aromatic groups	50-80 nm	[58]
Sphearanthus amaranthoids	Leaf	triangular	UV–Vis, HR-TEM, EDX,	flavonoids, carbohydrate, tannins, saponins, steroids, glycosides, terpenoids and alkaloids	39±5 nm	[59]
Stachys lavandulifolia	Vahl extract	spherical to triangular	UV-vis, FTIR, DLS, TEM		56.3 nm	[60]
Stevia rebaudiana	Leaves	well-dispersed octahedral	UV-Vis, TEM, EDX and XRD		8–20 nm	[61]

Plant	Part of Plant	Shape	Characterization	Phytochemicals	Size	Ref
Stevia rebadiauna	Leaf extracts	Spherical	UV–vis, FT-IR, TEM, SEM and XRD		5 to 20 nm	[62]
Sargentodoxa cuneata		hexagonal	UV-vis, XRD, TEM, EDX, HR-TEM and FTIR	phenylpropanoid glycosides	15 to 30 nm	[63]
Tanacetum vulgare	Fruit extract	triangular	TEM, XRD, EDX and FTIR and UV–Vis		11 nm	[64]
Terminalia Catappa	Leaf extracts	Spherical	UV-Vis, XRD, FTIR and TEM	Propane, Butyl hydrogen phthalate	21.9 nm	[65]
Terminalia arjuna	Fruit extract	Spherical	UV–vis, FTIR, XRD, AFM, EDX, TEM and ZP	tannin, terpenoid, saponins, flavonoids, glycosides and polyphenolic compounds	20–50 nm	[66]
Terminalia Arjuna	Bark extract	triangular, tetragonal, pentagonal, hexagonal, rod-like and spherical shapes	TEM, EDX, FTIR, AFM, XRD and UV-Vis	triterpenoids, saponines, tannins, flavanoids	15 – 20 nm	[67]
Trigonella foenum-graecum	Seeds	Spherical	UV–Vis, SAED, XRD, FTIR and TEM	alkaloids, lysine and L-tryptophan and steroidal saponins	18nm	[68]
Urtica dioica L	Leaves	crystalline	UV-Vis, TEM, XRD, DLS, FT-IR and ZP		1 nm to 195 nm	[69]

Like other synthesis routes like plants and other microorganisms, bacteria also have an intrinsic ability to synthesize nanoparticles of different sizes and morphologies, as shown in Table 2. This approach also has some challenges over other methods that are yet to be solved, like the synthesis of complex materials with the desired phase, a full understanding of the synthesis mechanism at the molecular level to achieve better control over shape and size, and scaling up to get a large number of nanomaterials. Chemical methods are already advanced to provide greater control of nanomaterials' shape and size, but this approach is eco-friendly and limits the drawbacks of the chemical synthesis [70]. However, lengthy procedures and contamination of cultures are the limitations of this approach.

Table 2. *Bacterial mediated synthesis of gold nanoparticles.*

Bacteria spices	Shape	Characterization	Size	Ref
P. aeruginosa	rod-shaped	SEM, TEM, HR TEM, FESEM and XRD	50–30 nm	[71]
Pseudomonas denitrificans	At 37°C pH 3 roughly spherical (blunt shaped nano-triangles)	SEM, TEM, HR TEM, FESEM and XRD	25–30nm	[72]
Pseudomonas fluo-rescens 417	Spherical	TEM, UV-vis, DLS, PDI, XRD and EDX	5−50nm	[73]
Pseudomonas veronii	rod-shaped	SEM, TEM, HR TEM, FESEM and XRD	5–25nm	[71]
Rhodopseudomonas capsulata	Spherical	TEM, FT-IR, EDX, XRD and FESEM	10–20 nm	[72]
Shewanella algae	Spherical	TEM, UV-vis, DLS, PDI, XRD and EDX	9.6 after 1 h(mean size), 100 nm after 6 h, 100–200 nm after 24 h (TEM)	[74]
Bacillus	Spherical	Zetasizer Nano system and FESEM	20–50nm	[75]
Escherichia coli	spherical	Zetasizer Nano system and FESEM	11.8–130nm	[76]
Klebsiella pneumonia	Spherical	SEM, TEM, HR TEM, FESEM and XRD	5–65nm	[77]
Bacillus stearothermophilus	Triangle	SEM, TEM, HR TEM, FESEM and XRD	5–30 nm	[72]
Magnetospirillum Gryphiswaldense	Spherical	TGA, TEM, EDS, SAED, FE-SEM, HAADF STEM	10−40 nm	[73]
Shewanellao neidensis	Spherical	TEM, UV-vis, DLS, PDI, XRD and EDX	2–50 nm	[74]
Sporosarcina koreensis	Spherical	FTIR, FESEM, EDX and XRD	30–50 nm	[75]
Bacillus licheniformis	Rod	SEM, TEM, HR TEM, FESEM and XRD	10-100 nm	[75]
Geobacillusstearo thermophilus	Spherical	PDI, TEM, DLS EDX and XRD	12–14 nm	[72]
Geobacillus stearothermophilus	Rod	SEM, TEM, HR TEM, FESEM and XRD	12-14 nm	[77]
Streptomyces clavuligerus		UV-vis, SEM, TEM, HR TEM, FESEM and XRD	8.2 nm	[78]
Stenotrophomonas maltophilia	Curved, straight or bean	TEM, FTIR, FESEM, DLS, PDI and XRD	40 nm	[79]
Lactobacillus casei	Rod	SEM, TEM, HR TEM, FESEM and XRD	7-56 nm	[79]

The fungi-mediated approach exhibits unique advantages because fungi's growth process is easy to handle, isolate, a large amount of biomass, and high yield of proteins. The entophytic fungi also secrete large amounts of bioactive substances necessary for the synthesis of nanoparticles in the presence of precursor substances, as shown in Table 3, during the fabrication of nanoparticles from the precursor solution, biomass (fungi) along with the supernatant act as a reduction medium [17]. Algae are aquatic microorganisms and used to a great extent for the synthesis of nanoparticles. Algae are also called bio-nano factories because they fabricated nanomaterials with high stability, easy to handle, no need for cell maintenance [78]. Algae are the key origin of phytochemicals that are involved in the fabrication of nanoparticles. The algae contain many bioactive metabolites like proteins and polysaccharides and various types of other phytochemicals that contain amino, hydroxyl, and carboxyl functional groups, and these groups are responsible for the

fabrication of nanoparticles, as shown in table 4. Algae are of different sizes. They may be microalgae or macro-algae [79].

Table 3. *Fungi Mediated synthesis of gold nanoparticles.*

Fungal species used	Characterization	Size	Shape	Ref
C. albicans	FTIs, TEM, UVFS	20–40 nm	Hexagonal, triangular, spherical	[80]
Chrysosporium tropicum	TEM, SEM, XRD	2–15 nm	Spherical	[81]
penicillium aurantiogriseum	FTIs, SEM, UVVs,	153.3 nm	Spherical	[82]
penicillium citrinum	FTIs, SEM, UVVs,	172 nm	Spherical	[82]
Penicillium rugulosum	XRD, FTIR, XPS, UV–vs	NA	Crystal	[83]
Aspergillus terreus	FTIR, XRD, AFM and SEM	20 to 50 nm	Spherical	[84]
Penicillium sp	UV–Vs, XRD, TEM, SEM, EDX	30 to 50 nm	Spherical	[85]
Fusarium acuminatum	UV-Vs, FTIRs, XRD, TEM	17 nm	Spherical	[86]
Aspergillus terreus	UV-Vs, HR-TEM, FTIRs, XRD, EDX, SAED	10-50 nm	anisotropic morphology	[87]
Fusarium solani	FTIRs, TEM, UV–vis	20 to 50 nm	spherical	[88]
Aspergillus niger	FTIR, SEM, TEM, XRD	12.79 ± 5.61nm	Spherical, elliptical	[89]
Helminthosporum solani	UV– vs, TEM,	2–70 nm	Spheres, rods, triangles	[90]
Volvariella volvacea	XRD, FTIR	20–150 nm	Triangular, spherical, hexagonal	[91]
Metal-tolerant fungal isolates	XRD, TEM	9–18 nm	Spherical, trigonal, cubic, tetragonal and hexagonal	[92]

Table 4. *Algae and Actinomycetes mediated synthesis of gold nanoparticles.*

Algal use	Characterization	Size	Shape	Ref
Spirulina platensis	UV–vis, HR-TEM, FTIR, EDAX	5 nm	uniform shape	[93]
Ecklonia cava	FTIR, XRD, TEM	30 ± 0.25 nm	spherical and triangular	[94]
Sargassum wightii	XRD, TEM,	8–12 nm	Spherical	[95]
Laminaria japonica	TEM, XRD, FTIR	15–20 nm	Spherical self-assembled	[96]
Gracilaria corticata	TEM, XRD, FTIR	45–57 nm	Spherical	[97]
Sargassum muticum	TEM, UV-VIS	<10 nm	Spherical and crystalline	[98]
Chlorella pyrenoidusa	HRTEM, UV-VIS	25–30 nm	Spherical	[99]
Acanthophora spicifera	TEM XRD	27–35 nm	Spherical	[100]
Sargassum myriocystum	FT-IR, TEM, SEM–EDAX, XRD	15 nm	Triangular and spherical	[101]
Tetraselmis suecica	UV-VS, TEM	79nm	Spherical	[102]
Cystoseira baccata	TEM, HRTEM, STEM	8.4±2.2 nm	Spherical & polycrystalline	[103]
Osmundaria obtusiloba	UVVIS, FTIR, HRTEM, SEMEDS, XRD	10–20 nm	spherical, triangular and diamond	[104]
Streptomyces griseoruber	XRD, FTIR, UV–vs	5–50 nm	NA	[105]
Nocardia farcinica	EM, XRD,	30 - 100 nm	crystal structure	[106]
Streptomycetes viridogens	TEM XRD	18-20 nm	spherical and rod shaped	[107]
Rhodococcus sp.	EM, TEM, XRD	5–15 nm	NA	[108]
Nocardiopsis dassonvillei NCIM 5124	TEM, SAED, EDS, XRD	10 to 25 nm	crystal structure	[109]
Streptomyces griseus isolate (M8)	FTIR, TEM	19 to 28 nm	Hexagonal	[110]

4. Biomedical Applications

4.1. Antibacterial Activity of Gold Nanoparticles

In the previous few years, nano-based therapies have been used to diagnose and treat diseases and construct novel drugs. Nanoparticles have excellent antibacterial activity, show effective results against different pathogenic bacterial strains, and open a new door for modern science [111]. Different Nanoparticle is used to treat different pathogenic strains of bacteria in which the gold nanoparticle perform a tremendous job due to its different sizes and shape have beneficial uses in biomedicine Bio-conjugated gold nanoparticles of different sizes and shapes recently exploited in hyperthermic destruction of MDRB because of its optical properties [112, 113]. In this method, gold nanoparticles use as ‘‘light-directed nano heaters’’, which are very beneficial in biomedicine, such as selective laser photo thermolysis of pathogens [114, 115]. Gold nanoparticles have a great ability to absorb light several million times stronger than the organic dye due to its nonradiative properties; there is the possibility to convert the absorbed light into heat [112-114, 116]. As a result, due to the electron-phonon relaxation process and presence of proper wavelength of light increase the temperature a few tens of degree which is enough for the destruction of MDRB via cell damage by different thermal effects, such as induction of heat- shock method, endothelial swelling, metabolic signaling disruption, denaturation of Enzymes/Protein and micro thrombosis, etc. [114, 115, 117]. Different strains of bacteria other than MDRB are identified, which is the leading cause of infection and mortality in humans, such as salmonella DT104, Pseudomonas aeruginosa, S. aureus, MRSA, E. coli, M. tuberculosis [118, 119]. Norman et al. reported photothermal therapy in which the gold nanorods are covalently bonded with antibodies for the destruction P. aeruginosa, which was isolated from the upper respiratory tract of sinusitis patients [120]. Xu’s group created vancomycin-functionalized gold nanoparticles (AuNPs) to overcome vancomycin-resistant enterococci (VRE) [121]. Different Bio-inspired gold nanoparticles are rapidly synthesized at room temperature from the grapefruit extract,

which showed excellent antimicrobial activity towards most of the tested fungal and bacterial cultures and shows good anticancer activity against HeLa cell lines. [122] Cefaclor AuNPs have good antimicrobial activity against both Gram-positive (Staphylococcus aureus) and Gram-negative (Escherichia coli) bacteria [123]. Bankar et al. (2010) reported the banana peel (Musa paradisiaca) extract mediated Au NPs displayed efficient antifungal and antibacterial activity towards the test pathogenic fungi, C. Albicans (BX and BH), bacterial cultures including Citrobacter kosari, E. coli, Proteus valgaris, Pseudomonas aeruginosa, Enterobacter aerogenes and Klebsiella sp [124].

4.2. Antifungal Activity of Gold Nanoparticle

Gold nanostructures have promising applications and focus on research due to their fascinating electronic, chemical, and optical properties in nanoelectronics, sensing, biomedicine and catalysis [125, 126]. It is well-identified that inorganic nanoparticles have a great ability to interact with microorganisms and can act as antifungal and antibacterial agents [127, 128]. It has been investigated that inorganic AuNPs have an antifungal ability due to their concentration, shape and size. It has been studied that the smaller size of Au-NPs has a better antifungal effect against Candida [129]. The synthesis of anisotropic gold nanoparticles by sonochemical method, which depends on gold size and shape, has the best fungicidal activity against various strains of Candida, which is the first report showing the antifungal activity of gold nanoparticles against the fungus Candida [130]. The following schematic diagram showing the antifungal activity of gold nanoparticles and some of Candida albicans strains are given below.

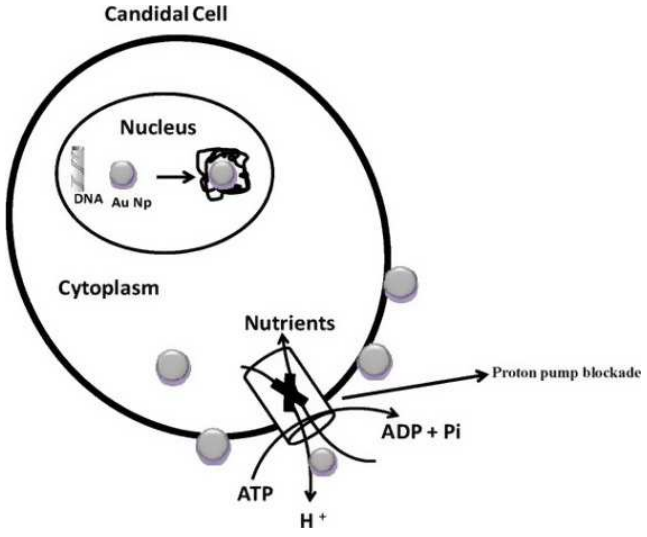

Figure 2. *Schematic diagram showing the action of gold nanoparticles on the fungal cell [130].*

Fluconazole coated Au-NPs have the best antifungal activity, which was observed from the zone of inhibition against Aspergillus niger, Aspergillus flavus and Candida albicans. The MIC of fluconazole coated Au-NPs showed variable MIC against C. albicans, A. niger (6.25, 3.125) and A. flavus (12.5, 6.25), respectively [131]. The Plant base Au-NPs using flower extract of Plumeria alba, which act as reducing agents, also have significant antimicrobial activity against broad-spectrum antibiotics against A. niger, A. flavu [132]. The Au-NPs were formed using P. pinnata, a medicinal plant, and the investigation shows that it has had good antifungal activity against plant pathogenic fungi SR1 and BP1120 fungal strain [133].

4.3. Antiviral Activity of Gold Nanoparticle

Measles virus (MeV) is a paramyxovirus that infects humans, principally children using garlic extract (Allium sativa), which acts as a reducing agent to make and evaluate the antiviral activity of gold nanoparticle. These nanoparticles inhibit the MeV replication in Vero cells at a 50% effective concentration (EC50) of 8.829 µg/mL, and the selectivity index (SI) obtained was 16.05. Au-NPs-As likely inhibit viral infection by blocking viral particles directly, showing a strong virucidal effect. Gold nanoparticles may be useful as a promising strategy for treating and controlling MeV infection and other related enveloped viruses [134]. The subunit vaccine of Au-NPs in which the epitopes of EDIII protein combined with Au-NPs have a carrier capacity to develop subunit vaccine against dengue virus show promising activity against dengue virus [135]. The Au-NPs have promising antiviral activity against HIV-1 by adsorption assays and cell fusion assays. The action of Au-NPs was observed [136]. The experimental result showed that they inhibit the viral entry bind with the gp120 protein of the virus and prevent CD4 attachment; this property makes them an effective antiviral inhibitor [137]. Human adenoviruses (HAdVs) are broad-spectrum DNA viruses possessing pathogenicity [138]. The gold nanoparticles covered with SiO2 shells have been synthesized and used as an antiviral agent against adenoviruses and possesses an antiviral and viricidal action against these viruses [139]. Ribavirin-Au-NPs had been produced and better activity against measles virus and used to treat measles infection and higher antiviral activity and might also be used as a prophylactic agent limit the spread of infection during outbreaks [140].

4.4. Anticancer Activity of Gold Nanoparticles

Worldwide, cancer is considered the leading cause of death. According to the National Cancer Institute (NCI), there were 8.2 million cancer and 14 million new cancer cases in 2012, and the number will be increased to 24 million within the next two decades. About 40% of people may be diagnosed with cancer during their lifetime [141]. Gold nanoparticle-based therapies have promising applications in the biomedical field; using anticancer agents is one of the most promising research areas in nanotechnology [142]. Eco-friendly gold nanoparticles were synthesized from marine bacteria Enterococcus sp takes 2 hours of incubation the nanoparticle produced give ruby red color in the reaction mixture and have SPR band centered at 545nm the

nanoparticle synthesized have an effective anti-cancer activity against HepG2 and A549 lung cancer cells and its anticancer activity increase with the concentration of nanoparticle increase. This synthesis approach opens a new door in the development of targeting cancer cells to increase the anti-cancer activity of gold nanoparticles because the method is simple and novel in biomedical application [142]. Chloroquine-conjugated gold (GNP-Chl) nanoparticles were developed. GNP-Chl nanoparticles have interesting anticancer properties and have good anticancer activity against MCF-7 breast cancer cells [143]. Theaflavin and theaflavin- gallates are tea extracted phenols that have selectively induce apoptosis of tumors cells; the conjugates of theaflavin and gold nanoparticles (Au-NPs) AuNP@TfQ increase its apoptotic ability as compared to bare theaflavin (Tf) due to the presence of quinone motif in AuNP@TfQ induces ROS generation through depolarization of mitochondria and result from caspase-mediated apoptotic cell death and is a magic bullet in mediated ovarian cancer treatment [144].

Gold nanoparticles (Au-NPs) synthesized from the green synthesis method used Marsdenia tenacissima plant extract is very efficient, simple and have excellent anticancer properties. Gold nanoparticles are excellent theragnostic nanoparticle Marsdenia tenacissima plant extracts Au-NPs activate caspase expression and down-regulate the anti-apoptotic protein expression in A549 in lung cancer cells M. tenacissima extract are a stabilizing agent who is an effective anticancer agent against lung cancer cell lines (A549) [145]. A. spectabilis plant extract act as a reducing source. The Au-NPs synthesized from this plant extract produces significant cytotoxicity on bladder T24 cancer cells which is confirmed from MIT cytotoxicity assay the Au-NPs induces apoptosis by increasing the nuclear fragmentation and DNA damage in bladder T24 cell it also inhibits the intrinsic apoptotic pathway the Au-NPs was synthesized from A. spectabilis plant extract as a reducing source Au-NPs produces significant cytotoxicity on bladder T24 cancer cells, the A. spectabilis plant extract-based synthesis of Au-NPs are faster, eco-friendly and easier and has been proven its potent anticancer activity [146].

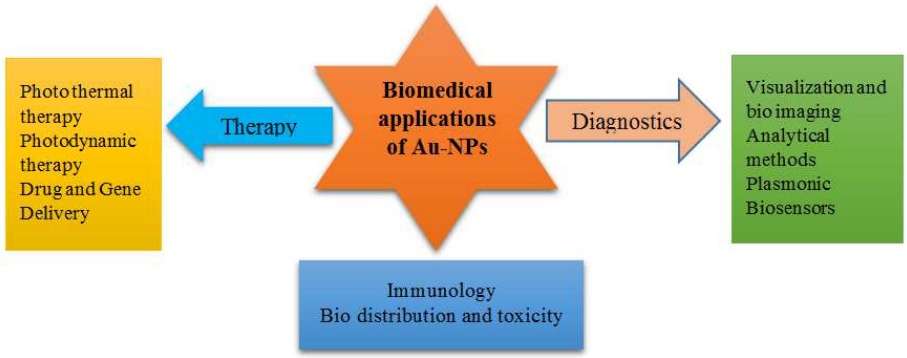

Figure 3. *Generalized scheme for the biomedical application of GNPs. Along with basic applications in diagnostics and therapy.*

5. Conclusion

Gold nanoparticles (Au-NPs) have a small size, higher dispersion, and large surface especially colloidal gold solution are subject of increased interest for the investigation of their cytotoxicity and application for application in medicine, water purification, food industry, and pharmacology etc. the Au-NPs are biocompatible materials due to this property it has numerous other biological application including drug delivery, tissue/tumor imaging, labeling, sensing and photothermal therapy [147]. Nanoparticles derived from gold take practical consideration lately. However, due to their flexibility, it has many applications in various fields, including use in biomedical application ablation thermal and radiotherapy development, drug delivery, gene delivery, and highly sensitive analytical assessment [148, 149]. Hybrid gold nanoparticles are developed, applied in molecules of biological interests (including peptides and proteins) also used for cancer diagnosis, therapy and radiolabelled bioconjugates [150]. Au-NPs have significant properties of surface plasmon resonance (SPR), and effective fluorescence quenching due to these features has have been utilized in photodynamic therapy [151]. Photodynamic therapy (PDT) is considered is an important treatment for oncological diseases and certain skin or infectious diseases in which laser and photosensitizer light-sensitizing agents is use (the wavelength associated with a peak of dye absorption) [152, 153]. GNPs have also been widely used in biological, chemical agent identification, bioimaging, and various visualizations [154, 155]. Other major uses of gold nanoparticles in biological and chemical sensing duo its efficient sensing properties use for the detection of different molecules and analytes such as nucleotides, saccharides, metals ions and anions [156] proteins [157, 158] and toxins [159]. Gold nanoparticles are also utilizes for detection of microbial metabolites and microbial cells [160] cancerous cells bioimaging [161, 162] and revelation of receptors on their surface, [163, 164] study of endocytosis and other purposes.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

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