

REVIEW PAPER

Biosynthesis of metallic nanoparticles using plant extracts and evaluation of their antibacterial properties

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ABSTRACT

The increasing attention being paid to metallic nano particles (MNPs) is due to their intensive applications in different areas of science such as medicine, chemistry, agriculture, and biotechnology. The main methods for nanoparticle production are chemical and physical approaches that are often costly and potentially harmful to the environment. Since the eco-friendly synthesis of NPs with different chemical compositions, sizes, shapes and controlled dispersity is an important aspect of nano biotechnology and green nanotechnology, biosynthesis of nanoparticles has been proposed as a cost-effective and environmental-friendly alternative to chemical and physical methods. Plants contain abundant natural compounds such as alkaloids, flavonoids, saponins, steroids, tannins and other nutritional compounds. These natural products are derived from various parts of the plant such as leaves, stems, roots, shoots, flowers, barks, fruits and seeds. Since the plant extract contains various secondary metabolites, it acts as the reducing and stabilizing agent for the bioreduction reaction to synthesize the novel metallic nanoparticles. This approach has been actively pursued in recent years as an alternative, efficient, inexpensive, and environmentally safe method for producing nanoparticles with specified properties. The present review focuses on the synthesis of MNPs with particular emphasis on biological synthesis using plant extracts and most commonly proposed mechanisms regarding the antibacterial properties of nanoparticles.

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INTRODUCTION

Nanotechnology is “the design, characterization, production and application of structures, devices and systems by controlling shape and size at nanometer scale” [1]. Normally, in nanotechnology, the curiosity lies on the matter with at least one dimension measuring between 1 and 100 nm. Within this range, materials may have properties considerably different from those expected when they have larger dimensions. Nanoscience is a new interdisciplinary subject that depends on the fundamental properties of nano size objects [2, 3]. A nanometer (nm) is a billionth of a meter, 10^{-9} . To

demonstrate this, the size of a human hair is 80,000 nm wide and a virus is around 100 nm in diameter. About ten atoms in a line make up one nanometer because one atom is 0.1 nm in diameter.

Nanomaterials can show atom-like behaviors which result from higher surface energy due to their large surface area, while a bulk material has constant physical properties regardless of its size, at the nanoscale, this is often not the case [4]. Several well-characterized bulk materials have been found to possess most interesting properties when studied in the nanoscale. There are many reasons for this including the fact that nanoparticles possess a very high aspect

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ratio. Due to the specific characteristics such as size, distribution and morphology, nanoparticles exhibit completely new or improved property, which impact all aspects of human life. Nanotechnology has opened a wide opportunity in the area of materials science, and the incorporation of other branches, such as photochemistry and electrochemistry to better understand its properties [5].

The metallic nanoparticles have been studied expansively because of their unique physicochemical characteristics including catalytic activity, optical properties, electronic properties, antibacterial properties and magnetic properties [6-11]. Noble metallic NPs, such as Ag, Au, Pd, have enticed tremendous interest in the scientific community [12, 13]. These materials have given rise to a busy area of research, due to the wide variety of applications in fields such as biomedicine, catalysis, preparation of nanocomposites with tunable electrical conductivity, thermal conductivity, tensile strength, superior rigidity, hardness and erosion resistance. So, they can be used for manufacturing of satellite components, aircraft spares, industry parts and electronic segments such as microchips processors [14-17].

The metallic nanoparticles are most promising; they have good antibacterial properties due to their large surface-area-to-volume ratio, which is of much interest to researchers due to the growing microbial resistance against metal ions, antibiotics, and the development of resistant strains. Silver nanoparticles show effective antimicrobial property compared to other nanoparticles due to their extremely large surface area, which provides better contact with microorganisms. In this way, nanoparticles are attached to the cell membrane and penetrate into the bacteria. The bacterial membrane contains sulfur-containing proteins, and the silver nanoparticles interact with these proteins in the cell as well as with the phosphorus-containing compounds like DNA. The nanoparticles preferably attack the respiratory chain and cell division finally leading to cell death. The nanoparticles release silver ions in the bacterial cells enhancing their bactericidal activity [18].

The highlight of this review is related to the green synthesis using plant extract and characterization of Cu, Zn, Ag NPs techniques and their antibacterial properties.

Techniques for the synthesis of nanoparticles

Generally, the methods for the synthesis of nanoparticles are usually classified into two categories: the physical and chemical techniques

[19]. Physical synthetic methods such as inert gas condensation, severe plastic deformation, high-energy ball milling and ultrasonic shot peeling can be used to synthesize metallic nanoparticles [20]. Several methods including the commonly grinding process and pyrolysis can be used for the physical synthesis of metallic nanoparticles. The grinding process is the most representative example of the physical methods, where highly efficient mills are used to separate the particles of nanometric sized. In grinding process, macroscale or microscale particles are ground by a size-reducing mechanism; e.g., an ordinary or a planetary ball mill. The resulting particles are subsequently air classified to recover oxidized nanoparticles. The factors that critically affect the properties of the resultant nanoparticles include the material and time of milling and the atmospheric medium. In pyrolysis, an organic precursor (either a liquid or a gas) is forced through an orifice at high pressure and is burned. The resulting ash is air classified to recover oxidized nanoparticles.

However, these techniques have not been a reliable system to obtain metallic nanoparticles because, generally, the obtained particles are larger than 100 nm, which could not be considered as nanometric size. Another disadvantage of physical methods is expensive and cumbersome for the large-scale production of nanoparticles [21]. A further drawback of “physical” approaches is enormous consumption of energy to maintain the high pressure and temperature used in the synthesis procedures.

Chemical methods involve the reduction of chemicals [22], electrochemical procedures [23], and reduction of phytochemicals [24], microemulsion, chemical coprecipitation, chemical vapor condensation, pulse electrodeposition [20]. A typical procedure involves growing nanoparticles in a liquid medium containing various reactants, in particular reducing agents, such as sodium borohydride or potassium bitartrate [25] or methoxy polyethylene glycol [26] or hydrazine [21]. To prevent the agglomeration of metallic nanoparticles, a stabilizing agent such as sodium dodecyl benzyl sulfate [21] or polyvinyl pyrrolidone [25] is also added to the reaction mixture. Most chemical methods used for the synthesis of nanoparticles are too expensive and also involved with the use of toxic and hazardous chemicals that are responsible for various biological risks.

Various chemical and physical methods have

been reported in order to synthesis nanoparticles, but some of the chemical procedures involved in the synthesis of these nanoparticles use toxic solvents which could potentially generate unsafe and hazardous byproducts and often involve high energy consumption [27-29].

Nanoparticle synthesis methods can also be classified as “bottom-up” and “top-down” by the direction of the nanoparticle formation. The “bottom-up” reaction begins from atomic level through forming molecules; however, in the opposite technique described as “top-down” the scale of the resultant nanoparticles is larger, so that a mechanical process or the addition of acids is required to reduce the particle size. Usually, the “top-down” technique requires the use of complex and complicated instrumentation (Fig. 1) [30].

The development of green processes for the synthesis of nanoparticles has been evolving into an important branch of nanotechnology as green nanotechnology deals with the safe and eco-friendly methods for nanomaterials fabrication which is considered as an alternative for the conventional physical and chemical methods.

Green nanotechnology is gaining importance due to the elimination of harmful reagents and provides the effective synthesis of expected products in an economical manner [11, 31-39]. Noble metallic nanoparticles (MNPs) such as silver, gold and platinum are widely applied in medicinal applications. There is a growing need to develop an environmentally friendly process for the synthesis of nanoparticles that does not employ toxic chemicals [40-42]. Thus, synthesizing nanoparticles by biological means, which has the advantages of nontoxicity, reproducibility in production, easy scaling-up, and well-defined morphology, has become a new trend in nanoparticle production. In particular, microorganisms and plants have been demonstrated as new resources with considerable potential for synthesizing nanoparticles. In the case of biological methods, nanoparticle synthesis using plant extracts is the most adopted method, because it is eco-friendly, the green production of nanoparticles, it can act as a source of several metabolites, it is much safer to handle, and easily available [37, 38, 43]. While fungi and bacteria require a comparatively longer incubation time

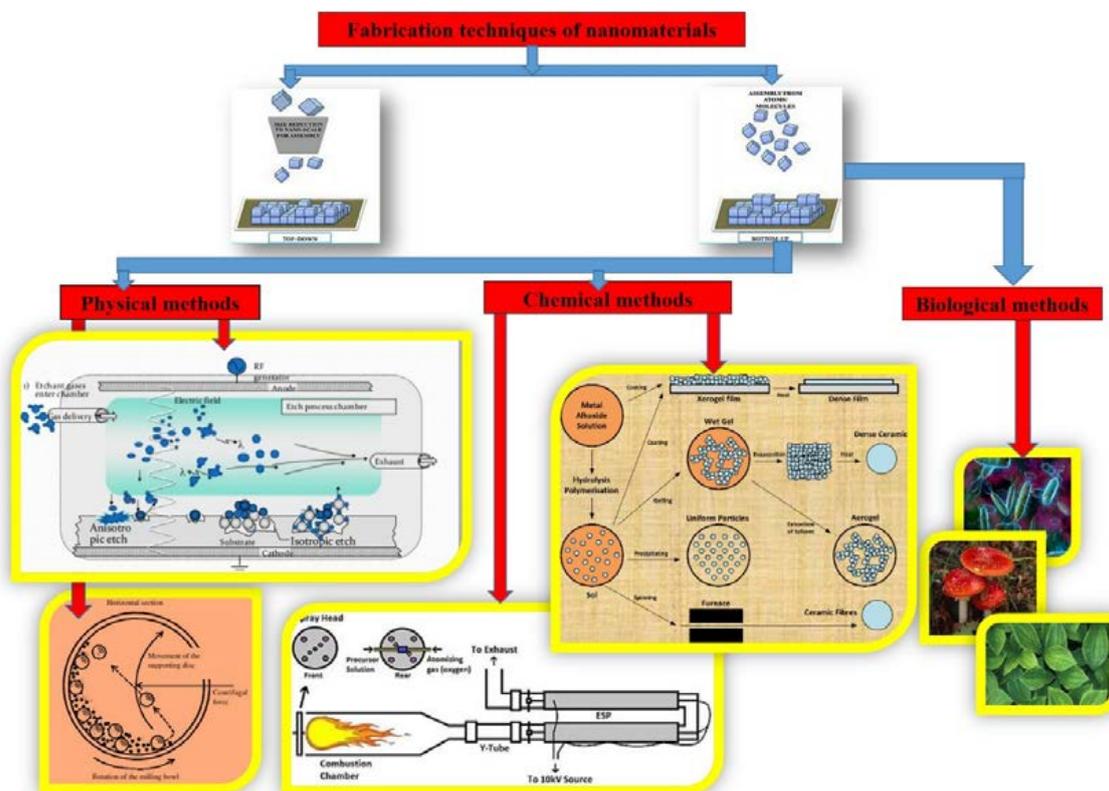


Fig. 1: Fabrication techniques of nanoparticles

in the growth media for reducing a metal ion, water-soluble phytochemicals do the same in a jiffy. Therefore, compared with bacteria or fungi, plant cells are among the suitable candidates for the synthesis of metallic nanoparticles. Plant-based synthesis of nanoparticles works at low temperatures and requires only modest and environmentally safe components [44]. In addition, the synthesis of nanoparticles using plants offers other advantages, such as the utilization of safer solvents, decreased use of dangerous reagents, milder response conditions, feasibility, and their adaptability in use for medicinal, surgical, and pharmaceutical applications [45]. Furthermore, physical requirements for their synthesis, including pressure, energy, temperature, and constituent materials, are trivial.

In the biosynthesis of metallic nanoparticles using plant extract, three important parameters are (1) metal salt, (2) a reducing agent, and (3) a stabilizing or capping agent for controlling the size of nanoparticles and preventing their aggregation [46]. Many biomolecules in plants such as proteins/enzymes, amino acids, carbohydrates, alkaloids, terpenoids, tannins, saponins, phenolic compounds, reducing sugar and vitamins [47] could be involved in bioreduction, formation and

stabilization of metal nanoparticles. The reduction potential of ions and reducing the capacity of plants which depend on the presence of polyphenols, enzymes, and other chelating agents present in plants have critical effects on the amounts of nanoparticle production (Fig. 2).

Antibacterial activity of metallic nanoparticles

Metal-based nanoparticles represent an alternative for biomedical treatments, mainly in the fabrication of biomedical devices with antimicrobial coatings. A high antimicrobial activity of nanoparticles depends on the particle size that allows greater surface contact and a direct interaction with the membranes of pathogenic microorganisms. The antibacterial activities of metallic nanoparticles were found to be related to their shapes and sizes. Nanoparticles smaller than 10 nm interact with bacteria and produce electronic effects, which improve the reactivity of nanoparticles. Thus, it is proven that the bactericidal effect of nanoparticles is size dependent [48].

The cell membranes of the microorganisms interact with the medium, so metal NPs will have some interactions to release metal ions that interfere with the processes of the DNA replication, cell membrane formation, cell division, and so

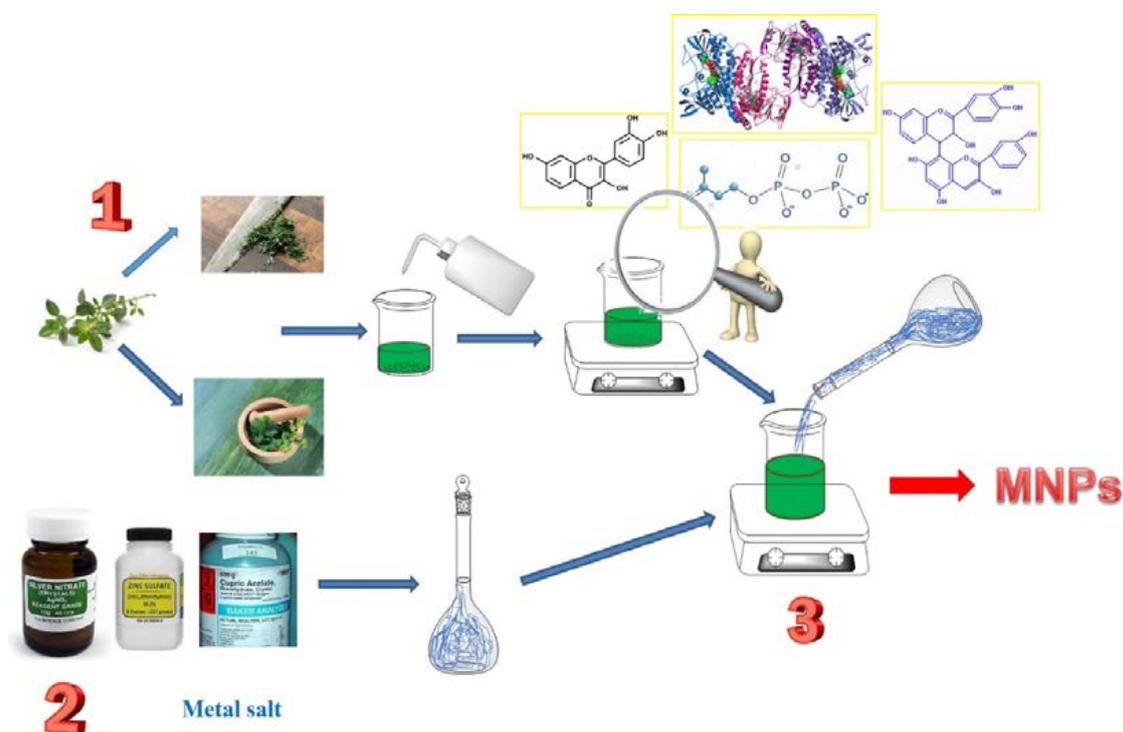


Fig. 2: Synthesis of nanoparticles using plant extracts

forth, of certain microorganisms such as bacteria, which results in an antimicrobial effect [48, 49].

Several studies propose that nanoparticles attach to the surface of cell membrane disturbing the permeability and respiration function of the cell [18, 24]. The damage to the cell may be caused by the interaction of nanoparticles with sulfur or phosphorus-containing biomolecules in the cell such as DNA. Therefore, sulfur-containing proteins in the membrane or inside cells and phosphorus-containing elements like DNA are likely to be preferential sites for binding Ag and Zn [50-52] or CuNPs. Other studies suggest that when bacteria are treated with silver ions, DNA tends to lose its ability to replicate. Lokini et al. [53] showed that AgNPs could destabilize the outer membrane and rupture the plasma membrane, thereby depleting intracellular ATP. The excellent antibacterial activity of silver nanoparticles is mainly attributed to their high surface area-to-volume ratio that enables greater presence of atoms on the surface and, in turn, greater contact with the environment. The smaller nanoparticles have more antibacterial activity that provide more surface exposure to the bacterial membrane [54]. In addition, these nanosized particles penetrate through cell membrane easier, interacting with intracellular materials and finally resulting in cell destruction in the process of multiplication. Luo et al. [55] documented that the nanoparticles induce oxidative stress to bacteria and induce ROS production. For example, the antibacterial activity could be explained based on reactive oxygen species (ROS) such as H_2O_2 , hydroxyl radicals, singlet oxygen, and Zn^{2+} ions released on the surface of ZnO which cause severe damage to bacteria [56-58]. The generation of hydrogen peroxide (H_2O_2) from the surface of ZnO is considered as an effective mean for the inhibition of bacterial growth according to some studies [59]. It has been reported that both UV and visible light can activate ZnO and consequently, electron-hole pairs (e^-/h^+) can be created. The generation of H_2O_2 is explained as follows: the holes split the H_2O molecule from the suspension of ZnO into OH and H^+ . Furthermore, dissolved oxygen molecules are converted to superoxide radical anions ($O_2^{\cdot-}$) which react with hydrogen ion (H^+) to produce HO_2^{\cdot} radicals. The collision of these hydroxyl radicals with electrons will produce hydrogen peroxide anions HO_2^{\cdot} , which react with hydrogen to generate H_2O_2 molecules. Therefore, the H_2O_2 molecules generated can penetrate into the cell

membrane and kill the bacteria [60, 61]. The e^-/h^+ pair recombination minimizes the chances of ROS generation. Lattice defects play an important role in the inhibiting e^-/h^+ pair recombination process [62]. These defects may act as trapping centers and inhibit photo induced e^-/h^+ pair recombination [63] resulting in higher antibacterial activity. Further, under normal circumstances, cells are able to defend themselves against ROS damage with antioxidant enzymes. However, when the nanoparticles are inside the cell, the nanoparticles could restrain antioxidative enzymes to inhibit the capability of removing ROS. Also reported that the nanoparticles break the balance of oxidant/antioxidant and generate the accumulation of ROS in bacteria. However, exact mechanism of AgNPs on different bacterial cells needs a further study. Priester et al. [64] suggested that the action mechanism of the copper NPs occurs through the interaction of enzymes and -SH groups causing damage in the DNA and therefore oxidative stress generation [65-67]. The mechanism of penetration of nanoparticles to the bacteria is not understood completely, but studies suggest that when bacteria are treated with zinc nanoparticles, changes taken place in its membrane morphology cause a significant increase in its permeability affecting proper transport through the plasma membrane [68, 69], leaving the bacterial cells incapable of properly regulating transport through the plasma membrane, resulting into cell death [70]. In addition, ZnO nanoparticles could be attributed to the damage of the bacterial cell membrane and extrusion of the cytoplasmic contents thereby resulting in the death of the bacterium [71]. Several investigations have suggested the possible mechanisms involving the interaction of nanomaterials with the biological macromolecules. It is believed that microorganisms carry a negative charge while metal oxides carry a positive charge. This creates an "electromagnetic" attraction between the microbe and treated surface [72]. However, to understand the mechanisms of action of these agents, more detailed chemical structure elucidation of the bioactive components followed by therapeutic investigations and toxicological assessment are required.

Techniques for characterization of metallic nanoparticles

The development of materials at nanometric scale is being increased in different fields. The properties of these nanomaterials are critical for

the technological revolution worldwide, which mainly depend on the methods of synthesis for the potential applications such as the bactericidal and antifungal effect [73]. For observation of formation and characterization of metallic nanoparticles, several experimental techniques are applied [74-76].

UV-Visible spectroscopy (UV-VIS) is a technique used to quantify the light that is absorbed or scattered by a sample. It is generally recognized that UV-Vis spectra could be used to examine the size and shape controlled nanoparticles in aqueous suspensions [77]. Some of the colloidal metal materials are different under the macroscopic scale and show distinct absorption peaks in the visible region; copper, silver, and gold are metal with prominent absorption peaks. The optical absorption spectra of noble metallic nanoparticles are known to exhibit unique optical properties due to the property of surface plasmon resonance (SPR), which shift to longer wavelengths with increasing the particle size. On the other hand, SPR of a multi-nanoparticle aggregate will be red-shifted to a longer wavelength compared with SPR of the individual particles. SPR is the effect of the oscillation of the conducting electrons aligned in resonance to the wavelength of the irradiated light [78]. The size and shape, the spacing between the metallic nanoparticles and dielectric constant of the medium and surface adsorbed species determine the spectral position of plasmon band absorption as well as its width [79]. According to Mie's theory, only a single SPR band is expected in the absorption spectra of spherical nanoparticles, whereas anisotropic particles could give rise to two or more SPR bands depending on the shape of the particles. The number of SPR peaks increases as the symmetry of the nanoparticle decreases [80-82]. The color appearing is due to excitation of surface plasmons in metallic nanoparticles [83]. Formation of MNPs by using plant extracts as a result of the reduction of the metal ions to metal is followed by color change and thus UV-Vis spectrum [84, 85].

Transmission Electron Microscopy Analysis (TEM) is the most common characterization technique to determine the size, shape and size distribution of the MNPs.

Scanning Electron Microscopy (SEM)

The SEM image provided insight into the morphology and size of the synthesized nanoparticles.

X-Ray Diffraction (XRD)

The crystal structure and average particle size of the nanoparticles were analyzed by XRD system [86]. Generally, the narrow and strong diffraction peaks indicate the well crystalline nature of synthesized nanoparticles. The mean size of nanocrystals was measured from the broadening of the diffraction peaks corresponding to the most intensive reflections according to the JCPDS (Joint Committee on Powder Diffraction Standards) database. Scherrer equation [87] was used to determine the crystallite size from XRD diffraction pattern measured for nanoparticles:

$$d = K\lambda / B \cos\theta$$

Where:

d- the average dimension of crystallites in nanometers,

λ - the wavelength of the X-ray radiation

K- the Scherrer constant (shape factor, usually taken as 0.94),

B- the line width at half-maximum height (FWHM) in radians,

θ - the Bragg angle, (the position of the diffraction peak maximum).

Energy Dispersive X-Ray Spectroscopy (EDS or EDX)

EDX spectroscopy is used for identification, purity and the elemental composition of the synthesized nanoparticles.

Scanning Electron Microscopy (SEM)-Energy Dispersive X-RAY Spectroscopy (EDX)

The morphology and chemical composition of the synthesized nanoparticles were examined by scanning electron microscopy (SEM) equipped with an energy-dispersive X-ray spectrometer (EDX or EDS). The main use of high-resolution EDS/SEM ($\sim 100 \text{ \AA}$) is the ability to obtain three-dimensional images with large depth fields by a simple sample preparation [88].

Dynamic Light Scattering (DLS) Analysis

The particle size distribution and zeta potential analysis of NPs were evaluated via dynamic light scattering (DLS) and zeta potential was analyzed using Malvern Zetasizer Nano range instrument. The particle size distribution spectra of the metallic nanoparticles were recorded as diameter (nm) versus frequency (%/nm) spectra with diameter (nm) on x-axis and frequency (%/nm) on y-axis. The zeta potential spectra of the

metallic nanoparticles were recorded zeta potential versus intensity spectra; zeta potential (mV) on x-axis and intensity (a.u) on y-axis. Zeta potential values reveal details about the surface charge and predicting the long-term stability of the dispersion of synthesized metallic nanoparticles [89]. Nanoparticles with zeta potential values greater than +25 mV or less than -25 mV typically have high degrees of stability. If the hydrosols have a large negative or positive zeta potential then they will tend to repel each other and there will be no tendency of the particles to agglomerate. On the other hand, the particles have low zeta potential values then there will be no force to prevent the particles coming together and flocculating [90]. The zeta potential of nanoparticles strongly depends on pH and electrolyte concentration of the dispersion [91]. The particle size and zeta potential values of the synthesized AuNPs using mushroom (*Agaricus bisporus*) extract were 32.1 nm, -45.8 mV respectively. Zeta potential measurements reveal the NPs are highly stable and have an average surface charge of -45.8 mV. As mentioned, the higher zeta-potential value is a key parameter to maintain the stability of suspension through the electrostatic repulsion between particles, which results in a high stability of suspension [92].

Fourier Transform Infrared (FTIR) Spectroscopy

Fourier transform infrared (FTIR) spectroscopy, used to evaluate chemical bonds in surface atoms and functional atoms on the surface of nanoparticles, can be used to characterize physical properties of nanomaterials and their functions [93]. In the biosynthesis of MNPs using plant extracts, FTIR spectroscopic measurements were carried out to identify the possible biomolecules in extracts responsible for capping leading to efficient stabilization of MNPs. For instance, FTIR spectra of as synthesized CuNPs (biocapped) [94] shows major peaks at 2362 cm^{-1} and 1382 cm^{-1} corresponding to aldehydic C–H stretching and C–N stretching vibration of the aromatic amine, respectively. These two peaks are absent when CuNPs washed in acetone/methanol/water in the ultrasonic bath. However, the remaining broadband around 3413 cm^{-1} in both cases indicates the presence of O–H stretching corresponding to poly phenols (flavonoids) present in the plant extract [95]. Also, the bands at 1714 cm^{-1} and 1108 cm^{-1} ascribed to C=O stretching and C–O bending indicate the presence of flavonoids and terpenoids which may be responsible for the reduction/stabilization process (Fig. 3) [96].

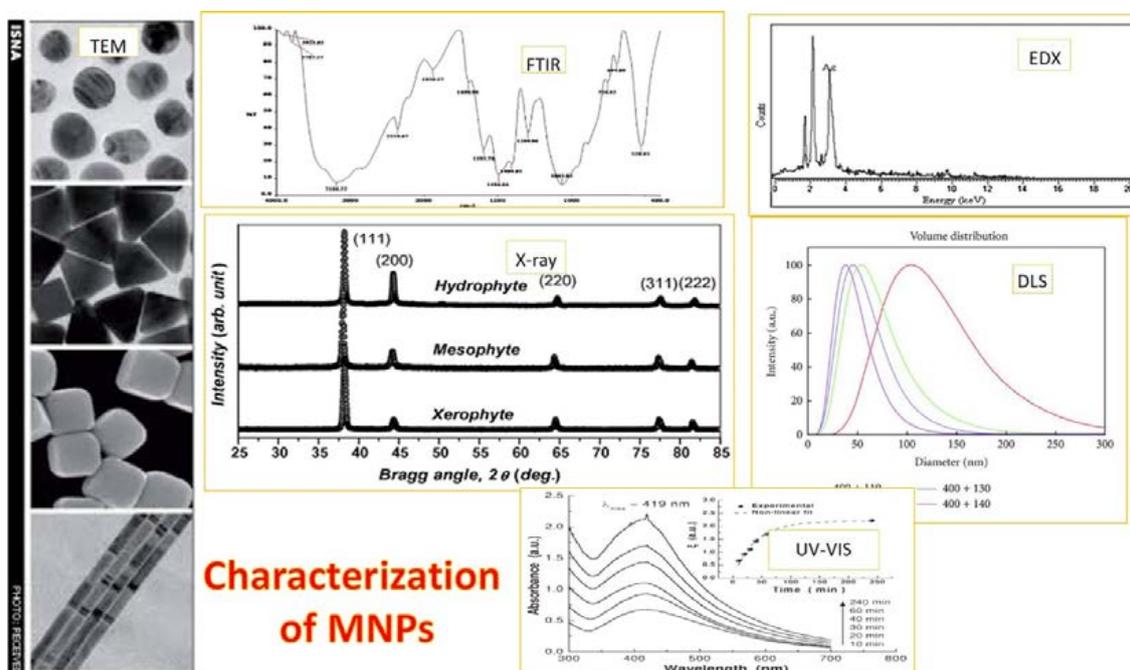


Fig. 3: Techniques for characterization of metallic nanoparticles

Synthesis of Nanoparticles Using Plant Extracts

Generally, nanoparticles are prepared by a variety of chemical and physical methods which are not environmentally friendly. Green synthesis of MNPs is an economical, eco-friendly and simple method in the synthesis route [32, 97-99]. A number of biomolecules act as reducing and protecting agents in the green synthesis of MNPs. Green/biosynthesis of MNPs were performed by using bacteria, fungi and plant extract [100-102]. Green synthesis appears to be a cost-effective alternative to conventional physical and chemical method of MNPs synthesis and would be suitable for developing a biological process for large-scale production. Nowadays, plant extracts act as reducing and capping agents for the synthesis of nanoparticles, which is more advantageous than chemical, microbial synthesis [103-107].

The rate of nanoparticle growth depends upon various variables, including the concentration of metal ions, amount of plant extract, pH and temperature [108]. Time is also a key parameter in the synthesis of nanoparticles. The availability of an enormous number of nuclei at a given time resulted in decreasing the size of nanoparticles, because smaller metal nuclei grow and use metal ions at the same time [109].

Vilchis-Nestor et al. [110] reported the synthesis of gold nanoparticles and silver nanostructures by using green tea (*Camellia sinensis*) extract in aqueous solution at ambient conditions. They also investigated the control of size, morphology, and optical properties of the nanostructures and reported initial concentrations of metal ions and plant extract as controlling factors. It was investigated that when the amount of *C. sinensis* extract is increased, the resulted nanoparticles are slightly bigger and more spherical. In another study, the amount of plant material was found to play a critical role in controlling the size and size disparity of metallic nanoparticles. Accordingly, smaller metallic nanoparticles and narrow size distribution occur when more plant extract is added in the reaction medium. The particle size distribution varied with the variation in the dosage of *C. zeylanicum* bark extract. The number of particles increased with increasing dosage due to the variation in the number of reductive biomolecules [111].

As metal particles are generated in the aqueous phase, they are unstable by nature, and these metal atoms tend to agglomerate to decrease the total

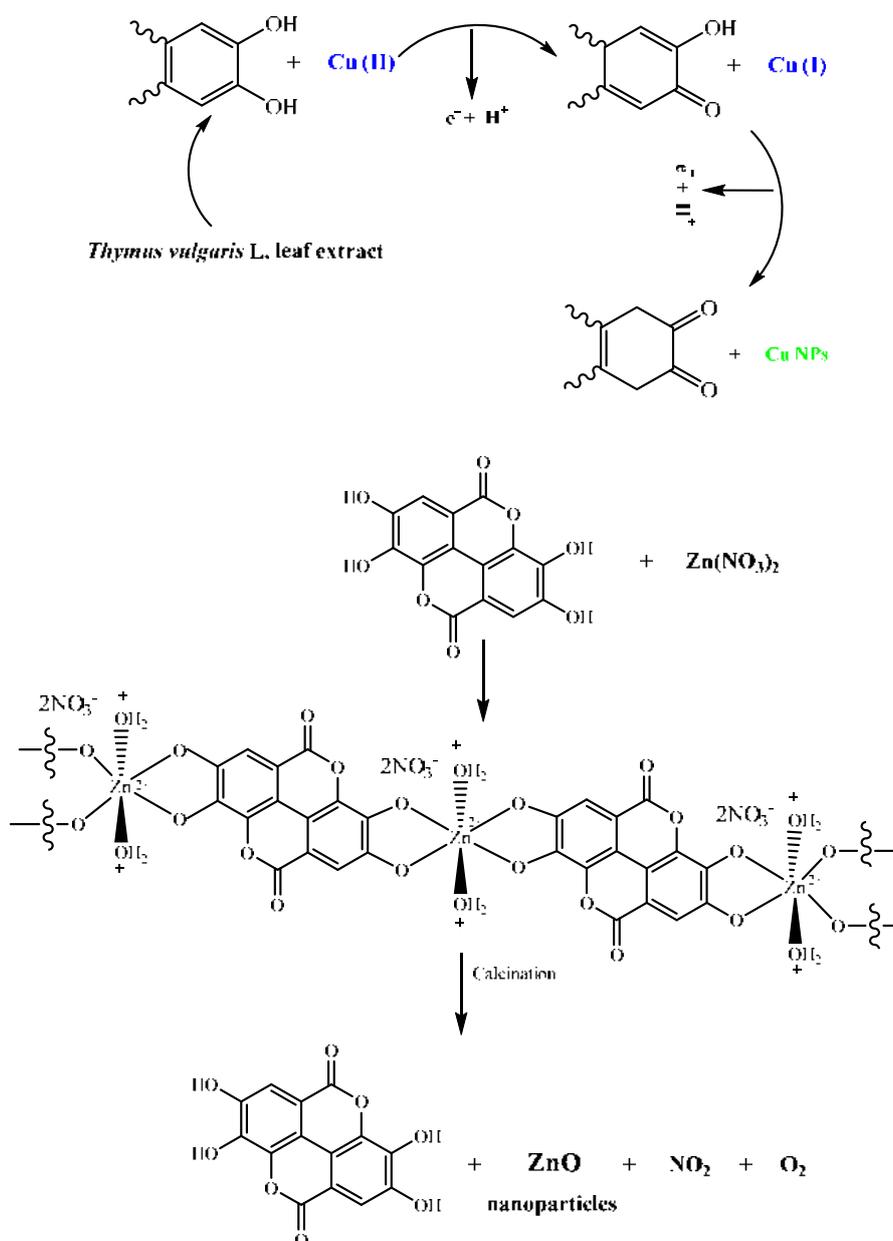
surface energy. In addition, some metals serve as nuclei for others to grow on. This agglomeration, which can be caused by attractive van der Waals forces between crystals, should be repressed to limit the final particle size at the nanometric scale [109]. The plant extract serves as a reducing and dispersing agent to separate metal ions from each other and hence provides better size control of nanoparticles. It also remains on the metal NPs as the capping agent and improves the biological activity. The plant extracts/bioextract often contains metabolites such as flavonoids, proteins, terpenoids, and polyphenols. These biomolecules not only act as reducing agents for metal ion reduction but also (remains on the metallic NPs) as the capping agents which helps to minimize the agglomeration of NPs thereby controlling the morphology and also helping to protect/stabilize the NPs, thus improving the biological potential. G. Sangeetha et al. [112] reported the formation of ZnONPs in the biosynthesis procedures by aloe barbadensis miller leaf extract. The overall observation proved the existence of some phenolic compounds, terpenoids or proteins that were bound to the surface of ZnO nanoparticles. The stability of ZnO nanoparticle could be due to the free amino and carboxylic groups interacted with the zinc surface. The bonds of functional groups such as -CO-C- , -C-O- and -C=C- were derived from heterocyclic compounds and the amide bands derived from the proteins were present in the leaf extract and were the capping ligands of the nanoparticle [113-115]. Moreover, the proteins presented in the medium prevented agglomeration and aided the stabilization by forming a coat, covering the metallic nanoparticles.

In green synthesis of CuNPs, biomolecules found in the *Thymus vulgaris* L. leaf extract induce the reduction of Cu^{2+} ions from $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ to copper nanoparticles [116] or in another synthesis, the plant extract of *Nephelium lappaceum* acts as ligation, and the aromatic hydroxyl group present in polyphenolic ellagic acid ligate with zinc ions to form zinc-ellagate complex (pH 5-7). Calcification of this complex at 450 °C in static air leads to the formation of ZnO NPs [117]. (Scheme 1)

In some of the studies, the influence of pH on the biosynthesis of NPs has been investigated. It was suggested that different values of pH affect nanoparticle size and shape. In the synthesis of silver and gold nanoparticles by fruit extract of *Tanacetum vulgare*, larger particle size could be

achieved by decreasing the pH [89]. In another study, Dwivedi and Gopal [118] determined that nanoparticles are more stable when exposed to higher pH conditions. Results of studies in the biosynthesis of AgNPs indicate that the size of nanoparticles decreases when pH increases. At lower pH, aggregation exceeds over nucleation to form large particles. Whereas, at higher pH, more functional groups are available for binding to silver leading to the synthesis of stable, small-

sized nanoparticles. However, as stated by Gan and Li [119], plant extracts which can produce a large number of stable nanoparticles over wide pH range can be more suitable for application in which there is a change in environmental PH. However, previous studies have indicated that neutral pH is optimal for the synthesis of AgNPs . At this pH, little or no assembly of AgNPs into the particles of suitable size and shape occurs [120]. In another study, nano-crystalline palladium particles



Scheme 1. Possible mechanisms of formation of Cu and ZnO NPs by using the extract of plants.

Table 1: The synthesis of NPs using plant extracts by modifying parameters such as temperature and time.

plants	Parts of plant	NPS	Size (nm)	morphology	T (°C)	Time	Ref
Eichhornia crassipes	leaf	ZnO	32	Spherical	60	1 h	[121]
Trifolium pratense	flower	ZnO	60-70	Spherical	90	4 h	[122]
Aloe vera	leaf	ZnO	25-40	Spherical	150	5-6 h	[112]
Boswellia ovalifoliolata	stem bark	ZnO	20	Spherical	-----	1 h	[123]
garlic (<i>Allium sativum</i>)	leave	ZnO	14	Spherical	90	3 h	[124]
<i>Althaea officinalis</i> L	flower	AgO	50	Spherical	62	15 min	[125]
Magnolia kobus	leaf	Cu	37	Spherical	95	24 h	[126]
Potato		ZnO	20	Hexagonal (wurtzite)	80	30 min	[127]
Aloe Vera	flower	Cu	40	Spherical	50	30 min	[128]
Potato		Fe ₃ O ₄	40	Spherical	80	35 min	[129]
Magnolia Kobus	leaf	Au	40	Hexagonal	95	3 min	[130]
Kalopanax pictus	leaf	MnO ₂	19.2	Spherical	rt	90 min	[131]
Diopyros kaki	leaf	Pt	2-20	Spherical - plates	95	2-3 h	[132]
<i>Tradescantia pallida</i>	leaf	ZnO	23-27	rod	60	4h	[133]
Magnolia kobus	leaf	Ag	16	Spherical	95	30 min	[134]
Kalopanax pictus	leaf	Ag	10	Spherical	90	-----	[135]
Kalopanax septemlobus	leaf	Ag	30.8	Spherical	rt	24 h	[136]
Calotropis procera	leaf	Ag	10	Spherical	rt	10 min	[137]
Alternanthera dentata	leaf	Ag	10-80	Spherical	rt	10 min	[138]
Cocous nucifera	flower	Ag	22	Spherical	rt	24 h	[139]
Abutilon indicum	leaf	Ag	7-17	Spherical	rt	15 min	[140]
Quercus brantii (oak)	leaf	Ag	0.83-6	Spherical	rt	5h	[141]
Cycas	leaf	Ag	2-6	Spherical	95	20 min	[142]
Punica granatum	peel	Cu	15-20	Spherical	rt	8 h	[143]
Ananas comosus	fruit	Ag	5-30	Spherical	rt	2 min	[144]
<i>Vitis vinifera</i>	fruit	Se	3-18	Spherical	95	15 min	[145]
Carica papaya	leaf	ZnO	50	Spherical	60	2 h	[146]
Banana	peel	CuO	23	Spherical	70-80	-----	[147]
Belgian endive	leaf	Ag	19-64	Spherical	75-80	-----	[148]
Sasa borealis	leaf	Au	10-30	Oval, Spherical	50	20 min	[149]
Elettaria cardamomum	seed	Au	15.2	Spherical	60	2 min	[150]
Camellia japonica	leaf	CuO	15-25	Spherical	60-80	-----	[151]
Ficus carica	fruit	Ag	54-89	Spherical	rt	24 h	[152]

(10–15 nm) have been synthesized using *Curcuma longa* tuber extract as biomaterial that pH and temperature have no major effect on size and shape of the nanoparticles.

Investigations showed that the rate of synthesis of the nanoparticles was related to the reaction and incubation temperature, and an increase in temperature levels leads to nanoparticle growth at a faster rate and reducing their average particle size. The reason for a decrease in particle size with temperature can be discussed as follows. As the reaction temperature increases, the reaction rate increases and thus most metal ions are consumed in the formation of nuclei, stopping the secondary reduction process on the surface of the preformed nuclei. For instance, synthesis rate and final conversion to silver nanoparticles became faster when reaction temperature increased. However, the average particle sizes produced by *D. kaki* leaf broth decreased from 50 nm to 16 nm when temperature

increased from 25 °C to 95 °C [84].

Table 1 summarizes the important examples of nanoparticle biosynthesis using various plant extracts. Moreover, some important features of the nanoparticles including size and morphology and a number of parameters such as temperature and time are mentioned.

CONCLUSION

It is known that green synthesis of MNPs is much safer and environmentally friendly compared to chemical and physical synthesis. The methodology employed by using plant extract is very simple, easy to perform, inexpensive, high efficient and eco-friendly. Plant extracts contain diverse chemical compounds such as proteins, carbohydrates, alkaloids, tannins, phenolics, oils, and saponins which have medicinal value and the same can act as reducing and capping agents for MNP synthesis.

The shape, size, and size distribution of MNPs can be controlled by optimization of reaction conditions, such as temperature, pH, and amount of plant material suggesting that extract can be used as both reducing and stabilizing agent for the preparation of MNPs. With the help of more detailed experimentation on reaction parameters such as pH, temperature, ratio and concentration of plant extract to the metal salt, it will be possible to optimize production process to obtain a large amount of stable, and small size MNPs.

Phytosynthesized MNPs have many applications such as antimicrobial, biomedical, agriculture, bioinsecticides, catalyst, biosensor, etc. The antibacterial activities were inversely proportional to the average nanoparticle sizes. The studies indicated that biologically synthesized metallic nanoparticles using plant extract have higher antibacterial activity than metallic nanoparticles chemically synthesized. Future prospect of plant-mediated nanoparticle synthesis includes an extension of laboratory-based work to industrial scale, elucidation of phytochemicals involved in the synthesis of nanoparticles using bioinformatics tools and deriving the exact mechanism involved in inhibition of pathogenic bacteria.

CONFLICT OF INTEREST

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

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