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Review Article

GREEN SYNTHESIS OF PLANT-MEDIATED METAL NANOPARTICLES: THE ROLE OF POLYPHENOLS

LATIF MS, ABBAS S, KORMIN F*, MUSTAFA MK

Department of Technology and Natural Resources, Faculty of Applied Sciences and Technology, Universiti Tun Hussein Onn Malaysia Kampus Pagoh, KM1, Jalan Panchor, 84000 Muar, Johor, Malaysia. Email: faridahk@uthm.edu.my

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ABSTRACT

The use of metal nanoparticles (MNPs) in various fields is increasing day-by-day leading to a genuine concern about the issues related to their environmental and biological safety. The major approaches for the synthesis of NPs include physical and chemical methods which are expensive and hazardous to health in addition to being toxic to the environment. This review highlights the potential of plant extracts to carry out the synthesis of MNPs with a special emphasis on the role of flavonoids in nanosynthesis. This green and clean approach have been actively utilized in recent years as an alternative to conventional hazardous approaches. It has proved as cost-effective, non-toxic, less time and labor consuming, efficient, and eco-friendly method for the synthesis of MNPs with specific biological actions. This review also focuses on the role of polyphenols, including the flavonoids as bioreductants of metal salts for the synthesis of NPs along with their biomedical applications. Various examples of the MNPs, along with their biological actions, have also been summarized.

Keywords: Green synthesis, Metal nanoparticles, Polyphenols, Flavonoids, Plant extract.

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INTRODUCTION

The synthesis of nanoparticles (NPs) can be performed using different methods, including physical, chemical, and biological techniques [1]. The NP synthesis by conventional physical and chemical techniques carries the risk of toxicity and environmental pollution as they release toxic by-products, which are potentially hazardous to the environment [2]. In addition to it, the NPs synthesized by such hazardous methods are unfit for the medical field due to the health-related concerns, particularly in clinical applications [3].

Although the conventional methods are suitable for the synthesis of large quantities of particles, in a lesser period of time, with defined sizes and shapes, these techniques have the drawbacks of being complicated, costly, inefficient, and out fashioned. The recent years have witnessed a growing interest in the nanosynthesis of environment-friendly particles without involving the production of toxic by-products as part of the synthesis process [4-6].

This task is achievable only through adopting environment-friendly synthesis procedures using biotechnology tools of biological nature that is described as safe and environmentally benign for nanosynthesis as an alternative to conventional physical and chemical methods [7,8]. This concept has led to the approach of green technology or green nanobiotechnology. In general, the nanosynthesis procedures involving biological routes such as those which are based on microorganisms (viruses, bacteria, fungi, and algae), plants, plant extracts, or their by-products, for example, proteins, lipids, alkaloids, and flavonoids by applying different biotechnology tools and techniques [9,10]. A graphical summary of plant-based NP synthesis is shown in Fig. 1.

The superiority of NPs synthesized by green technology to those produced by conventional methods is quite evident due to several features. For instance, green technology employs the use of cost-effective chemicals, less energy, and produces eco-friendly products, and by-products. The nanobiotechnology is more advantageous over other conventional procedures due to the fact the more components are available by the biological system for the synthesis of NPs [11,12].

By virtue of the rich biodiversity of biological systems, it is now possible to synthesize the bionanomaterials which are environment-friendly and have the potential to use in a variety of medical applications. Due to the synthesis of environment-friendly chemical products and by-products, the 12 principles of green chemistry are now considered as a reference guide in related research around the world [13]. Consequently, the green nanobiotechnology has now become a promising alternative route for the synthesis of biocompatible and stable NPs [14,15]. In context to the importance of polyphenols including flavonoids of plant extracts in mediating the synthesis of metal NPs (MNPs), this review attempts to highlight and summarize the role of polyphenols in the synthesis of MNPs as described in recent literature.

Biosynthesis of NPs uses a bottom-up approach in which synthesis is performed by the application of reducing and stabilizing agents [16]. There are three main factors which are described for the biosynthesis of NPs based on a biological system: The choice of solvent medium, the choice of an eco-friendly and environmentally benign reducing agent, and the choice of a nontoxic material as a capping agent to stabilize the synthesized NPs [6].

BIOLOGICAL NANOSYNTHESIS AND ITS APPLICATIONS

In contrast to the physical and chemical methods of nanosynthesis, the biological nanosynthesis relies on the use of microorganisms (bacteria and fungi), enzymes, and plants to produce MNPs [17] (Table 1).

There are numerous examples of a variety of applications of the MNPs in the fields of biomedicine, physicochemistry, agriculture, and environment [9,18], as shown in Fig. 2.

PLANT-BASED NANOMATERIALS

The plant resources based green synthesis of a number of MNPs including copper (Cu), gold (Au), nickel (Ni), platinum (Pt), titanium (Ti), selenium (Se), silver (Ag), and zinc NPs have already been reported [19,20]. The plant-based MNPs have been shown to possess various activities such as antimicrobial, anticancer, antidiabetic, anti-inflammatory, antioxidant, and immunomodulatory [21-24]. In recent

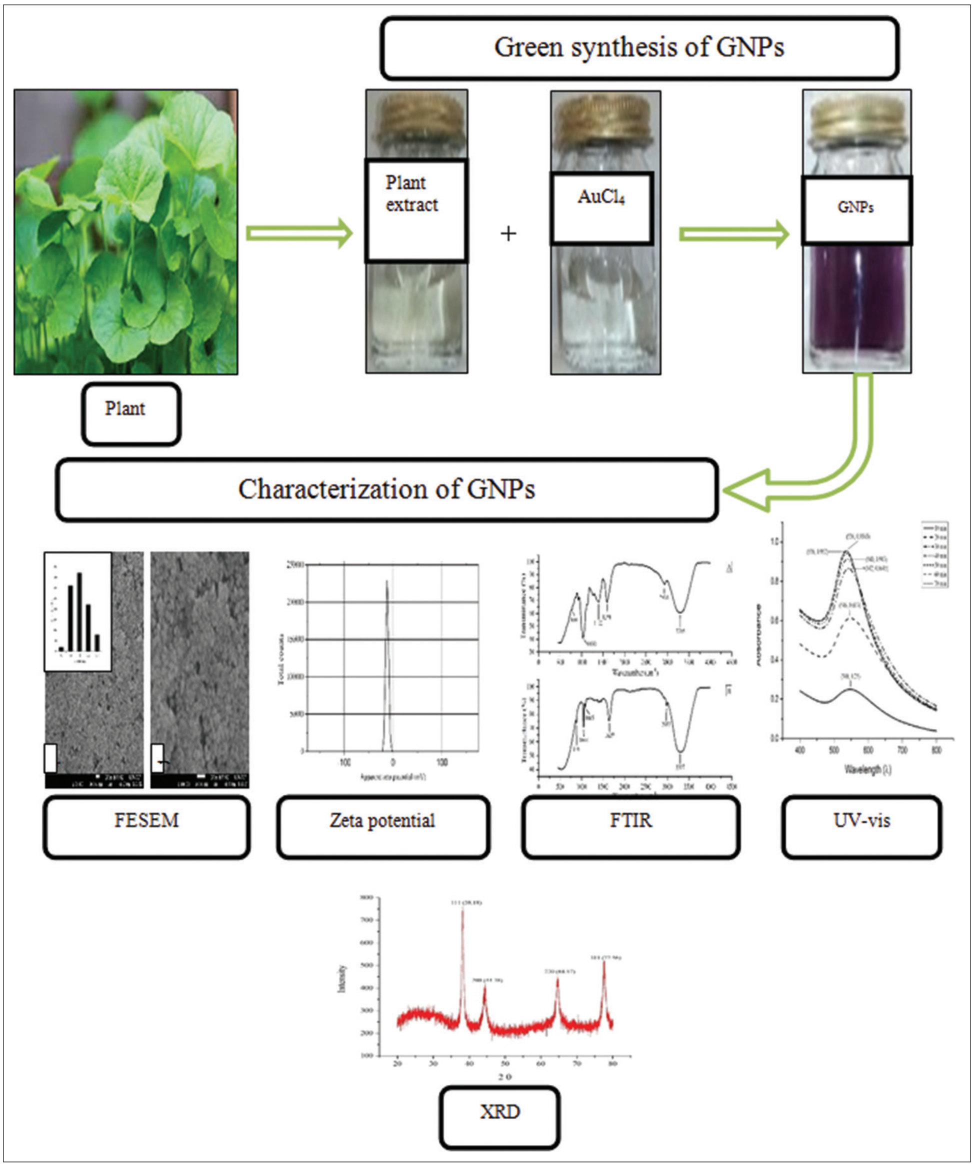

Fig. 1: Green synthesis and characterization of nanoparticles using plants

Table 1: Methods of nanoparticle synthesis

Physical	Chemical	Green/biological
Mechanical methods	Coprecipitation	Plant extracts-mediated
Vapor deposition	Sol-gel	Microbial culture-mediated
Sputter deposition	Microemulsions	Agricultural waste-mediated
Electric deposition	-	Enzymes-mediated
Ion beam method	-	-

reviews, the MNPs synthesis using various plant extracts has been reported for cobalt, copper, gold, magnetite, platinum, palladium, and zinc oxide which have been proved as a potent remedy against a variety of infectious diseases along with other acute ailments [19,25]. The role of various phytochemicals such as alkaloids, flavonoids, phenols, sugars, proteins, and terpenoids has been confirmed in most of the previous reports emphasizing their involvement in the bioreduction, capping, and stabilization of metal ions [26,27].

Despite the ease involved in the purification of NPs synthesized using only one single active substance in plant extract, it is important to further study the MNPs with a biomedical perspective for the treatment of particular diseases. At present, limited information is available in the scientific literature regarding the use of a single substance from plant extract for the synthesis of MNPs. Recent reports in literature on this issue show that the flavonoids which have a wide existence in the plant extracts have a major contribution toward the bioreduction, capping, and stabilization of metal ions into NPs formation [28-31].

Plant extracts-mediated synthesis of NPs

To prepare the plant extract, different parts of the plants are used as fresh or dry material such as the fruit, leaf, peel, petal, and shoot. The extraction procedure usually involves soaking the plant material in a green solvent with or without stirring followed by filtration and centrifugation. The filtered extract is rich in the reducing and capping agents required for the bioreduction of metallic ions. The advantage of using dried plant is that it has a long shelf life at room temperature, but it is important to store the fresh plant at −20°C to avoid any deterioration. In addition, the use of dry plant material ensures the elimination of effects of seasonal variations leading to variations in plant constituents [32,33].

Various factors such as temperature, concentrations of the extract, and the metal ions and pH may affect the size and shape of the synthesized NPs [34]. The plant extract based synthesis procedures usually have

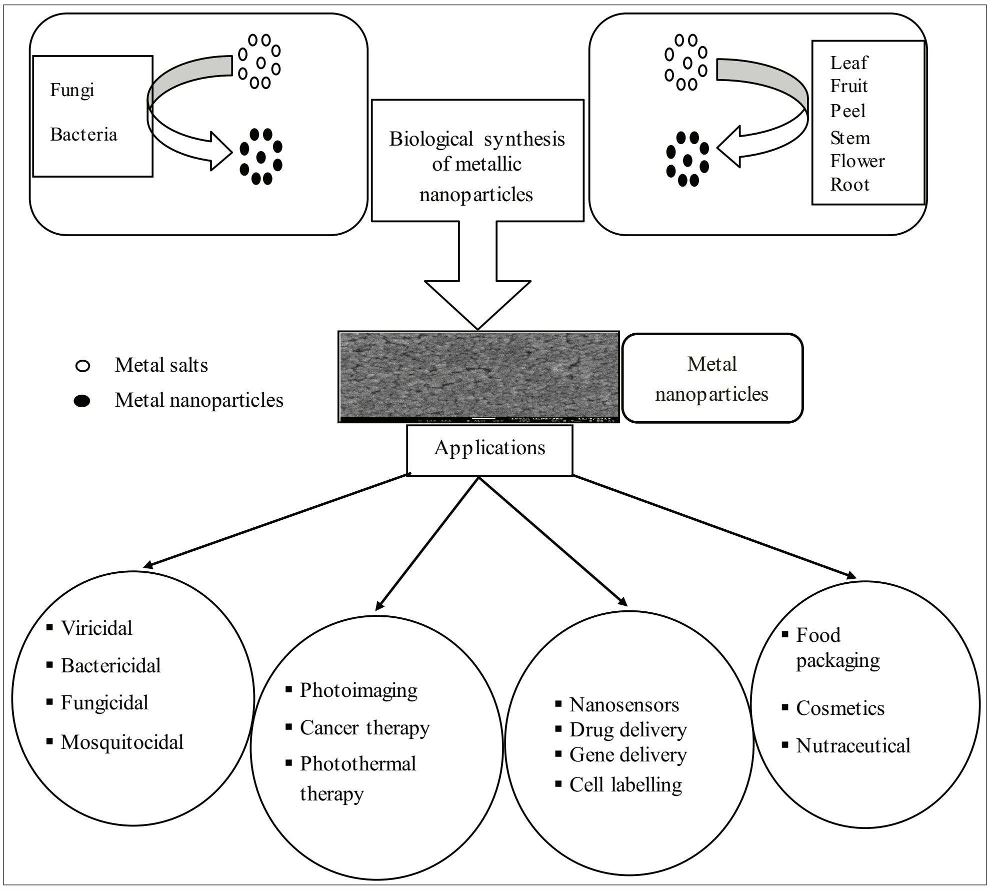

Fig. 2: Biological synthesis and applications of metal nanoparticles

a high rate of reaction, taking several minutes to several hours for completion, depending on the type and amount of the plant extract. Most plants, especially the perennial plants, are almost always naturally available. Usually, the plant extract-based synthesis of metallic NPs is carried out at room temperature, whereas heating of the reaction mixture or culture medium is required for the synthesis of metallic NPs using microorganisms. Due to the ease of handling and flexible reaction conditions, plant extract-mediated synthesis of MNPs is considered as more suitable for large-scale production as compared to microorganisms-based nanosynthesis [5,35,36].

Polyphenols and flavonoids-based MNPs and their biomedical applications

The detail of polyphenols and flavonoids employed in the synthesis of MNPs along with their biomedical efficacy is summarized in Table 2. Recently, it was reported that the major contribution for the synthesis of silver NPs (AgNPs) was of the total flavonoids present in the *Alternanthera tenella* and *Coriandrum sativum* leaf extracts [7]; and shown to be efficacious as antiacne, antidandruff, and anti-breast cancer agent as they were found active against *Propionibacterium acnes*, *Malassezia furfur*, and human breast adenocarcinoma cells, respectively [28,29].

The bioreduction of Ag^+ to AgNPs was carried out by the water-soluble flavonoids present in *Myrmecodia pendan* extract [37]. It was inferred that the flavonoids of *Dalbergia spinosa* leaf extract may be adsorbed onto the metal ions surface by interacting with carbonyl groups or electrons, thereby exhibiting increased anti-inflammatory, and antibacterial (against *Bacillus subtilis*, P*seudomonas aeruginosa*, *Staphylococcus aureus*, and *Escherichia coli*) activities [38]. The flavonoids functionalized clove buds extract mediated AuNPs were reported to possess the anticancer activity against various cancer cells [39].

Mechanisms of flavonoids-mediated NP synthesis

There are some studies which proposed the plausible mechanism for polyphenols-mediated the synthesis of MNPs, as shown in Table 2. It was proposed that the hydroxyl groups present in the B and C rings of kaempferol participated in the AuNPs synthesis [76,112]. Moreover, the radical scavenging activity of NPs may be attributed to the A ring of kaempferol coating the surface of AuNPs. It was described that the formation of the enol form of luteolin, releasing reactive hydrogen, may be responsible for the reduction of Ag^+ to Ag^0 [113].

It was proposed that the dihydromyricetin (DMY)-mediated synthesis of AuNPs occurred through the oxidation of hydroxyl to carbonyl groups. The study reported a shifting in the stretching vibration of the hydroxyl groups of DMY to higher wavenumber after bioreduction of Ag, which indicated the possible participation of hydroxyl in the reaction. In addition, there was a shift in the stretching vibration of carbonyl groups to lower wavenumber due to the oxidation of hydroxyl groups leading to the intramolecular hydrogen bonding [64].

Quercetin was found to chelate at three positions involving the carbonyl and hydroxyl groups at the C3 and C5 positions and the catechol group at the C3′ and C4′ positions. These groups were proposed to chelate different metal ions by the following steps: (1) Adsorption onto the metal surface, (2) budding of NP, (3) aggregation, and (4) bioreduction [59]. The possible mechanism for genistein AuNPs was proposed as follows: (1) Transfer of the electron from genistein into the Au center, (2) reduction of the Au^{3+} to Au^0 by genistein, and (3) further acted as a stabilizing agent to form a layer of negative ions leading to the formation of the AuNPs [71].

The work of Kasthuri *et al*. [47] revealed that the reduction of Au^{3+}/Ag^+ ions occurred in a 2-step reaction involving the reduction by hydroxyl groups of the apiin followed by the oxidation of hydroxyl

Table 2: Mechanism of synthesis and applications of MNPs

Source	MNP (size)	Mechanism	Application	Reference
Abutilon indicum (Polyphenols)	AuNPs (1–20 nm)	Hydroxyl and carbonyl groups of polyphenols mediated bioreduction of Au metal ions	Anticancer	[40]
Acacia rigidula (Phenolic compounds)	AgNPs (8–66 nm)	Hydroxyl groups of polyphenols mediated bioreduction of Ag metal ions	Antibacterial	[41]
Acalypha indica (Phenolic compounds)	AgNPs (20–30 nm)	Hydroxyl groups of phenolic compounds mediated bioreduction of Ag metal ions	Antibacterial	[42]
Achyranthes aspera (Phenolic compounds)	AgNPs (7–14 nm)	Hydroxyl groups of phenolic compounds mediated bioreduction of Ag metal ions	Larvicidal against mosquito	[43]
Allium sativum (Phenolic compounds)	AgNPs (3–6 nm)	Hydroxyl groups of polyphenols mediated bioreduction of Ag metal ions	Antibacterial Antioxidant	[44]
Alpinia calcarata (Phenolic compounds)	AgNPs (27 nm)	Hydroxyl groups of flavonoid/phenolic mediated bioreduction of Ag metal ions	Antibacterial Antioxidant	[45]
Andean blackberry (Flavonoids)	AgNPs (12–50 nm)	Hydroxyl and carbonyl groups of flavonoid mediated bioreduction of Ag metal ions	Antioxidant	[46]
Apiin (Apigenin glycoside)	AuNPs (21 nm) AgNPs (39 nm)	Apiin hydroxyl groups-mediated reduction of metal ions and subsequent formation of carbonyl groups that bind to metal ions leading to apiin coated NPs	Anticancer	[47]
Azadirachta indica (Phenolic compounds)	AgNPs (34 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	-	[48]
Baicalein	AuNPs (26.5 nm)	Hydroxyl groups of baicalein mediated reduction of Au metal ions -	Antibiofilm activity against *P. aeruginosa*	[49]
Brassica oleracea	AgNPs (24 nm)	Hydroxyl groups of polyols-mediated reduction of Ag metal ions	Cytotoxicity	[50]
Butea monosperma (Polyphenols)	AuNPs (10–30 nm) AgNPs (20–80 nm)	Hydroxyl groups of polyphenols/protein-mediated reduction of Au metal ions	Anticancer	[51]
Cassia fistula (Flavonoids/ polyphenols)	ZnNPs (5–15 nm)	-	Dye reduction Antioxidant Antibacterial	[52]
Catechin	c-SiNPs	Hydroxyl groups mediated reduction of Si metal ions	Enhanced antioxidant activity and hippocampal cell survival	[53]
Centella asiatica (Flavonoids/polyphenols)	AuNPs	Hydroxyl groups of flavonoids/polyphenols mediated reduction of Au metal ions	-	[54]
Citrullus lanatus (Phenolic compounds)	AuNPs (20–140 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Au metal ions	Antiproteasome Antibacterial Antioxidant	[55]
Citrus maxima (Flavonoids, phenolic compounds)	AuNPs (15–35 nm)	Hydroxyl and amide groups mediated reduction of Au metal ions	Catalytic dye reduction	[56]
Citrus sinensis (Phenolic compounds)	AgNPs (10–35 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antibacterial	[57]
Clove buds (Flavonoids)	AuNPs and AgNPs	-	Anticancer against cancer of the human cervix, human chronic myelogenous leukemia, human colorectal adenocarcinoma, and human renal carcinoma	[39]
Coleus aromaticus (Phenolic compounds)	AgNPs (44 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antibacterial	[58]
Coriandrum sativum (Flavonoids)	AgNPs (37 nm)	Hydroxyl groups mediated reduction of Ag metal ions-	Antiacne (*Propionibacterium acnes*), antidandruff (*Malassezia furfur*) and anticancer against human breast cancer	[28]
Coriandrum sativum (Luteolin)	AgNPs (13 nm)	Conversion of Ag^+ to Ag^0 by the freely released reactive hydrogen from the enol form of luteolin.	Antibacterial against *B. subtilis*	[59]
Costus afer (Flavonoids, phenolic compounds)	AgNPs (5–38 nm)	Hydroxyl groups of flavonoids and phenolic compounds mediated reduction of Ag metal ions	Antibacterial Antioxidant	[60]
Curcuma longa (Phenolic compounds)	AgNPs (58 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Anticancer	[61]

(Contd...)

Table 2: (*Continued*)

Source	MNP (size)	Mechanism	Application	Reference
Dalbergia spinosa (Flavonoids)	AgNPs (18 nm)	Interaction of carbonyl groups or electrons with the metal surface	Anti-inflammatory activity. Antibacterial against *E. coli, P. aeruginosa, S. aureus,* and *B. subtilis*	[38]
Decalepis hamiltonii (Phenolic compounds)	AgNPs (32 nm)	Hydroxyl groups of flavonoids and phenolic compounds mediated reduction of Ag metal ions	Antibacterial	[62]
Delonix regia (Polyphenols)	PdNPs (2–4 nm)	Polyols mediated reduction of Pd metal ions	Catalytic dye reduction	[63]
Dihydromyricetin	AuNPs (24–43 nm)	Hydroxyl/carbonyl groups mediated reduction of Au metal ions	-	[64]
Dioscorea bulbifera (Phenolic compounds)	AgNPs (8–20 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Synergism with antibacterial agents	[65]
Durio zibethinus (Phenolic compounds)	AgNPs (20–72 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antioxidant Photocatalytic dye reduction Cytotoxicity	[66]
Ecklonia cava (Phenolic compounds)	AgNPs (43 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antioxidant Anticancer Antibiotic	[67]
Epicatechin and Theaflavin	AgNPs (31 nm)	Carbonyl groups-mediated bioreduction of $AgNO_3$ leading to synthesis and stabilization of AgNPs	Anticancer against human epidermoid larynx carcinoma cells	[68]
Erythrina suberosa (Flavonoids, phenolic compounds)	AgNPs (15–34 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antimicrobial Antioxidant Anticancer	[69]
Galenia africana (Flavonoids, phenolic compounds)	AuNPs	Hydroxyl/carbonyl groups mediated reduction of Au metal ions	Antibacterial	[70]
Genistein	AuNPs (64.64 nm)	Reduction of Au^{3+} to Au^0 by the transfer of an electron from genistein leading to the formation of AuNPs by stabilizing them with a layer of negative ions	Anticancer against human epithelial lung carcinoma and human melanoma cells	[71]
Gloriosa superba leaf extract	Ag/Au (20 nm)	-	Antibacterial Antibiofilm	[72]
Glycyrrhiza glabra (Phenolic compounds)	AgNPs (9 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antimicrobial	[73]
Glycyrrhiza uralensis (Phenolic compounds)	AgNPs (8 nm) AuNPs (12 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag and Au metal ions	Antioxidant Antimicrobial Cytotoxicity Catalytic dye reduction	[74]
Hybanthus enneaspermus (Phenolic compounds)	AgNPs (16–26 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Larvicidal against mosquito	[75]
Hypoxis hemerocallidea (Flavonoids, phenolic compounds)	AuNPs	Hydroxyl/carbonyl groups mediated reduction of Au metal ions	Antibacterial	[70]
Kaempferol	AuNPs (16.5 nm)	Hydroxyl Groups B and C rings of kaempferol mediated the synthesis of k-AuNPs The A ring of k-AuNPs involved in antioxidant activity	Anticancer against human breast cancer	[76]
Lawsonia inermis (Phenolic compounds)	CuNPs	-	-	[77]
Lantana camara (Phenolic compounds)	AgNPs (23–30 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antibacterial catalytic dye reduction	[78]
Lilium casa blanca (Flavonoids rich extract)	AuNPs (9–13 nm)	Hydroxyl/carbonyl groups mediated reduction of Au metal ions-	Catalytic dye reduction-	[79]
Luma apiculata (Phenolic compounds)	FeONPs (7–13 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Fe metal ions	Photocatalytic dye reduction	[80]
Mimusops elengi (Phenolic compounds)	AgNPs (12–30 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antioxidant Antimicrobial	[81]
Morinda citrifolia L. (Phenolic compounds)	AgNPs (10–60 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antibacterial	[82]
Myrtus communis (Phenolic compounds)	FeNPs (20–40 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Fe metal ions	Antioxidant	[83]
Nigella arvensis (Flavonoids, phenolic compounds)	AgNPs (2–15 nm)	Hydroxyl, carbonyl, and amide groups mediated reduction of Ag metal ions	Antimicrobial Anticancer	[84]
Ocimum sanctum (Phenolic compounds)	AgNPs (18 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antibacterial	[85]

(Contd...)

Table 2: (*Continued*)

Source	MNP (size)	Mechanism	Application	Reference
Potentilla fulgens (Flavonoids)	AgNPs (10–15 nm)	Hydroxyl, carbonyl, and amide groups mediated reduction of Ag metal ions	Anticancer against human breast cancer and human glioblastoma cancer cells Antibacterial against *E. coli* and *B. subtilis*	[86]
Proanthocyanidin	AuNPs (17–29 nm)	Hydroxyl/carbonyl groups mediated reduction of Ag metal ions	The efficient cardioprotective potential with good biocompatibility	[87]
Pueraria tuberosa (Flavonoids/phenolic compounds)	AgNPs (162 nm)	Hydroxyl groups of flavonoids/phenolic compounds mediated reduction of Ag metal ions	Antioxidant Anticancer	[88]
Pulicaria glutinosa (Phenolic compounds)	AgNPs (40–60 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	-	[89]
Punica granatum (Flavonoids, phenolic compounds)	AgNPs (40–70 nm)	Hydroxyl groups of flavonoids/polyphenols mediated reduction of Ag metal ions	Anticancer	[90]
Quercetin	Ag-SeNPs (30–35 nm)	Hydroxyl/carbonyl groups mediated reduction of Ag/Se metal ions	Antioxidant, antimicrobial, and anticancer activities	[91]
Quercetin	Metal NPs	Metal ion chelation by three positions of quercetin involving the carbonyl and hydroxyl groups at the C3 and C5 positions and the catechol group at the C30 and C40 site	-	[59]
Quercus brantii (Phenolic compounds)	AgNPs (6 nm)	Hydroxyl groups of flavonoids/polyphenols mediated reduction of Ag metal ions	-	[92]
Ranunculus muricatus (Flavonoids)	Au/TiO_2 (50–90 nm)	Hydroxyl groups interact with metal ions through a covalent bond	Antibacterial against *S. aureus* and *E. coli*	[93]
Rosmarinus officinalis (Phenolic compounds)	AgNPs (10–30 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antimicrobial	[94]
Salacia chinensis (Phenolic compounds)	AgNPs (40–80 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Anticancer	[95]
Satureja intermedia (Phenolic compounds)	AgNPs (28 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antioxidant	[96]
Sesbania grandiflora (Flavonoids, polyphenols)	AuNPs (7–34 nm)	Hydroxyl/carbonyl groups mediated reduction of Au metal ions	Catalytic dye reduction	[97]
Siberian ginseng (Phenolic compounds)	AgNPs (126 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antimicrobial	[98]
Sterculia acuminata (Polyphenols)	AuNPs (9–38 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Au metal ions	Catalytic dye reduction	[99]
Suaeda monoica (Phenolic compounds)	AuNPs (3-25 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Au metal ions	Antioxidant	[100]
Sunflower oil (Phenolic compounds)	AgNPs (50 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Anticancer	[101]
Syzygium cumini (Phenolic compounds)	AgNPs (20–60 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Antibacterial	[102]
Syzygium cumini (Phenolic compounds)	AgNPs (30–92 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	-	[103]
Syzygium samarangense	AgNPs	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Anticancer	[104]
Tamarindus indica (Phenolic compounds)	AuNPs (52 nm)	Hydroxyl/carboxylic groups mediated reduction of Au metal ions	-	[105]
Tea extract (Phenolic compounds)	AuNPs (8–24 nm)	Hydroxyl groups of phenolic compounds mediated reduction of Ag metal ions	Catalytic dye reduction	[106]
Tephrosia tinctoria (Flavonoids)	AgNPs (<100 nm)	Hydroxyl/carboxylic groups mediated reduction of Au metal ions	Antidiabetic	[107]
Terminalia arjuna (Polyphenols)	AuNPs (20–50 nm)	Hydroxyl/carboxylic groups mediated reduction of Au metal ions	Enhancement of seed germination activity in *Gloriosa superba*	[108]
Terminalia catappa (Phenols)	AuNPs (10–35 nm)	Hydroxyl/carbonyl groups mediated reduction of Au metal ions	-	[109]
Walnut green husk (Polyphenols)	AgNPs (31.4 nm)	Hydroxyl groups of polyphenols mediated reduction of Ag metal ions	Antioxidant Antimicrobial Anticancer	[110]
Zingiber officinale (Phenolic compounds)	AgNPs (10–20 nm)	Hydroxyl groups of polyphenols mediated reduction of Ag metal ions	Antibacterial	[111]

B. subtilis: Bacillus subtilis, P. aeruginosa: Pseudomonas aeruginosa, S. aureus: Staphylococcus aureus, E. coli: Escherichia coli, MNP: Metal nanoparticle, AgNPs: Silver nanoparticles

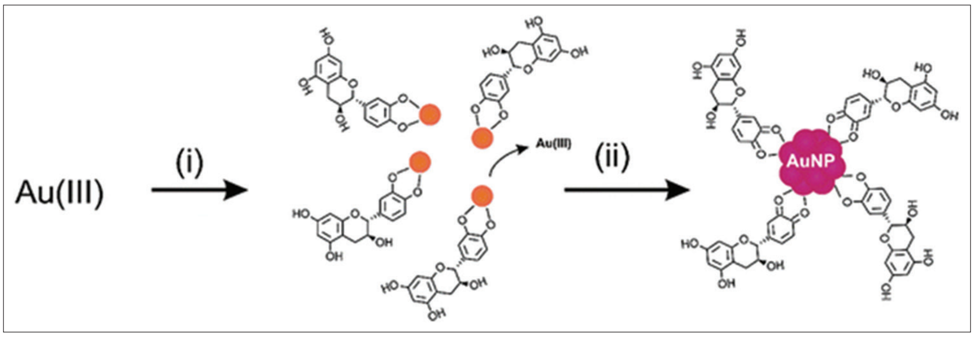

Fig. 3: Mechanism of polyphenols-mediated GNP synthesis: (1) Polyphenols and (2) synthesis and stabilization of gold nanoparticles [114]

groups to the carbonyl groups. Finally, the binding of carbonyl groups of apiin to the metal ion, thereby coating the NPs surfaces to prevent agglomeration. Most of these cited references from available literature give a clear indication that both the hydroxyl and the carbonyl groups of polyphenols collectively play a key role in the formation of MNPs.

Fig. 3 depicts the mechanism of polyphenols-based GNP synthesis. The adjacent hydroxyl groups of polyphenolic compounds from a 5-member chelate ring structure followed by oxidation of the chelated dihydroxy groups to quinones. Due to the high oxidation-reduction potential of Au^{3+}, the quinones subsequently reduce the gold metal ions from Au^{3+} to Au^0. The synthesis of gold NPs occurs after a collision between the adjacent Au^0 atoms, and the NPs thus formed are stabilized by polyphenolic compounds including the quinones [114].

CONCLUSION

The emerging threats related to the toxic and hazardous nature of the conventional methods of NP synthesis have led to the plant extracts-mediated synthesis of MNPs. The green nanosynthesis approach thus adopted is cost and time effective, and environment-friendly with the potential to easily scale up the product. Such a non-toxic approach is especially desirable to synthesize the NPs that must not be toxic if they are destined for the therapeutic applications. The NPs of controlled size and shape can be synthesized using various plant extracts of which the polyphenols, including flavonoids, are considered as the most active bioreductants of metal ions. The MNPs synthesized using natural polyphenols and flavonoids have shown a number of biomedical applications, including their therapeutic activity against various ailments.

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AUTHORS' CONTRIBUTIONS

All the authors of this review paper have contributed equally in retrieving, collecting, and compiling the data as well as writing and proofreading of the manuscript.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this review paper.

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