International Nano Letters (2021) 11:273–293
https://doi.org/10.1007/s40089-021-00341-1

ORIGINAL ARTICLE

Potentials of phytosynthesized silver nanoparticles in biomedical fields: a review

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Received: 17 February 2021 / Accepted: 10 May 2021 / Published online: 18 May 2021

Abstract

Nanoscience and nanotechnology are currently undergoing several developments that will impact several industries across the global in due season. The wide applications of nanoparticles in biomedicine, pharmacy, phytochemistry, research institute, catalysis, textile, waste water management, chemistry, food preservatives, and paint have led to new area of discoveries for many researchers and industries. The biological method of synthesizing silver nanoparticles (AgNPs) had tremendously gained wide popularity due to its environmental friendly conditions of synthesis. Numerous biological entities namely; plants, bacteria, essential oil, fungi, algae, and yeasts had been used as reducing and capping agent for the synthesis of AgNPs. All scientific investigations have ascertained the uniqueness of AgNPs as therapeutic agent against cancer, virus, bacterial, and fungal infections. This review provides detailed scientific information about the various methods of synthesis, optimization conditions, mechanism, and characterization techniques for the synthesis of AgNPs with efficient yield and morphological properties. Furthermore, concise advancement in the antibacterial, antiviral, antifungal, antioxidant, and anticancer activities of AgNPs mediated from plant sources from recently published articles were enumerated.

Keywords Nanoparticles · Synthesis · Optimization conditions · Mechanism · Characterization techniques · Biological activities

Introduction

Presently, the world at large is threatened with infections from coronal virus and other bacterial attack that had pose a lot of disturbances on the world health sector as many antibiotics and vaccines have lost their usefulness in preventing or curing this diseases caused by microbes [1]. Several decades ago, antiviral and antimicrobial agents played a crucial role in combating infectious diseases that emanates from virus, bacteria, and fungi, but the existence of precarious and antibiotic-resistant virus and bacteria are major concern these days. Drug resistance developed by viruses and microbes can be worrisome, therefore, overcoming this kind of challenge is tasking [2]. Hence, the exploration of

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compounds with efficacy to inhibit the growth of these pathogenic organisms and their resistant to modern drugs is very crucial [3]. Nanotechnology had be announced as an imperative approach used in combating various viral and microbial infections in pharmaceutical industrial, research institutes, and biomedical sciences [4]. Silver nanoparticles are found to exhibit unique properties such as conductivity, chemical stability, catalytic and biological (antibacterial, antiviral, antifungal, and anti-inflammatory) activities [5]. The use of AgNPs as bio-labeling, food preservation, anticancer, wound healings, therapeutic agents for microbial infection, water purifications, antioxidant, and cosmetics have been on wide range recently [6]. Green synthesis of metal nanoparticles has attracted a lot of attention due to different optical, chemical, and electronic properties and important use in textile, catalysis, and paint industries [7]. Advancement in nanotechnology with the easy in production of AgNPs with improve antimicrobial efficiency had increase its medicinal application rendering it as an anti-decay agent [8]. Recently, AgNPs have been reported to exhibit an effective lethal agent against fungi, bacterial (Gram-positive and Gram-negative bacteria), and even against antibiotic-resistant strains [9]. Regardless of the various methods of AgNPs synthesis, the biological method has been the most preferred [10]. Beside microbial synthesis, plant mediated synthesis of AgNPs rank the most celebrated owing to its reproducibility, availability, reliability, and possibility of been easily scaled up for large-scale production [11]. Plant's parts namely, bark, flower, root, stem, fruit, pulp, seed, callus, peel, bulb, and leaves had been reported as a good sources for the synthesis of AgNPs [12]. Optimum conditions to control the factors affecting the synthesis of AgNPs from plants had been established [13]. This review centered on recent scientific findings on the procedures involved in the biosynthesis of AgNPs from plants sources and its biological applications.

Synthesis of AgNPs

The rapid increase in the applications of AgNPs had led to several methods of synthesis. The popular methods of synthesizing AgNPs are physical, chemical, and biological methods [14].

Physical method

This method entails the production of AgNPs through either condensation and vaporization process. This can only be attainable by proper maintenance of the furnace tube at atmospheric pressure. The constituent in a fixed vessel will be evaporated through the carrier gas in the furnace [15]. This method has been used for some decades till now [15]. It has been noted that the use of this method in the synthesis of nanoparticles is prone to some limitations and difficulties which include consumption of high quantity of energy in kilowatts, wastage of time as it required long period of time, it generate high amount of heat to the environment due to long duration of time in attaining thermal constancy, and huge spaces are also required when producing cylinder-based furnace [16]. However, the production of high amount of AgNPs with efficient yield is achievable with this method. The formation of AgNPs via laser ablation has been reported. Laser method of synthesizing AgNPs is advantageous because it requires no chemical entities or reagent and production of pure colloids is also possible [17].

Chemical method

The chemical method of synthesizing AgNPs involves the reduction of silver ions in aqueous solutions via chemical process, diverse methods such as photo reduction in reverse micelles, radiation chemical reduction, catalytic reduction, and thermal decomposition has been reported as reduction processes but all these methods are complex, very expensive, generate toxic waste that causes pollution and harm to the environment [18]. Capping oxidants, metal-based precursors, and reducing agents are essential in the production of AgNPs via the chemical method. Interestingly, the deposition of AgNPs on silica and polymer nanoparticles has been documented as a good technical strategy for the stabilization of nanoparticles [19]. However, this method encouraged the production of spherical shape AgNPs with smaller particle sizes but it requires efficient control of the growth of metal-based precursors and the use of adequate capping agents [20]. Sariyeh et al. reported that the chemical method of synthesizing nanoparticles is rapid but difficulties in controlling the growth, stability, and particles aggregation are worrisome and the cost of purchasing the required capping agents for the stabilization of particle size is another limitation [21]. The diagrammatic expression of the chemical method of synthesis of AgNPs is showed in Fig. 1.

Biological methods

The biological method of synthesizing AgNPs adopt the use of microorganism (such as bacteria, algae, and fungus), polysaccharides, and plants extracts as reducing agents [22, 23]. The intracellular and extracellular activities of bacteria enhance its usage as reducing agent in AgNPs synthesis [24]. AgNPs had been synthesized from numerous extracts of plant's species and essential oil obtained from plants [25]. Spherical-shape AgNPs with particle size in the range of 30 and 70 nm was synthesized from the root extract of *Berberis vulgaris* [25]

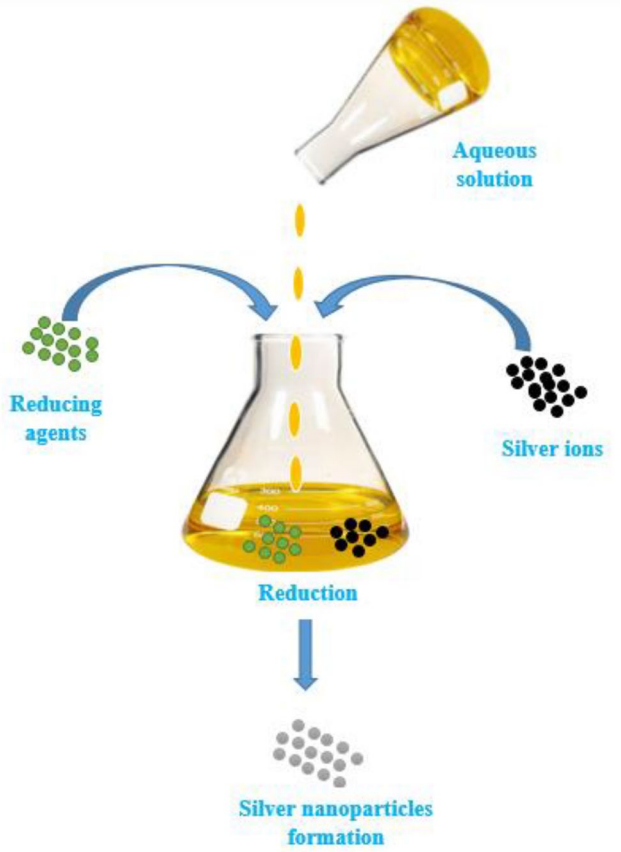


Fig. 1 Flow chart illustrating the chemical method of synthesis of AgNPs

Compounds found in plant have been reported to possess great affinity for the surface of nanostructures, which enhance stability, prevent aggregation, and puffer improved biological activities of synthesized nanoparticles [26]. Aside the eco-friendliness of AgNPs obtained from plant sources, numerous advantages such as cost effectiveness, nontoxic reducing and capping agents, improved morphological, and biological activities had been stated [27]. Both the synthesis of AgNPs from microorganisms and plant extracts offer similar advantages but the use of microorganism as reducing agent suffers the following set back; expensive cost of isolation, difficulties in maintaining aseptic conditions and culture media, and toxicity of some microorganism [28]. Flow chart illustrating the synthesis of AgNPs is represented with (Fig. 2). List of some plant metabolites that have been used as reducing agents are showed in Fig. 3.

Mechanism for the synthesis of AgNPs from plant sources

The biological reduction of silver by plants' secondary metabolites during the synthesis of AgNPs from plant extract occurred when silver ion binds to the surface of secondary metabolites present in plant extracts as a result of the electrostatic interactions between the metabolites and silver ions. The secondary metabolites (phytochemical) reduced the silver ion by altering the silver nuclei which produced an observable coloration. The buildup of the silver nuclei result into AgNPs [29]. The interaction of the charges on the functional groups of the phytochemical present in plant extract with silver ion has been reported as the mechanism behind the biosynthesis of AgNPs from plant sources [30]. Schematic representation for the synthesis of AgNPs from plant source is presented in Fig. 4.

Optimization

Optimization entails all the activities involve in controlling all the reaction parameters such as concentration of the plant extract, pH, time of incubation, concentration of silver salt, and temperature to attain optimum conditions for the production of AgNPs with efficient yield and desire morphological properties [31].

Effect of silver salt concentration on AgNPs synthesis

Increase in the concentration of silver salt has been documented to produce an improved UV absorption because of the increase in the concentration of metal ions and hence the complete reduction of silver ions [32]. High concentration of silver salt is required to shorten the reaction time for the AgNPs synthesis and also to aid stability when the metabolites serving as reducing agents are in minimum amount. The optimum concentration of $AgNO_3$ solution for the synthesis of finer AgNPs from *Tragopogon Collinus* extract was recorded at 0.0025 M [32]. Concentration above10 mM results in increase in the SPR band, agglomeration buildup of silver, and blurred surfaces. Interestingly, the optimum concentration of silver salt for the synthesis of AgNPs with appropriate morphological properties and applications has been set in the following (0.1, 0.5, 1, and 2 mM), (0.5, 1, and 2 mM) and (20, 50, and 100 mM) [33, 34].

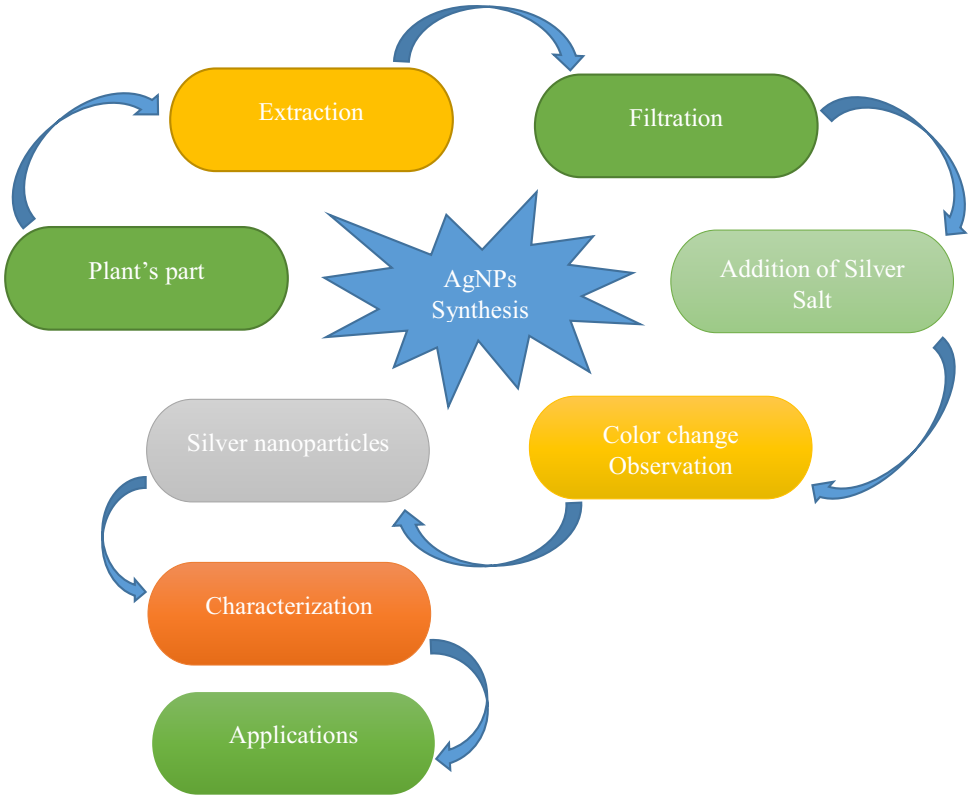


Fig. 2 Flow chart illustrating the synthesis of AgNPs from plant

Effect of concentrations of plant extracts on AgNPs synthesis

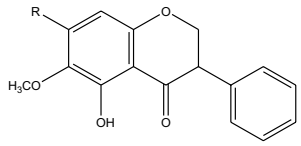
The green synthesis of nanoparticles using plants depends greatly on the phytochemicals that function as the reduction agent of the silver ions and stabilizing for the synthesized AgNPs [35]. The nature or type of metabolites found in the extracts also has influence on the optimum concentration of extract required for synthesis of AgNPs with desired properties [32]. Some reporters have stated that changing the concentrations of plant extracts has massive influence on the biological and morphological activities of synthesized AgNPs [36, 37]. An increase in concentration of extract has been shown to cause an increase in the yield of synthesized AgNPs, because more functional groups are readily available to react with the silver salt to produce improved absorption [38]. Below the optimum concentration of the extract, low yield and unstable AgNPs are obtainable because the metal ions are partially reduced [32].

Effect of pH on AgNPs synthesis

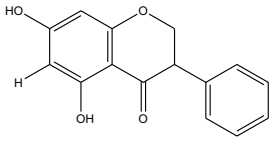
The pH of a reaction has great impact on the morphology of AgNPs which could affect the stability and macromolecules charges [35]. In an attempt to ascertain the effect of pH on particle size of AgNPs Muthu and Priya studied the catalytic activity of separated fraction of AgNPs biosynthesized from the flower of *Cassia auriculata* flower and concluded that large particle size nanoparticles are produced at low pH while nanoparticles with small particle sizes are obtained at high pH [39]. An increase in the pH value of a reaction has been reported to cause an increase in the reaction rate that produced a rapid color change of the solution within a few minutes when AgNPs is synthesized from carob leaf [40]. Decrease in pH values has also been stated as the optimum pH value for the synthesis of AgNPs from banana peel extract [41]. Formation of stable AgNPs from *Fagonia cretica* extract was achieved at pH 4 [31]. However, another study had shown that pH value between 2 to 9 had no effect on the AgNPs' morphological properties [42].

Effect of reaction time on AgNPs synthesis

The length of time used in the synthesis of AgNps had a significant effect on the stability of AgNps produced [32]. Scientific report had shown that the variation in reaction time depends large on the species of plants extract, the conditions of synthesis, such as concentration of silver salt, volume of extracts, temperatures, and pH are other co-factors that influence reaction time of synthesis [32, 43]. Therefore, it is difficult to obtain a single optimum condition for the synthesis of AgNPs from plant extract. Constant color range



Glycitein



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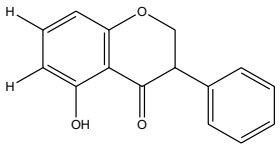
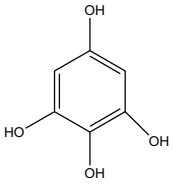
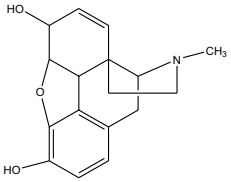


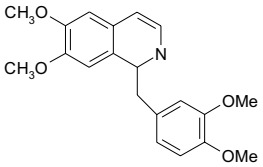
Daldzein



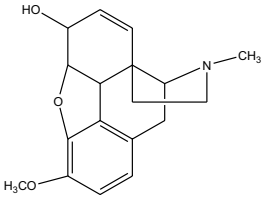
Gallic acid



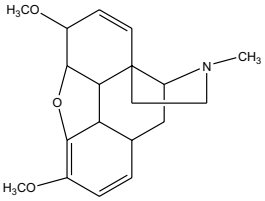
Morphine



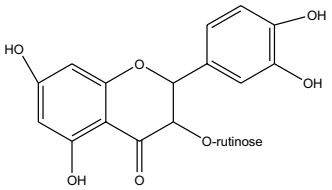
Papaverine



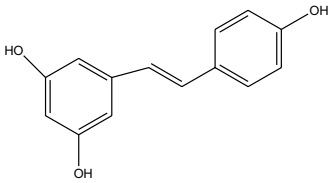
Codein



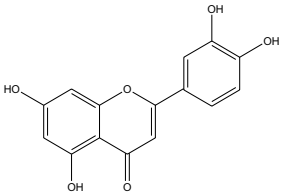
Heroine



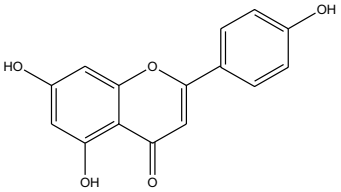
Rutin



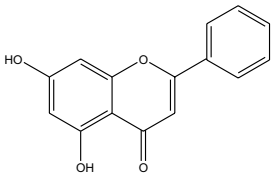
Resveratrol



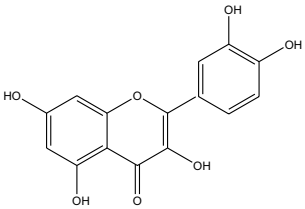
Luteolin



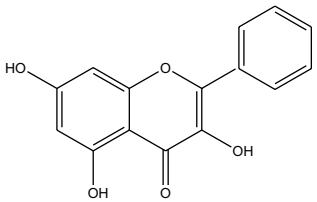
Apigenin



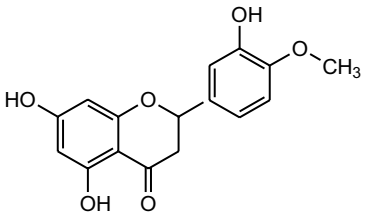
Chrysin



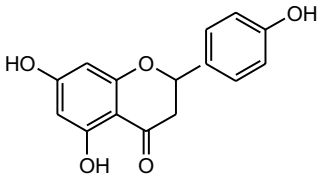
Quercetin



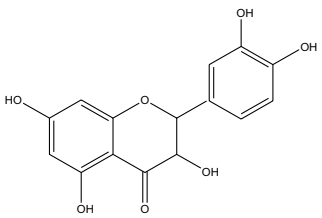
Galangin



Hesperetin



Naringenin



Taxifolin

Fig. 3 Structures of some secondary metabolites used as stabilizing and reducing agents in AgNPs synthesis

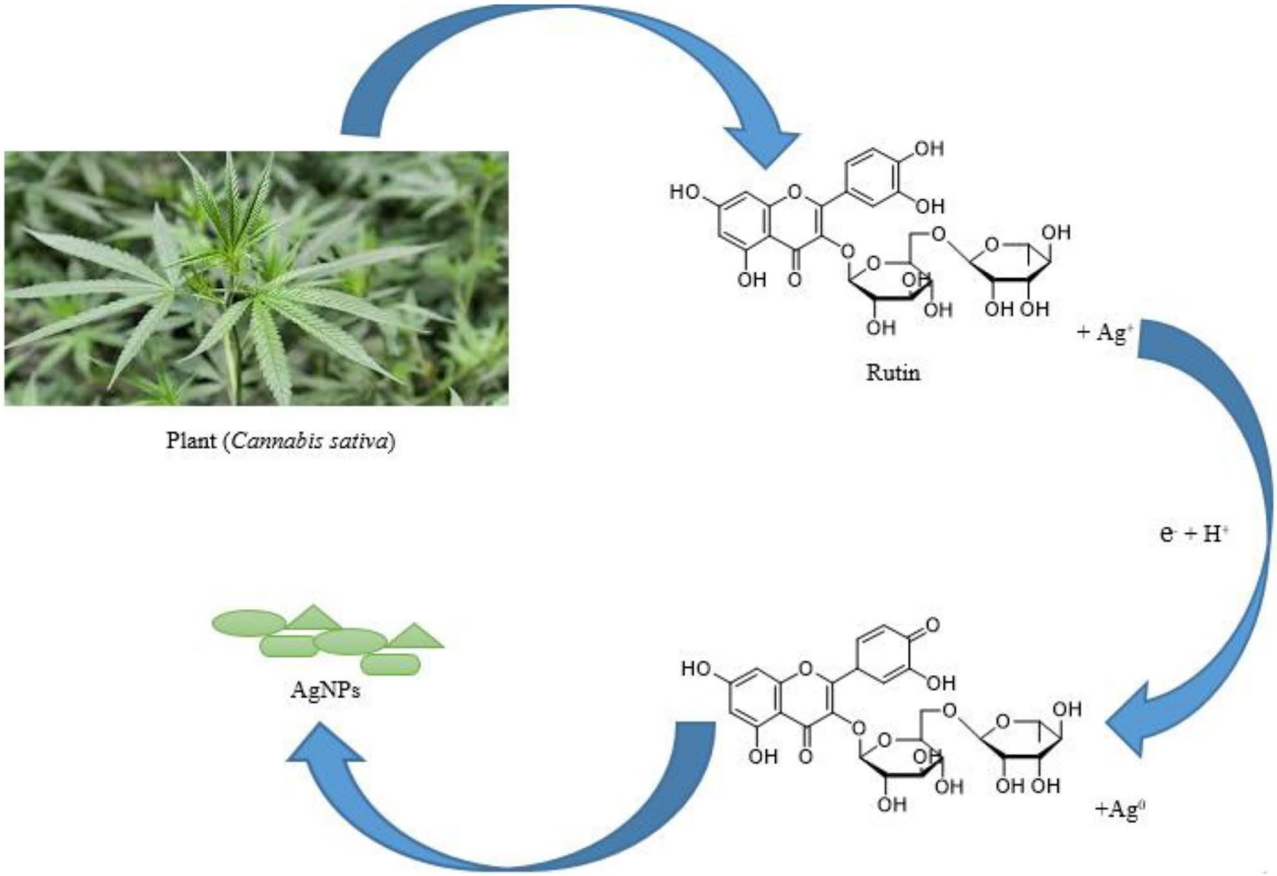


Fig. 4 Schematic representation for the mechanism involved in the synthesis of AgNPs from plant source

change for a long time has been reported as an indication of uniformly dispersed AgNPs without any no agglomeration [44]. Furthermore, an increase in the duration of synthesis of AgNPs corresponds to improved nanoparticles formation [45]. Duration of 90 min has been recorded as the optimum time for the synthesis of AgNPs from *Tragopogon Collinus* Leaf [32]. A period of ten (10 min) has been regarded as the optimal incubation time for the AgNPs [33]. However, the reaction time of several days had also been reported for a complete reduction of silver ion and stabilization of AgNPs [46]. Increased reaction time had been documented to improve the morphological identity (such as particle size and shape) of synthesized AgNP [47]. This claim is linked to gradual oxidation of nanoparticles.

Effect of the temperature on AgNPs synthesis

Temperature is also an important factor to be considered in the synthesis of AgNPs. The reduction of silver nitrate occur quickly at higher temperatures with rapid color change [35]. The synthesis of AgNPs at room temperature has been reported suitable due to the fact that the stability of plant metabolites requires working at ambient temperature. Many reports on the synthesis of AgNPs at room temperature have been shown [48]. Conversely, to establish the complete reduction of silver ion from Ag^+ to Ag^0 in the synthesis of AgNPs at a short reaction time, the use of at higher temperatures have been experimented [49]. Interestingly, the synthesis of AgNPs from *Tragopogon Collinus* extract at elevated temperature 40 °C and above had been successful without any effect on the size or shape of the nanoparticles [32].

Characterization of synthesized AgNPs

The evaluation of the properties of synthesized AgNPs is of great importance in estimating their morphological identities such as shape, surface area, crystallinity, size, and dispersity. This is achieved by characterization using some readily available and special techniques [50]. Major techniques adopted for the characterization of nanoparticles are as follows: UV–visible spectrophotometry, Fourier transform

infrared spectroscopy (FTIR), scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy-dispersive spectroscopy (EDS), powder X-ray diffraction (XRD), and dynamic light scattering (DLS) [51, 52].

UV–visible spectrophotometry

UV–visible spectrophotometry is a cheap and readily available technique that allows identification of compounds and characterization of metal nanoparticles. Reports showed that UV produces the surface plasmon resonance (SPR) absorbance bands are in the region of 400–500 nm (Table 2). The interaction of the mobile surface electrons of AgNPs and light had been linked with the production of these SPR bands in the mentioned region of the UV spectrophotometer [6, 53]. However, study had showed SPR bands below 400 nm for synthesized AgNPs [54]. This had also been traced to the occurrence of impurities in the silver salts and plant phytochemicals. There is huge influence of SPR on the morphological properties of AgNPs [55]. Synthesis conditions and plant extracts used in the green synthesis of AgNPs also have its contribution in the variation of SPR bands. Findings had showed that decrease in concentration of silver salt will amount to increase in AgNPs size and SPR peaks [56]. Therefore, the regulation of concentrations of salt and volume of plants extracts are of high importance in synthesizing AgNPs with desired particle size and other morphological properties. It is a point worth knowing that the green method of synthesizing AgNPs suffers a great limitation in producing AgNPs with controllable morphological properties. This limitation is associated with the different capping and reducing secondary metabolites used [34]. The UV–Vis spectrum of the AgNPs synthesized with a strong and sharp SPR band at 400 nm has been reported [52]. Other findings and documentation on AgNPs SPR bands are recorded in Table 1.

Table 1 SPR bands of AgNPs synthesized from plant sources

S/no.	Plant name	Part of plant	SPR peak (nm)	References
1	*Impatiens balsamina*	Leaf	452	[57]
2	*Lantana camara*	Leaf	420	[57]
3	*Cassia auriculata*	Leaf	452	[37]
4	*Azadirachta indica*	Leaf	420–450	[58]
5	*Cymodocea serrulata*	Leaf	454	[59]
6	*Acalypha hispida*	Leaf	424	[60]
7	*Mangifera indica*	Leaf	420	[61]
8	*Cassia occidentalis*	Leaf	461	[62]
9	*Datura stramonium*	Leaf	444	[63]
10	*Phyllanthus amarus*	Leaf	421	[64]
11	*Rubus glaucus Benth*	Leaf	422	[65]
12	*Ricinus communis*	Leaf	442	[66]
13	*Nigella sativa*	Seed	432	[53]
14	*Pimpinella anisum*	Seed	442	[67]
15	*Tamarindus indica*	Fruit	432	[68]
16	*Piper nigrum*	Fruit	441	[69]
17	*Tectona grandis*	Seed	440	[70]
18	*Quercus*	Fruit	421	[71]
19	*Fagonia cretica*	Whole plant	440	[72]
20	*Cyperus rotundus*	Whole plant	446	[73]
21	*Acacia seyal*	Gum	421	[74]
22	*Dimocarpus longan*	Peel	432	[75]
23	*Acorus calamus*	Rhizome	437	[76]
24	*Erythrina indica*	Root	460	[77]
25	*Calotropis procera*	Latex	454	[78]
26	*Capparis decidua*	Stem	460	[79]
27	*Cymodocea serrulata*	Whole plant	441	[80]

Fourier transforms infrared spectroscopy (FTIR)

FTIR technique is used to predict the surface chemistry of AgNPs. It also helps in identification of the functional groups present in plant extracts and the synthesized AgNPs. The variation in the absorption bands of the extract and synthesized AgNPs is an important factor used in ascertaining the complete reduction of the metal ion and formation of nanoparticles. Some of the secondary metabolites reported as reducing and capping agents in AgNPs synthesis revealed by FTIR analysis are polyphenols, alkaloids, tannins, terpenes flavonoids, and quinones [81, 82]. The occurrence of various secondary metabolites in plant extracts used in reducing the metal ions has led to the production of polydisperse AgNPs which is a limitation to green method of synthesizing AgNPs. Report had proven that the use of pure secondary metabolites could solve the aforementioned limitation [83]. Further scientific information on the use of FTIR technique in green synthesis of AgNPs are documented in Table 2.

Table 2 FTIR absorption wavelengths and functional groups of AgNPs synthesized from plant sources

S/N	Plants name	Plants parts	FTIR absorption wavelength (cm^{-1})		Functional group prediction	Ref
			Extract	AgNPs		
1	*Nyctanthes arbortristis*	Leaf	3942.45	3854	O–H	[87]
			2922.43	–	C–H	
			1706.26	–	C=O	
			1604.23	1698	C=C	
2	*Diospyros montana*	Bark	3364.92	–	N–H	[88]
			2940.05, 1099.58	–	C–H	
			1581.48	–	H–C=O	
3	*Tragopogon collinus*	Leaf	–	3385	OH	[32]
			–	2921	NH	
			–	1640	C=O	
4	*Aspilia pluriseta*	Leaf	–	3488	O–H	[89]
			–	2920	C–H	
			–	1379	C–N	
5	*Teucrium polium*	Leaf	–	3425	O–H	[90]
			–	1641	C=O	
6	*Pterodon emarginatus*	Leaf	3400	3410	O–H	[91]
			2900	2930	C–H	
			1626	1628	C=O	
			1380	1384	NO_2	
7	*Launaea taraxacifolia*	Leaf	–	3780	N–H	[19]
			3459	3459	O–H	
			1550	1636	C=O	
8	*Mimosa pigra*	Leaf	3631	3300	OH	[92]
			2917 2849	2917 2849	CH	
			1727	1611	C=O	
9	*Datura inoxia*	Flower	1684	1710	C=O	[93]
			1589	1645	N–H	
			1546	1587	C–C	
			1509	1460	C–H	
			1299	1291	N–O	
			1205	1141	C–N	
			690	687	C–Br	
10	*Satureja hortensis* L	Leaf	3634	3440	OH	[94]
11	*Symphytum officinale*	Leaf	3256	3437	OH	[95]
			2921	2917	C–H	
			1722	1613	C=O	
12	*Alternanthera sessilis*	Leaf	3426	3452	OH	[5]
			2900	2989	CH	
			1615	1634	C=O	
13	*Oregano*	Roots	3426	3452	OH	[5]
			2900	2989	CH	
			1615	1634	C=O	
14	*Lactuca indica*	Leaf	3428	3232	OH	[96]
			2923	2916	CH	
			1632	1601	–C=C	
15	*Morus alba* L	Fruit	3990	3414	OH	[97]
			2955	2925	CH	
			–	1704	C=O	

Table 2 (continued)

S/N	Plants name	Plants parts	FTIR absorption wavelength (cm^{-1})		Functional group prediction	Ref
			Extract	AgNPs		
16	*Tarragon*	Leaf	1616	1626	–C=C	[21]
			3396	3408	OH	
			1625	1607	C=O	
17	*Cinnamomum tamala*	Leaf	3458	3457	OH	[98]
			2098	2093	CH	
			1638	1635	C=C	
18	*Psoralea corylifolia*	Seed	3293	3405	NH	[99]
			2958 2852	2956 2856	N–H	
			654	1632	C–OH	
19	*Capparis decidua*	Stem	3274	3279	N–H	[79]
			1636	1637	C=C	
20	*Cassia auriculata*	Flower	3393	3406	O–H	[100]
			2925	2925	C–H	
			1629	–	C=O	
			1605	1602	C=C	
21	*Coffea arabica*	Seed	3500	3420	O–H	[101]
			2925	2960	C–H	
			1744	1742	C=O	
22	*Fagonia cretica*	Leaf	3729.37	3739.15	O–H	[72]
			3467.80		N–H	
			1636.56	–	–C=O	

Morphological characterization AgNPs synthesized from plant sources

TEM analysis

In an attempt to envisage the size and shape of AgNPs synthesis from *Saraca indica* leaf extract, Shyam et al. [102] performed a transmission electron microscope (TEM) analysis on a JEOL JEM-2010 (HT) electron microscope at voltage of 200 kV by dissolving the AgNPs in deionized water solution with concentrations of 0.5 mg/mL, and few drop was loaded on Cu grids precoated with carbon films which produced a distinct spherical AgNPs with average particle size of 23 ± 2 nm.

Sariyeh and his research team reported a quasi-spherical shape and 25.12 nm particle size for the morphological exploration of AgNPs mediated from *Tarragon* leaf extract which was carried out on a Zeiss EM 10C/CR TEM microscope (Zeiss, Germany) at 100 kV by placing AgNPs suspension on a drop-casted carbon-coated copper grid at 25 °C to dry overnight [21]. The morphological investigation of AgNPs biosynthesized from the extracts of *Pterodon emarginatus* leaves during both the summer and winter periods showed round shapes with smooth edges with an average diameters of 33.20 ± 4.85 nm from the TEM image obtained from JE M-1011, Jeol, Japan) operated at 100 kV, 25 °C and drying period of 12 h [103]. The size and morphology analysis of AgNPs formed from *Morus alba* fruit extract via TEM images obtained with Philips EM 208 electron microscope at 100 keV. The AgNPs with spherical shape and average size of 150 nm was reported [104]. The shape and size of synthesized AgNPs from phlomis leaf extract investigated by TEM showed well dispersed spherical shape and an average size around 25 nm [105].

SEM analysis

The morphology of AgNPs observed by conducting an electron microscopic studies on AgNPs mediated from *Alternanthera sessilis* leaves and *Oregano* root by sputtering the nanoparticles with gold to analyze the surface characteristics revealed closely arranged AgNPs that are spherical in shape with sizes ranging from 17.58 to 23.44 nm [5]. SEM technique was adopted to deduce the surface morphology and topography of synthesized AgNPs. The SEM analysis showed that the size of AgNPs was in the range of 19–30 nm and spherical in shape [105].

Report had shown that the following techniques namely; dynamic light scattering, high-resolution transmission electron microscopy, field emission scanning electron

microscopy particle size analyzer and atomic force microscopy, and selected area electron diffraction are also used for metal nanoparticles characterization [106–108, 170].

Biological applications of AgNPs synthesized from some plants sources

Studies had shown that phytosynthesized AgNPs possess diverse applications in biomedical fields. Some of the biomedical applications of AgNPs are showed in Fig. 5.

Antibacterial activity

The results from the antibacterial investigation of AgNPs synthesized from both garlic and ginger and their extracts against Gram positive bacteria namely; *B. subtilis* and *S. aureus* and Gram-negative bacteria which includes *E. carotovora*, *P. vulgaris* and *K. pneumoniae* conducted by [109] revealed that the AgNPs possess higher activities than the extractsonly, it was also noted that garlic extract showed no antibacterial activity against all the bacterial strains. Scientific information from some researchers emphasized that compounds based on metals and their ions are tremendously toxic to bacteria species and displayed a significant biocidal activities owing to the reactive species with a large surface area found in them [110–112]. Antibacterial assessment of AgNPs formed from *Launaea taraxacifolia* leaf extract on *P. aeruginosa* and *P. mirabilis* showed great cytotoxicity kinetics. For *P. aeruginosa*, the estimated minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were 0.10 and 0.15 mg/mL, while the MIC and MBC of 0.05 and 0.25 mg/mL were recordedfor *P. mirabilis.* This specified that the high penetration of AgNPs across the cell walls of the bacteria even at low concentration [113]. The antibacterial tests of AgNPs mediated from *Satureja hortensis* leaves on *Escherichia coli* and *Staphylococcus aureus* strains of bacteria showed strong antibacterial efficiency comparable with some antibiotics namely; kanamycin and vancomycin [114]. The evaluation of t anti-proliferative potency of AgNPs against *Labeo rohita* fish infected with *Pseudomonas aeruginosa* revealed that all the hematological parameters of the bacterial intoxicated fish were close to normal when treated with AgNPs, showing that AgNPs increased the immunity of thefish against bacterial challenge [115]. The bactericidal action of AgNPs was linked to the strong electrostatic forces that occur when the positive charge of Ag+ ion coupled with negative charge of bacterial cell wall causing the disruption and damage of the cell membrane which ultimately cause bacterial cell death [115, 116]. Antibacterial activities of AgNPs synthesized from some plants sources are showed in Table 3.

Antifungal activities

Antifungal potency of synthesized AgNPs from plants have higher potential when compared with some available antibiotics like amphotericin and fluconazole judging from the membrane damage and damage in fungal intracellular components of *Candida* sp. when treated with AgNPs which later resulted to the death of *Candida* sp. cell [117]. The antifungal efficiency of garlic, ginger extracts and AgNPs synthesized fromthem against *C. albicans* strain revealed that the synthesized AgNPs are more potent than the extracts [109]. The activity of AgNPs against spore-producing fungus and its effectiveness in growth retardation of fungi has been reported. A broad noticeable changes occur when fungal spore is bound with AgNPs causing a significant changes in their membrane structure [118]. Antifungal activities of AgNPs synthesized from some plantssources are showed in Table 3.

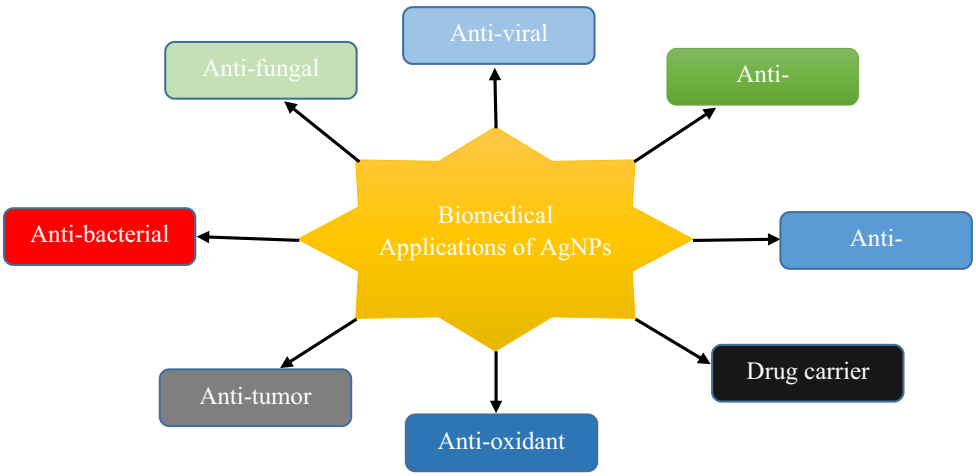


Fig. 5 Biomedical applications of AgNPs

Table 3 Characterization techniques, morphological properties, and biological activities of AgNPs synthesized from plant sources

S/no.	Plants name	Plants part	Techniques	Sizes	Shapes	Biological activities	References
1	*Pimpinella anisum*	Seeds	TEM, UV, FTIR, EDS, XRD	3.2–16	Spherical	Antibacterial	[137]
2	*Phyllanthus amarus*	Leaf	XRD, UV–Vis, SEM, TEM	30–42	Flower	Antifungal	[138]
3	*Artemisia absinthium*	Whole plant	UV–Vis, SEM, FTIR	15–35	Spherical	Antibacterial	[139]
4	*Azadirachta indica*	Leaf	TEM, FTIR, UV–Vis, DLS	34	Spherical	Antibacterial	[140]
5	*Coffea arabica*	Seed	TEM, FTIR, UV–Vis, DLS	20–50	Spherical	Antiviral	[141]
6	*Phoenix dactylifera*	Root	EDX, SEM UV, FTIR, XRD	15–40	Spherical	Anticancer	[142]
7	*Acacia rigidula*	Stem	TEM UV, FTIR, XRD	15–25	Spherical	Antibacterial	[143]
8	*Cleome viscosa* L	Fruit	UV, FTIR, XRD, FESEM-EDAX, TEM	20–50	Spherical	Antibacterial	[144]
9	*Allium rotundum*	Aerial part	TEM UV, FTIR, XRD	20.5	Spherical	Antibacterial	[145]
10	*Catharanthus roseus*	Leaf	FTIR	–	–	Antidiabetic	[146]
11	*Parkia speciosa*	Leaf	UV, SEM, TEM, DLS	26–39	Spherical	Antioxidant	[147]
12	*Ocimum sanctum*	Leaf	DLS	–	–	Antibacterial	[148]
13	*Azadirachta indica*	Leaf	DLS	–	–	Antioxidant	[148]
14	*Buddleja globosa*	Leaf	–	16	Spherical	–	[149]
15	*Pandanus odorifer*	leaf	UV, FTIR, XRD, HRTEM	5–9	Spherical	Anticancer	[150]
16	Plant derived 4-N-methyl benzoic acid	Leaf	UV, FTIR, XRD, HRTEM	7–23	Spherical	Antioxidant	[151]
17	*Tamarindus indica*	Fruit	HRSEM, HRTEM, UV, FTIR, XRD	10	Spherical	Antibacterial	[152]
18	Spice blend	-	SEM, TEM, UV, FTIR, EDX	6–28	Cubic	Antioxidant	[153]
19	*Phyllanthus acidus* L	Fruits	UV, EDX, XRD, SEM, TEM	10.29–45.57	Irregular	Antiinflammatory	[154]
20	*Erythrina suberosa*	Leaf	FTIR, UV–Vis, DLS	15–34	Spherical	Antioxidant	[155]
21	Turmeric (green tea)	Leaf	UV, EDX, XRD, SEM, TEM	6.13–8.46	Spherical	Antioxidant	[156]
22	*Phoenix dactylifera*	Root	UV, FTIR, EDX, FESEM, TEM	15–40	Spherical	Anticancer	[157]
23	*Allium sativum*	Fruit	UV, FTIR, EDX, SEM, TEM, XRD	3–6	Cuboidal	Antibacterial	[158]
24	*Zingiber officinale*	Fruit	UV, FTIR, EDX, SEM, TEM, XRD	3–22	Spherical	Antioxidant	[158]
25	*Capsicum frutescens*	Vegetable	UV, FTIR, EDX, SEM, TEM, XRD	3–18	Spherical	Antibacterial	[158]
26	Cauliflower	Flower	UV, FTIR, EDX, SEM, XRD	25–100	Globular	Antibacterial	[159]
27	*Cassia auriculata*	Flower	UV–VIS, FTIR, SEM, EDAX, XRD	50–100	Cubic	Antifungal	[37]
28	*Lantana camara* L	Leaf	UV, FTIR, SEM, XRD	410–450	Spherical	Antibacterial	[160]
29	*Scindapsus officinalis*	Fruit	UV, FTIR, SEM, TEM	50	Spherical	Anticancer	[161]
30	*Foeniculum vulgare*	Seed	UV, FTIR, SEM	11–25	Spherical	Antibacterial	[162]
31	*Moringa oleifera*	Leaf	UV, FTIR XRD, SEM, TEM	9–11	Spherical	Antifungal	[163]
32	*Malus domestica*	Fruit	UV, SEM	200	Spherical	Antioxidant	[164]
33	*Tribulus terrestris*	Leaf	UV, FTIR, SEM	16–28	Spherical	Antibacterial	[165]
34	Tea green	Leaf	UV, DLS, SEM, XRD	25–75	Cubic	Antibacterial	[166]
35	*Ferula asafoetida*	Leaf	FTIR, FESEM, TEM, DLS, UV	20–60	Spherical	Anticancer	[167]
36	*Parthenium hysterophorus*	Leaf	UV, FTIR, SEM	10–40	Spherical	Antibacterial	[168]
37	*Padina tetrastromatica*	Leaf	UV, FE-SEM	40–50	Round	Anticancer	[169]

Table 3 (continued)

S/no.	Plants name	Plants part	Techniques	Sizes	Shapes	Biological activities	References
38	*Hibiscus rosasinensis*	Leaf	CPS, UV, FTIR, SEM	12–17	Spherical	Antibacterial	[170]
39	*Mangifera indica*	Leaf	XRD, PSA, SEM, UV	32.4	Cube	Antibacterial	[171]
40	*Syzygium aromaticum*	Stem	UV, FTIR, HRTEM	5–40	Spherical	Anticancer	[172]
41	*Nigella sativa*	Seed	UV, DLS, FTIR, TEM	10–20	Spherical	Antioxidant	[173]
42	Palm date	Fruit	SAED, DLS, EDX, TEM	3–30	Spherical	Antibacterial	[174]
43	*Salvinia molesta*	Leaf	AFM, EDX, XRD, UV	12.46	Spherical	Antibacterial	[175]
44	*Fagonia cretica*	Leaf	UV, TEM, FTIR	11–15	Spherical	Antibacterial	[176]
45	*Enicostemma axillare* (Lam.)	Leaf	XRD, TEM, DLS, UV, SEM	15–20	Spherical	–	[177]
46	*Ficus carica*	Leaf	UV, FTIR, SEM	2–15	Spherical	Antibacterial	[178]
47	*Clerodendrum inerme*	Leaf	UV, FTIR, TEM	5–60	Spherical	Antibacterial	[179]
48	*Curcuma longa*	tuber	UV, FTIR, SEM	44	Spherical	Antibacterial	[180]
49	*Dillenia indica*	Fruit	UV, SEM	11–24	Spherical	Antibacterial	[181]
50	*Persea americana*	seed	UV, FTIR, TEM	2.35	Semispherical	Antibacterial	[182]
51	*Carica papaya*	peel	UV, FTIR, XRD, SEM, TEM	6–20	Spherical	Antibacterial	[183]
52	*Berberis vulgaris*	Root	UV, TEM, XRD,	30–70	Spherical	Antibacterial	[184]
53	*Paulownia tomentosa*	Leaf	UV, FTIR, XRD, SEM TEM	10 and 42	Spherical	Antibacterial	[185]
54	*Capparis zeylanica* L	Leaf	UV, FTIR, XRD, FESEM and TEM	28	Spherical	Anticancer	[186]
55	Black pomegranates	Fruit peel	UV, FTIR, XRD, FESEM	15.6	Spherical	Antioxidant	[187]

DLS dynamic light scattering, *HRTEM* high-resolution transmission electron microscopy, *FESEM* field emission scanning electron microscopy, *CPS* particle size analyzer, *AFM* atomic force microscopy, *SAED* selected area electron diffraction

Antioxidant activities

The antioxidant activity of silver nanoparticles synthesized from ginger and ginger extracts and using free radical scavenging ABTS\+ and DPPH assays was investigated by Ahmed et al. [109]. The results obtained from the antioxidant inhibition of the assays were well-matched. AgNPs synthesized from ginger showed higher antioxidant inhibition (74.18 and 62.05%) than the garlic extract (72.14 and 60.2%) for DPPH and ABTS + assays, respectively. The antioxidant activity of AgNPs formulated from *Symphytum officinale* leaf extract was reported to belesser than that of commercially available vitamin C which was the positive control, however, the antioxidant activity (DPPH inhibition ratio) of the AgNPs increased to 59.5 and 65.2%, at concentration of 500 and 1000 µg/mL, respectively [95]. The DPPH inhibition displayed by the AgNPs had been traced down to the fact that silver can easily lose electrons, the interaction of plant metabolites with silver ions during the formation of nanoparticles is another possibility [119]. The antioxidant activity for biosynthesized AgNPs has been estimated via modified DPPH assay by [120] with ascorbic acid as referenced control showed potential inhibition activity of AgNPs in comparison with the reference (ascorbic acid) and it was stated that the DPPH radical inhibition activity was enhanced with the AgNPs. At concentration 25 and 30 µL, the inhibition activities were 63.6 and 64.9%, respectively. The AgNPs show enhanced activity when compared with the standard which indicated the antioxidant ability of the obtained AgNPs [121–123]. Antioxidantactivities of AgNPs synthesized from some plants sources are showed in Table 3.

Anticancer

Documentation from recent article indicated that AgNPs mediated from *Abutilon indicum* possessed dose dependent anticancer potency against colon cancer in human. Their anticancer activity was ascribed to the depletion of mitochondrial membrane potential that caused DNA fragmentation and cell cycle arrest [124]. Findings of some researchers revealed that AgNPs synthesized from *Teucrium polium* leaf extract wereobserved to be effective against MNK45 human gastric cancer cell line [90]. The cytotoxicity of AgNPs obtained biologically from *Pimpinella anisum* seeds against colon cancer cells and neonatal skin stromal cells in human has been testified [67]. Biosynthesized silver nanoparticles and *Scindapsus officinalis* extract showed in-vitro cytotoxic activity against HepG-2 and MCF7 cancer cell lines [125]. Biosynthesized AgNPs

had shown efficient anticancer activity against breast MCF7 cancer cell lines [126]. The anticancer activity of AgNPs mediated from the fruit extract of *Lycium chinense* has been reported [127]. The anticancer activity of AgNPs synthesized from *Perilla frutescens* leaf extract (PF@AgNPs) against human colon cancer (COLO205) and human prostate adenocarcinoma (LNCaP) cell lines via the MTT assay revealed an anticancer activity which was concentration dependant. It was deduced that the PF@AgNPs displayedmaximum inhibition of 91.6 and 87.9% cell viability against LNCaP and COLO205 cells, respectively, at concentration of 100 µg/mL. The investigation of the morphological activities of PF@AgNPs against tested cells via phase-contrast microscope proved that the anticancer mechanism of PF@AgNPs entails cell shrinkage, membrane destruction, chromatin condensation, protrusion of microspikes, fragmentation of nuclei, and formation of apoptotic bodies [128]. The report obtained from the cytotoxicity effect of AgNPs based on *T. ljubarskyi* through the MTT assay at concentrations of 40–120 µg/mL against lung cancer cells (A549) and breast cancer cells (MCF7) showed cell viability of 21–67% and cell inhibition of 33–79% for A549 cell lines and 16–67% cell viability and 33–83% cell inhibition were recorded for (MCF7) cell lines. Moreover, the control showed 100% cell viability and 0% cell inhibition. It was recorded that the higher the concentrations of AgNPs used, the lower the cell viability and higher cell inhibition for the investigated cancer cells. This indicated that the synthesized AgNPs were effectively potent against lung and breast cancer cell lines [129]. Anticancer activities of AgNPs synthesized from plant are showed in Table 3.

Antiviral activity

The antiviral efficacy of AgNPs synthesized from the root of *Panax ginseng* had showed great potential in inhibiting type A Influenza viruses when compared with commercially available antiviral drug [130]. Several studies have reported the antiviral activities of AgNPs against different types of human and other ruminate animal viruses namely, human immunodeficiency virus type 1 [131], human parainfluenza virus type 3 [132], H1N1 influenza A virus [133], Pestedes petits ruminants virus [134], adenovirus type 3 [135], herpes simplex virus 1 [132], and hepatitis B virus [130]. Antiviral activities of AgNPs synthesized from plant are showed in Table 3. Furthermore, the evenly distribution of non-aggregated AgNPs per volume unit and the presence of cetyltrimethylammonium bromide in the nanocomposite pores has been reported to provide improved antiviral activity of AgNPs and other nanomaterials [136].

In vitro toxicity of AgNPs

The in vitro toxicity assessments are used for the characterization of the biological response to AgNPs to detect the risks associated with exposure to AgNPs. Several studies on the in vitro toxicity of AgNPs had been conducted. Examples include neuroblastoma cells, alveolar epithelial cells (A549), monocytic cells (THP-1), stem cells, and embryonic kidney cells (HEK293T) [188]. The RNA sequence has been combined with functional assays to examine the in vitro toxicity of AgNPs using low dosage and prolong exposure duration of (1 µg/mL) and 1.5 months against BEAS-2B cells which cause an epithelial–mesenchymal transition, upregulation of TGFB1, and cell transformation. This finding proved that the studied cellular effects are dose, size, and duration dependent [189]. In addition, the in vitro toxicity effect of 30 nm CT-AgNPs on RAW 264.7 cells lines through cytostatic form, oxidative stress, and viability at 2 days of exposure displayed a decrease in cell proliferation and viability at a concentration of only 75 µg/mL which highlighted the low sensitivity of RAW 264.7 cells to lower AgNPs doses [190].

In vivo toxicity of AgNPs

Findings on the in vivo toxicity of AgNPs have been carried out on animals such as rats and mice via inhalation, injection, and ingestion administration. These techniques allow the detection of AgNPs in blood of these animals causing toxicity to their organs (lung, intestine, kidney, heart brain, and liver. Inhalation has been major route of exposure to AgNPs especially during the preparation of AgNPs and usage of aerosolized products. Inhalation study on exposure of mouse to freshly produced aerosols during pregnancy for a duration of 4 h in a day during the first 15 days of gestation at a particle number concentration of 3.80×107 part/cm^3 revealed that the AgNPs crossed the placenta and induce some effects on the foetus [191]. Alterations in brain gene expression from a short-term exposure (2 weeks) of mice to 20 nm AgNPs at concentration of 1.91×107 particles/cm^3 have been reported [192]. Report from investigation of the in vivo toxicity of AgNPs on male and female rats via inhalation for a duration of 1 month at exposure dose of 11–14 nm AgNPs at concentrations of 1.73×104/cm^3, 1.27×105/cm^3, and 1.32×106 particles/cm^3 showed no harmful biochemical, hematology, and pathological effects [193].

Future challenges and recommendation

Despite the acclaimed benefits of the phytosynthesis of AgNPs the following are its major challenges; several optimization studies are needed for the synthesis of AgNPs

with physicochemical characteristics such as specific size and shape especially for biomedical applications [194–197]. In Addition, the regularization of optimizing factors such as volume of plant extract, pH, concentration of silver precursors, contact time, and temperature to obtain stable AgNPs with high yield varies according to biological and this requires multitask [198–200]. Hence studies on optimization conditions for the synthesis of AgNPs from plant sources should be encouraged. Scaling-up phytosynthesized AgNPs for commercialization purpose is challenging due to variation of plant biomolecules with period of plant collection and difficulties in preservation of plant extract for a longer period of time. Also, the specified mechanism for the reduction of silver ions during green synthesis of AgNPs from plant extract requires more investigation due to varieties of phytochemicals found in plants [201–203]. Therefore, identification of plant's biomolecules that are responsible for silver salt reduction are necessary.

Conclusion

Biosynthesis of AgNPs from plants sources offer numerously advantages over chemical and physical method, in that it is inexpensive, ecofriendly, nontoxic, and easily forming. It possess better morphological and biological properties. High temperature, pressure and energy required for physical and chemical methods of AgNPs synthesis. Hence, the synthesis of AgNPs from plant offers great opportunity to medicinal institutes due to its biological activities and other industries due mode of synthesis. The method of synthesis, mechanism, optimization conditions and characterization techniques of AgNPs has been reviewed. The antifungal, antibacterial, antioxidant, antiviral, and anticancer activities of AgNPs have been comprehensively discussed and its efficiency indicate it as a potential therapeutic source to combat diverse infectious diseases. Despite the numerous scientific information and findings on AgNPs synthesis from plants. The need to find natural reducing constituents for AgNPs synthesis still remain imperative as the variation in phytochemical make up of plant extracts remain worrisome. Therefore, the identification of biomolecules responsible for the reduction of silver salt and stabilization of AgNPs will pave way for rapid production of AgNPs in commercial quantity.

Declarations

Conflict of interest The authors declare that there is no conflict of interest toward the publication of this manuscript.

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