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REVIEW

Green synthesis of silver nanoparticles mediated by traditionally used medicinal plants in Sudan

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Abstract

Sudan has a tremendous wealth flora due to its unique geographical location and diverse climate. Vast records of plants and plants' secondary metabolites are reported to possess redox capacity and can be exploited for the biosynthesis of nanoparticles. Plant-mediated synthesis of silver nanoparticles is preferred due to their availability and their various metabolites. The present review explores the potentiality and diversity of biological activities of silver nanoparticles that originated from the combination of silver and phyto-constituents of mostly traditionally used Sudanese medicinal and aromatic plants. The green synthesis methods of silver nanoparticles mediated by more than 45 traditionally used medicinal plants are critically reviewed. In addition, parameters that affect the synthesis of plant-mediated silver nanoparticles, their characterization techniques and various biological activities are summarized and discussed. Thus, the study of green synthesis of silver nanoparticles and its applications can be extended to involve vast plant diversity of Sudan.

Keywords Green synthesis · Characterization · Silver nanoparticles · Medicinal plants

Introduction

Nanoparticles that are defined to have at least their dimensions in the range of 1–100 nm have received steadily growing interest as a result of their unusual properties, arrangement to form superstructures and applications superior to their bulk counterparts. The nanoparticles are unlike bulk counterparts; their characteristics properties are governed by the rules of quantum mechanics rather than classical physics [1]. Silver nanoparticles, in particular, have been known to fascinate people since Middle Ages because of their unique properties and applications [2].

At present, silver nanoparticles have received high attention due to their extraordinary biological activities. They are used in drug delivery, bio-labeling, sensing, food preservation, wound healings, water purifications and cosmetics. Moreover, silver nanoparticles have other interesting applications such as textiles, electronics, catalysis and paints [3].

Recently, plant-mediated green synthesis of silver nanoparticles is developing into a new and important branch of nanotechnology. It has emerged and gained importance because it is eco environmental and effective cost, with lesser toxicity when related to chemical hazards [4]. Among physical and chemical nanoparticles synthesis, green synthesis has several advantages. For example (1) less toxic and hazardous materials and environmentally benign solvents, (2) simple, rapid and cost effective, (3) consumes less energy and performs under moderate operation conditions, (4) combines the potency of both silver nanoparticles and plant active ingredients. In this respect, plant-mediated silver nanoparticles have been reported to possess more biological activities than nanoparticles synthesized by chemical methods [5].

Previous studies stated the use of different plant parts such as leaf, root, stem, bark, fruit, bud and latex for the synthesis of silver nanoparticles. Plant mediated synthesis of silver nanoparticles is preferred over microbe-mediated synthesis. The latter is not feasible and requires high aseptic conditions, time taking process and long incubation periods. In addition, the reduction properties of plants secondary metabolites are attributed to the higher potential

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ability of plant extracts to synthesize nanoparticles with improved characteristics [6]. In the synthesis of silver nanoparticles, plant extracts and microbes act as reducing agent for reducing Ag^+ to Ag^0 and capping or stabilizing agents for preventing the aggregation of the nanoparticles.

The diversity of climates in Sudan results in a wide range of ecological habitats and vegetation zones. This diverse climatic condition holds the potential of an immense wealth of flora. The present review article reveals the current knowledge about the potential biosynthesis of silver nanoparticles from plants extracts and presents a database that could benefit researchers on their future work regarding the green synthesis of silver nanoparticles. Authors summarize and compare the synthesis procedures by Sudanese medicinal plants, parameters, characterizations and biological activities of silver nanoparticles.

Methods of silver nanoparticles green synthesis

The green synthesis of silver nanoparticles proceeds through the reduction of silver ions by the phytochemicals as initial step in the nanoparticles formation. The phytochemicals also involved in the subsequent steps by stabilization and directing the shape and size of nanoparticles [7].

The green synthesis of silver nanoparticles depends on several parameters such as concentration of substrate, temperature, reaction time and pH. Importantly, these reaction parameters affect the silver nanofabrication such as size, shape and distribution. The most important factors are summarized and discussed as follows.

Silver ion concentration

In the present review, the most frequently reported silver ion concentration was 1 mM. However, other concentrations were reported. Typically, the following concentrations of silver ions were used 1.75, 2, 3, 5, 8, 10, 53, 100 and 200 mM [8–17]. Employing high concentration of silver ions is probably to shorten the reaction time for the nanoparticle's formation. This is especially important if the amount of reducing phytochemicals in plant extract is not high enough. Interestingly, other researchers have examined and optimized the effect of changing concentrations of silver ions on the morphologies and applications of nanoparticles. Specifically, concentration sets of (0.1, 0.5, 1, and 2 mM), (0.5, 1, 2 mM), (20, 50, 100 mM) and (1–5 mM) were used by several authors [18–21].

Concentration of plants metabolites reducing agents

It is assumed that the phyto-constituents which are responsible for the reduction of silver ions are tannins, terpenoids, flavonoids, ketones, aldehydes, amides, and carboxylic acids [22]. These constituents are capable of donating electron for the reduction of Ag^+ ions to Ag^0 [23]. Tannins were found to play a key role in the reduction and capping of silver nanoparticles [24]. Other Water-soluble secondary metabolites, most likely proteins, were mainly responsible for the biosynthesis of silver nanoparticles as in *Foeniculum vulgare* [25].

The effects of changing the concentrations of plant extract have been studied extensively. Many researchers have found that the concentrations of plant extract affect largely the shape and size and hence the nanoparticles biological activities [13, 14, 18, 19, 21, 26, 27].

The effect of temperature

Synthesis of silver nanoparticles is largely affected by temperature. Mostly, it had been carried out at room temperature as a simple and natural method. In the reviewed articles, synthesis procedures follow the same pattern. It is evident that the stability of plant metabolites requires working at ambient temperature. However, to shorten the synthesis time and enhance complete conversion of Ag^+ to Ag^0, some researchers have attempted synthesis at higher temperatures [8, 9, 14, 28–33]. Interestingly, Krishnan et al. has synthesized silver nanoparticles from *Piper nigrum* at room temperature, 40, 60 and 80 °C and studied the surface plasmon resonance (SPR) of the resultant nanoparticles by UV spectroscopy and found that nanoparticles synthesized at 80 °C gave an intense surface plasmon resonance band [28]. An intense SPR band would indicate the formation of high amount of nanoparticles. Microwave irradiation has also been employed to synthesize silver nanoparticles from *Tamarind indica* [12] and *Eucalyptus globulus* [34].

Effect of pH

pH has an important effect on the fabrication of nanoparticles in many ways such as altering the charge on the metabolites and hence affect the redox reaction and binding between metal and the phytochemical capping agents. Consequently, the shape and size of the nanoparticles are affected by acidity and basicity of the reaction medium. Moreover, the stability of nanoparticles is also sensitive to medium pH [7]. In spite of the key role, few researchers have considered pH in their synthesis of nanoparticles. Muthu and Priya studied the effect of changing pH on the synthesis of silver nanoparticles

[35]. They found that large-sized nanoparticles were formed at low pH; whereas high dispersed and small-sized nanoparticles at high pH. Similarly, Khalil et al. revealed that the rate of formation of silver nanoparticles increased at high pH [36]. Stability of the synthesized silver nanoparticles colloid at pH 4 was also reported [19]. Similarly, Krishnan et al. described the stability of silver nanoparticles under different pH (2–9) and found no effect on the nanoparticles morphology and their SPR peak [28]. Interestingly, Sahni et al. have reported formation of monodisperse silver nanoparticles by addition of ammonia [37].

Effect of reaction time

Less time taking and mild processes are the most obvious advantages of plant-mediated synthesis of silver nanoparticles. Usually, brown color change takes place immediately after mixing the Ag^+ ions with plant extracts indicating formation of the nanoparticles. However, reaction time is an important factor for smooth formation of nanoparticles and their shapes, sizes and stabilities. For example, the size of the nanoparticles increases with time [11]. The reaction time is varied according to the synthesis conditions; such as concentration and type of plant extracts, reaction temperatures and pH. Generally, the reaction requires short periods as indicated by most of reviewed works. However, some researchers reported several days for a complete conversion of Ag^+ and stabilization of the nanoparticles [11, 18]. Some researchers have monitored the SPR band by UV–vis spectrophotometer and reported noticeable enhancement over time [21, 24]. In contrast, Sathyavathi et al. found blue peak shift in the absorbance from 440 to 427 nm with increasing reaction time [38]. The blue shifted band indicates particle size reduction, which is probably due to gradual oxidation of nanoparticles.

Separation and characterization of silver nanoparticles

The purification of silver nanoparticles by centrifugation technique is widely used to get rid of unreacted materials and by products. Proper separation and purification are highly required for the nanoparticles characterizations and applications [7, 23]. Various characterization techniques can be used to identify the shape, size, surface and dispersity of the nanoparticles. The common useful methods include UV–visible spectrophotometry, dynamic light scattering, scanning electron microscopy, transmission electron microscopy, zeta potential, Fourier transform infrared spectroscopy, X-ray diffraction, energy dispersive spectroscopy, auger electron spectroscopy, scanning tunneling microscopy, atomic force microscopy. In the current review, results obtained from the most important techniques will be summarized and discussed.

UV–visible spectrophotometry

UV–visible spectrophotometry is a readily available technique allows fast identification and characterization of silver nanoparticles. It gives strong absorbance band known as surface plasmon resonance (SPR) in the range 400–500 nm due to the interaction between light and mobile surface electrons of silver nanoparticles [16, 39, 40].

In the current work, most of SPR peaks are within the anticipated wavelength range, however, some researchers have reported SPR peaks below 400 nm for their synthesized nanoparticles [9, 15, 31, 41, 42]. The absorbance bands below 400 nm are probably due to absorption of silver ions, complexes, impurities and plant phytochemicals. The characteristic of SPR is largely affected by the shape and size of the nanoparticles and dielectric constant of the surrounding medium [43]. The high sensitivity of SPR to the change of surrounding medium could be the reason for having wide range variations of absorption bands.

In the present work, the examination of the particle sizes and SPR peaks did not result in a clear correlation when data in Table 1 were analyzed. This is probably due to variation in the synthesis conditions and type of plant extracts. However, proportional relationships between size and SPR peaks have been observed by examining the silver colloids synthesized using different concentrations of plant extract or silver ions. Specifically, Roy et al. reported SPR peaks of 420 and 430 nm for particles with diameters of 65.67 and 66.98, respectively [26]. Similarly, changing of silver ions concentrations in the range 0.02 to 0.1 M have been found to result in nanoparticles with SPR peaks and diameters that increase with decreasing the silver ions concentrations [20]. Other researchers, synthesized silver nanoparticles using varied plant extract concentrations and reported a blue shift of SPR peak and decrement of particle size with increasing the amount of plant extract [13, 36, 44].

Obviously, the green synthesis resulted in various shapes and sizes dominated by spherical, polydisperse and have been found to be efficient for silver nanoparticles formation as seen in the reviewed articles. However, it is clear that the green synthesis results in less controllable morphologies compared to the physical and chemical synthesis methods. This is probably due to the presence of different reducing/capping phytochemicals that make multi rates of redox reaction and growing processes of the silver nanoparticles.

Fourier transforms infrared spectroscopy (FTIR)

The surface chemistry of the nanoparticles is revealed by FTIR. This technique helps to identify the functional groups

Table 1 Green synthesis of silver nanoparticles using plants extracts

Plant name	Part of plant	Characterization techniques	NP size (nm)	SPR peak (nm)	Reference
Abutilon indicum	Leaf	UV, DLS, EDX, TEM, SEM, XRD	5–25	455	[24]
Acacia nilotica	Leaf	UV, EDX, FTIR, SEM	30–150	450	[45]
Acacia senegal	Leaf	UV, TEM, XRD, FTIR	10–19	467	[46]
	Gum	UV, AFM, XRD, FTIR	81.45 ± 2.07	421	[14]
Acacia seyal	Gum	UV, AFM, XRD, FTIR	81.45 ± 2.07	421	[14]
Acalypha hispida	Leaf	UV, XRD. FTIR, TEMGCMS	20–50	424	[8]
Adansonia digitata	Fruit, leaf	UV, FTIR, XRD, AFM, SEM, EDX, TEM	5–64	431	[33]
Allium cepa	Fruit	TEM, ZPM, FTIR	14.8 ± 3.2	436	[47]
	Bulb	UV, TEM	10	401	[37]
Allium sativum	Fruit	UV, SEM, TEM, XRD, FTIR	3–6	375	[15]
	Fruit	TEM, ZPM, FTIR	47.2 ± 14.8, 7.4 ± 3	428	[47]
Azadirachta indica	Leaf	UV, DLS, TEM,	34	436–446	[21]
	Leaf	UV, DLS	65.67, 66.98	420–450	[26]
Calatropis procera	Latex	UV, TEM, XRD, FTIR, LDPSA	12.33	290	[9]
Capparis decidua	Stem	UV, TEM, FTIR,	1–19	460	[48]
Capsicum frutescens	Fruit	UV, SEM, TEM, XRD, FTIR	3–18	480	[15]
Carum carvi	Leaf	TEM, SEM, EDS, XRD	10	450	[17]
Fagonia cretica	Whole plant	UV, HPLC, FTIR, TEM	16	440	[19]
Jatropha curcas	Leaf	UV, SEM, EDX, TEM, AFM, FTIR, XRD, AE	20–100	430	[10]
Cassia auriculata	Leaf	UV, XRD, TEM	10–35	435	[35]
	Leaf	UV, FTIR, SEM, EDAX, XRD, TEM	50–100	452	[27]
Cassia occidentalis	Leaf	UV, TEM, SEM, XRD, EDX	31	461	[49]
Catharanthus roseus	Leaf	UV, XRD, FTIR, EDX, SEM	35–55	423	[50]
Citrus sinensis	Peel	UV, XRD, AFM, FTIR	34	420	[51]
Coffee arabica	Seed	UV, XRD, TEM, SEM–EDX, FTIR, DLS	10–40, 10–50, 20–150	447, 459, 445	[20]
Coriandrum sativum	Seed	UV, XRD, FTIR, SEM,	13.09	421	[16]
	Leaf	UV, XRD, FTIR, TEM	26	427	[38]
Cyperus rotundus	Whole plant	UV, FTIR, SEM, EDX	20.5 ± 9.6	446	[52]
Datura stramonium	Leaf	UV, FTIR, TEM, XRD	18	444	[53]
Eucalyptus globulus	Leaf	UV, FTIR, XRD, TEM, SEM, EDX, TGA	1.9–4.3, 5–25	428	[34]
Fagonia cretica	Fruit	UV, HPLC, FTIR, TEM	16	440	[19]
Foeniculum vulgare	Seed	UV, SEM, FTIR	11–25	475	[25]
Hibiscus sabdariffa	Flower	TEM, SEM, EDX, XRD,FTIR	3.9	–	[54]
Jatropha curcas	Leaf	UV, SEM, EDX, TEM, AFM, FTIR, XRD	20–200	430	[10]
Kigelia Africana	Fruit	UV, FTIR, XRD, SEM, EDX, TEM	10	285–350	[31]
Lantana camara	Leaf	XRD, SAED, XPS, FTIR, AFM, TEM	24–11, 34–20, 31–17, 27–14	436, 421, 413, 400	[44]
	Leaf	UV, FTIR, XRD	–	439	[55]
Lawsonia inermis	Leaf	UV, FTIR, TEM, XRD	30	445	[56]
Magnifera indica	Leaf	XRD, LDPSA, SEM, EDS, UV	31.7	393	[42]
	Leaf	UV, FTIR, SEM	100	420	[57]
Mentha piperta	Leaf	UV, SEM, TEM	35	420	[58]
Moringa oleifera	Leaf	TEM, SEM, FTIR	9, 11	450, 440	[59]
		UV, TEM	57	430–440	[30]
Nigella sativa	Seed	UV, ZPM, FTIR, TEM	10–20	432	[40]
Olea europaea L.	Leaf	UV, FTIR, SEM, TGA	20–25	441	[36]
Phoenix dactylifera	Leaf	SEM, XRD	30–85	439.5, 447	[13]
Phyllanthus amarus	Leaf	UV, FTIR, XRD, TEM	36	421	[60]
	Whole plant	UV, FTIR, TEM, DLS	33.7	420	[29]
Pimpinella anisum	Seed	TEM, EDS, XRD, UV	8.3	442	[11]

Table 1 (continued)

Plant name	Part of plant	Characterization techniques	NP size (nm)	SPR peak (nm)	Reference
Piper nigrum	Fruit	UV, FTIR, TEM	20	441	[28]
Ricinus communis	Leaf	UV, UHRTEM, SAED, XRD, FTIR, TGA	30–40	430, 442	[61]
Tamarindus indica	Fruit	UV, XRD, SEM, EDX, TEM	10	432	[12]
Tinospora cordifolia	Whole plant	UV, FTIR, DLS	35.4	420–430	[29]
Tribulus terrestris	Fruit	TEM, AFM, XRD, FTIR, UV	16–28	435	[62]
Withania somnifera	Leaf	UV, LDA, TEM, SEM, XRD, AFM	70–110	430	[18]
		UV, SEM, TEM, XRD	12–36	430	[63]
Zingiber officinale	Rhizome	UV, SEM, TEM, XRD, FTIR	3–22	400–480	[15]

UV UV–visible spectrophotometry, *FTIR* Fourier transforms infrared spectroscopy, *SEM* scanning electron microscopy, *TEM* transmission electron microscopy, *XRD* X-ray diffraction, *DLS* dynamic light scattering, *AFM* atomic force microscopy, *LDPSA* laser diffraction particle size analyzer, *EDS* energy dispersive spectrometry, *ZPM* zeta potential measurement, *EDX* X-ray energy dispersive spectrophotometer, *XPS* X-ray photoelectron spectroscopy, *TGA* thermogravimetric analysis, *SAED* selected area electron diffraction, *LDA* laser doppler anemometry, *GCMS* Gas chromatography–mass spectrometry, *HPLC* high performance liquid chromatography, *AE* atomic emission

of both plant extracts and the resulting silver nanoparticles. Table 2 summarizes the FTIR data of the reviewed articles. It is important to note that the FTIR technique is used at least to characterize the synthesized silver nanoparticles. Examining FTIR of the plant phytochemicals in free form or bounded to silver nanoparticles sometimes reveals slight band shifts as shown in Table 2. These shifts are taken as an evidence for the metal reduction and formation of nanoparticles.

The most important phytochemical constituents responsible for the reduction and capping of silver nanoparticles as revealed by FTIR and phytochemical studies are alkaloids, flavonoids, tannins, terpenes and quinones [64]. Table 3 summarizes the phytochemical constituents of the reviewed plants. Obviously, within a plant extract there are different reducing and capping agents. Thus, most of silver nanoparticles mediated by plant extract result in polydisperse and several shapes and sizes. Few research articles studied the employment of pure phytochemical compounds on silver nanoparticles synthesis and applications. In this respect, Jain and Mehata reported synthesis of silver nanoparticles using quercetin [65]. The use of pure phytochemical compounds on the synthesis of nanoparticles may probably control the nanoparticles morphology and results into new scopes for nanoparticles applications.

Microbe-mediated silver nanoparticles synthesis

As mentioned earlier, the microbe-mediated synthesis is not preferred and less common. In this respect there are few reports on the synthesis mediated by yeast, fungi, bacteria, algae and viruses [66]. Microbe-mediated synthesis involves the bio-reduction of metal salts to elemental metal. Fungi such as *Aspergillus fumigates*, *Fusarium oxysporum*, *Trichoderma reesei* and *Coriolus versicolor* have been used for the synthesis of silver nanoparticles [67]. Another study reported the synthesis of silver nanoparticles from Mushroom polysaccharides [68]. Interestingly silver nanoparticles produced by pellet of *Escherichia coli* showed a marked activity against *Salmonella typhi, Bacillus subtilis, Klebsiella pneumonia* and *Vibrio cholera* [69]. Alternatively, biological molecules such as nucleic acids have also been reported to mediate silver nanoparticles synthesis by acting as reducing agents [66].

Biological activity

The present review article reveals the current knowledge about the biosynthesis of silver nanoparticles from plants extracts and their potential biological activities.

Anti-microbial activity

Anti-microbial effect of silver nanoparticles has been widely investigated, yet their mode of actions is not fully elucidated. This activity was attributed to many factors summarized as small size of the nanoparticles and increased surface area provide opportunities for interactions with bacterial cell because it leads to increased membrane permeability and cell destruction to bacteria and fungi. Silver nanoparticles can cause cell breaking down and changes in the cell membrane permeability. In addition, silver nanoparticles attach the surface of the cell membrane, penetrating in bacteria and disturb the cell function, interactions of silver nanoparticles with amino acids and enzymes: bonding with amino acids (especially to –SH group), generation of ROS. It is also attributed to the fact that cells are majorly made up of sulfur and phosphorus which are soft bases and DNA has sulfur and phosphorus as its major components; silver

Table 2 Comparison of FTIR data of selected plant extracts and plant synthesized silver nanoparticles

Plant name	FTIR absorption bands (cm^{-1})		Possible functional group	References
	Plant extract	AgNP		
Abutilon indicum	3321	3290	–OH	[24]
	2925	2931	C–H	
	1627	1653	N–H (amide I)	
	1393	1383	C=O	
	1114	1064	C–O	
Capparis decidua	3274	3279	N–H	[48]
	1636	1637	C=C (alkene, aromatic)	
	524	549	C–Br	
Cassia auriculata	3393	3406	O–H	[35]
	2925	2925	C–H	
	1629	–	C=O	
	1605	1602	C=C	
	1389	1389	Amide, NO_3 of $AgNO_3$	
	1068	1082	C–O	
Coffea arabica	876–880	780–1100	C–C, C–OH, C–H (ring), C–CO	[20]
	1036–1150	–	C–O, C–O–C, C–C	
	1408	–	COO–	
	1517	–	C=C	
	1603	–	COO–	
	1650–1550	1597–1630	C=O	
	1639	1632	N–H, C=O, C–C, C–N	
	1744	1742	COO– (ester)	
	2800–3500	3420–3770	O–H	
	2925	2960	C–H (CH3)	
	2855	2850	C–H (–CH2)	
Cyperus rotundus	3363	–	O–H	[52]
	2976	2976	C–H	
	1715	1715	C=O	
	1248	1248	C–O	
	1099	1099	P–O	
	726	726	N–H	
Eucalyptus globulus	3437	3437	O–H	[34]
	2927	2927	C–H	
	1743	1743	C=O	
	1607	1607	C=C	
	1382	1382	O–H	
	1247	1247	C–O–H	
	1060	1060	C–O	
Euphorbia hirta	3312	3340	O–H	[52]
	2921	2921	C–H	
	1715	1715	C=O	
	1100	1100	P–O	
	726	–	N–H	

Table 2 (continued)

Plant name	FTIR absorption bands (cm^{-1})		Possible functional group	References
	Plant extract	AgNP		
Fagonia cretica	3864.44	–	O–H	[19]
	3729.37	3739.15	O–H	
	3626.26	–	O–H	
	3467.80	–	N–H	
	2916.00	–	C–H	
	2358.74	–	N–H	
	1636.56	–	C=O	
	1472.89	–	N–H	
	1401.80	–	C–O–H	
	1114.29	–	C–O–C	
	1061.73	1050.90	C–O	
	869.08	–	C–C, C–OH, C–H (ring)	
	627.47	643.89	C–H bending	
Olea europaea	3409	3395	O–H	[36]
	1733	–	C=O	
	1624	–	Amide I carbonyl	
	1077	–	C–N	
	651	–	=C–H bend	
Phoenix dactylifera	3330	3330	N–H, O–H	[13]
	2976	2976	C–H	
	2128	2128	C–O	
	1658	1635	C=O	
	1453	1453	C=C	
	1377	1377	C–N	
	1278	1278	C–O	
	1052	1052	C–O	
	873	873	=C–H	
Piper nigrum	3416	3421	O–H	[28]
	2921	–	C–H	
	2388	–	C–H	
	1625	1645	C=O	
	1388	–	N=O	
	–	1230	C–N	
	1221	–	C–F	
	1023	–	C–O	
	565	–	C–I, OH bending	
	526	–	C–I, OH bending	
Tamarind indica	3384	3398	O–H	[12]
	2941	2940	C–H	
	1730	1740	C=O	
	–	1632	C=C aliphatic	
	1406	1415	C=C aromatic	
	1069	1075	C–O (ester)	

Table 2 (continued)

Plant name	FTIR absorption bands (cm^{-1})		Possible functional group	References
	Plant extract	AgNP		
Tribulus terrestris	3489	3419	O–H	[62]
	2811	2812	C–H	
	2728	2726	C–H	
	2164	2171	C=C	
	1591	1613	C=C	
	1388	–	C–N	
	1349	1349	C–N aromatic amine	
	1124	1125	C–N aliphatic amine	

nanoparticles can act on these soft bases and destroy the DNA which would definitely lead to cell death.

In the current review, more than 35 medicinal plants have proven to show significant anti-microbial activities against various Gram-positive and Gram-negative bacteria as well as anti-fungal effects. It is reported that green silver nanoparticles showed more efficient anti-microbial activity than the plant extract alone as in cases of *Azadirachta indica* [21], *Calatropis procera* [9], *Fagonia cretica* [19], *Tinospora cordifolia* [29]. While antimicrobial activity of synthesized silver nanoparticles from *Phyllanthus amarus* was reported to be higher than that of the standard drug used in the study [29]. Silver nanoparticles from *Lawsonia inermis* gel in combination with antibiotics showed a synergistic anti-microbial effect [56]. Whereas Dias et al. stated that a cream incorporated with silver nanoparticles biosynthesized from *Withania somnifera* possessed a significantly higher antimicrobial activity [18].

Some green synthesized silver nanoparticles have exhibited a prominent antifungal activity such as *Calatropis procera* [9], *Lawsonia inermis* [56], *Phyllanthus amarus*, *Tinospora cordifolia* [29] and *Withania somnifera* [18]. The actual mechanism behind the antifungal activity of silver nanoparticles is not yet fully understood. However, it is assumed that disrupting the structure of the cell membrane by destructing the membrane integrity could be responsible for this biological action [23]. Nanoparticles synthesized from spice medicinal plants e.g. *Allium sativum* (garlic), *Zingiber officinale* (ginger), and *Capsicum frutescens* (cayenne pepper); which are important spices with well-known medicinal uses; were evaluated. These spices were reported to have various biological activities including antimicrobial and antioxidant activities. Silver nanoparticles synthesized from these spices exhibited broad-spectrum antibacterial activities thus, being suggested as valuable potential alternatives [15]. However, it was noted that the antimicrobial activity of silver nanoparticles against Gram-positive bacteria was reported to be less compared to Gram-negative bacteria and this may be attributed to the presence of the peptidoglycan layer which is negatively charged and prevents the free entry of silver ions into the cell wall of the bacteria [26].

Anticancer activity

Induced cell death in cancer cells was assumed to be mediated by increased oxidative stress leading to apoptosis of these cells. In the present article, it was found that silver nanoparticles synthesized from *Abutilon indicum* showed a dose dependent anti-cancer activity against human colon cancer at a very low concentration. Their anticancer activity was attributed to the enhancement of intracellular ROS generation and depletion of mitochondrial membrane potential that leads to further DNA fragmentation and cell cycle arrest [24]. Whereas silver nanoparticles synthesized using *Pimpinella anisum* seeds has shown cytotoxicity on human neonatal skin stromal cells and colon cancer cells [11]. Biosynthesized silver nanoparticles and *Piper nigrum* extract showed promising anticancer activity against breast cancer cells (MCF-7) and human pharynx cancer cell line (Hep-2) [28]. Other findings revealed that silver nanoparticles from *Nigella sativa* seeds were found to be effective against hepatocellular carcinoma using HepG2 cell lines [40].

Anti-oxidant activity and radical scavenging activity

In biological systems, uncontrolled accumulation of H_2O_2 leads to the formation of oxygen free radicals which causes massive damage to cell membranes. The antioxidant ability of green silver nanoparticles could be attributed to the functional groups adhered to them that came from the medicinal plant extracts. Many studies have investigated the anti-oxidant activity of silver nanoparticles from various medicinal plants, e.g. *Abutilon indicum* [24], *Allium sativum*, *Capsicum frutescens*, *Cassia occidentalis* [49] and *Zingiber officinale* [15].

Table 3 Phytochemical constituents of plants mediated green synthesis of silver nanoparticles

Plant	Phytochemicals	References
Acacia nilotica	Flavonoids, tannins, saponins, glycosides, alkaloids, sterols, terpenoids, anthraquinones	[70]
Acacia senegal	Saponins, sterols, tannins	[71]
Acacia seyal	Flavonoids, alkaloids, tannins, terpenoids, cardiac glycosides	[72]
Allium cepa	Steroids, alkaloids, tannins, flavonoids, cardiac glycosides, anthraquinones	[73]
Allium sativum	Saponins, steroids, tannins, cardiac glycosides	[74]
Azadirachta indica	Alkaloids, glycosides, phenols, steroids	[75]
Cajanus cajan	Alkaloids, flavonoids, tannins, saponins, terpenes	[76]
Calatropis procera	Glycosides, sterols, triterpenes, saponins, cardiac glycosides	[77]
Capparis decidua	Alkaloids, glycosides	[78]
Capsicum frutescens	Phenolic compounds, active compound (capsaicin)	[79]
Carum carvi	Alkaloids, glycosides, sterol, terpenes	[80]
Coriandrum sativum	Flavonoids, isocoumarins, fatty acids, sterols, coumarins	[81]
Cassia auriculata	Alkaloids, flavonoids, steroids, saponins, tannins	[82]
Cassia occidentalis	Flavonoids, phenols, tannins, amino acids, saponins, glycosides, terpenoids, steroids	[83]
Catharanthus roseus	Alkaloids, phytosterols, phenolic compounds, tannins	[84]
Citrus sinensis	Flavonoids, steroids, hydroxyamides, fatty acids, coumarins, carotenoids	[85]
Croton zambesicus	Diterpenes	[86]
Cyperus rotundus	Essential oils (active compound cyperone)	[87]
Datura stramonium	Tannins, alkaloids	[88]
Fagonia cretica	Saponins, cardiac glycosides, tannins	[89]
Foeniculum vulgare	76 volatile components in the essential oil	[90]
Jatropha carcus	Phenols, tannins, phytic acid	[91]
Kigelia africana	Iridoids, naphthoquinones, flavonoids, terpenes, phenylethanoglycosides	[92]
Lantana camara	Triterpenoids, flavonoids, fixed oil, tannins	[93]
Lawsonia inermis	Quinones, phenylpropanoids, flavonoids, terpenoids, phenolic compounds, fatty acids	[94]
Magnifera indica	Terpenoids, flavonoids, saponins, tannins	[95]
Mentha piperta	Alkaloids, flavonoids, phenols, steroids, tannins	[96]
Moringa oleifera	Phenolic acids, flavonoids, alkaloids, glucosinolates, tannins, saponins, oxalates, phytates, steroids, triterpenoids, flavonoids, anthraquinones,	[97]
Nigella sativa	Alkaloids, tannins, flavonoids, sterols	[98]
Olea europaea L.	Flavonoids, triterpenes, sterol	[99]
Phoenix dactylifera	Phenolic acids, flavonoids and tanins	[100]
Phyllanthus amarus	Saponins, alkaloids, tannins, cardiac glycosides	[101]
Ricinus communis	Tannins, saponins, terpenoids, polyuronoids, reducing sugars, flavonoids, alkaloids, anthraquinones	[102]
Tamarindus indica	Alkaloid, anthraquinone, saponins, glycosides	[103]
Tinospora cordifolia	Terpenoids, steroids, glycosides, flavonoids, phlobatannins	[104]
Vernonia amygdalina	Terpenoids, flavonoids, saponins, tannins, alkaloids, cardiac glycosides	[75]
Withania somnifera	steroids, phenols, alkaloids, flavanoids, glycosides, tannins and saponins	[105]
Zingiber officinale	Alkaloid, flavonoids, glycosides, resins, saponins, sterol terpenes, tannins, carbohydrates	[80]

dgnr

Other biological activities of green silver nanoparticles

Acacia Seyal silver nanoparticles significantly reduced cellular infiltration and granulamatous inflammation in ankle joints tissues of induced arthritic rats. So, it is concluded that gum arabic- silver nanoparticles worked as nano-cargo for enhanced anti-arthritic hesperidin (standard drug) in induced arthritic rats [14].

Anti-plasmodial effect against *Plasmodium falciparum* was detected using silver nanoparticles from *Catharanthus roseus* extract [50]. However, no proper mechanism for anti-plasmodial action of silver nanoparticles from this plant was demonstrated. Alternatively, *Magnifera indica*

silver nanoparticles enhanced dual dentistry applications and hence can be used for dental restoration [42].

Cytotoxicity

The effect of silver nanoparticles synthesized from aqueous-leaf-extract of *Mentha piperita* was detected on one of the most important neurological enzymes, i.e. acetylcholinesterase (AChE). It showed that these green synthesis nanoparticles from this plant extract might cause neurotoxicity via inhibiting AChE activity. This activity was confirmed by conduction of enzyme kinetic studies which revealed that silver nanoparticles were capable of binding to both the free AChE enzyme and to the enzyme–substrate (AChE-AChI) complex [58]. Results of this study showed that; due to their small size, nanoparticles may easily cross the blood brain barrier and could interact with various neurological targets, which in turn causes neurotoxic effects. This may draw the attention that even green silver nanoparticles are not safe and could cause some neurotoxicity due to their interaction with AChE. While *Cassia occidentalis* silver nanoparticles showed lower heomolytic activity (1.7%) to human blood i.e. less toxicity [49].

Effect of size and shape of the nanoparticles on biological activity

It is noted that almost all silver nanoparticles of the present plant extracts included in this review attained a spherical shape. Studies showed that spherical shaped silver nanoparticles have high surface to volume ratio to interact with the cell walls of pathogens which gives better antimicrobial activity [33]. Nanoparticles with a size range of 11–15 nm is highly suitable for biomedical application because the size of synthesized nanoparticles is within the tolerable range and will not cause toxicity within the cell [19].

In the current review, it is stated that small size nanoparticles have more penetration power to cell membranes, however, too small size brings the issue of enhanced toxicity compared to larger size nanoparticles, thus, an appropriate size is highly desirable for specified biological applications. Small particle size proves its higher potential antimicrobial activity as in *Cassia auriculata* [27] and *Adansonia digitata* [33].

Conclusion

The current review describes the green synthesis of silver nanoparticles mediated by several medicinal plants. The nanoparticles fabrication conditions, characterizations and biological activities presented a database that could benefit researchers on their future work regarding green synthesis of silver nanoparticles.

Wide range of medicinal plants traditionally used in Sudanese folk medicine has been exploited for the green synthesis of silver nanoparticles as simple, cost-effective, ecofriendly and rapid technique. However, this area is still dormant and more researches are required to explore the potentiality of other Sudanese flora. The silver nanoparticles synthesized using reducing and capping plants extracts are reported to have wide variations in shapes and sizes; which showed an impact on their biological activities. However, more studies are required to elucidate the effect of pure secondary metabolites that may control the morphology of the silver nanoparticles and hence their biological activities and other applications. These kinds of studies could provide better understanding of mechanism and efficiency of silver nanoparticles.

A thorough research on Sudan flora is in way to exploit green synthesized silver nanoparticles. This would be associated with a possible warranty on their safety and realization of their full potentiality in the era of green nanotechnology.

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