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REVIEW

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Vitex negundo assisted green synthesis of metallic nanoparticles with different applications: a mini review

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Abstract

Background: Several attempts have been made for green synthesis of nanoparticles of different metals and metal oxides, revealing the significance of plant extracts in reducing metal source to nanoparticles and applications in various scientific domains.

Main body: The present article focus on applications of *Vitex negundo* leaves extract in fabrication of nanoparticles of various metals like silver, gold, zinc oxide, and copper oxide. *Vitex negundo* is evergreen, perennial shrub, belonging to family Verbenaceae. Its leaves are reported to contain several phytochemicals like iridoids, flavonoids, and their glycosides, terpenoids. In respective research attempts, these metallic nanoparticles were evaluated for one or more applications like anti-microbial activity and/or photocatalytic activity.

Conclusions: Use of *V. negundo* polar extract indicated involvement of its polar phytocompounds in reducing the metal source and stabilizing the nanoparticles. In conclusion, it could be noted that metal nanoparticles have better antimicrobial activity and photocatalytic potential over aqueous leaves extract.

Background

Since few decades, many research groups are working hard for the development of simple and facile methods for the synthesis of metallic nanoparticles. The reason lies in their applications in various scientific domains. Applications so explored can be classified into two types. Biological applications include applications of nanoparticles explored for their anti-bacterial [1], anti-fungal [2], anti-viral [3], anti-inflammatory [4], anti-cancer [5, 6], anti-diabetic [7], and anti-oxidant potentials [8]. Non-biological applications include photocatalysis of pollutant dyes like methylene blue, reduction of 4-nitrophenol and its derivatives used in pesticides [9], use in dye-sensitized solar cells (DSSCs) [10]. Using *C. gigantea* latex, yttrium nitrate, europium nitrate, sodium chloride, and water, Ramakrishna et al. synthesized Eu3+ doped Y_2SiO_5 nanophosphors; those can be used in light-emitting diodes (LEDs) [11]. Recently, Wang et al. modified zinc oxide nanoparticles using uniformly dispersed silver nanoparticles and found enhancement in ethanol fumes and H_2S gas sensing performance [12].

For synthesis of metallic nanoparticles, several biological systems have been tried. Shivaji et al. employed cell-free culture supernatants of psychrophilic bacteria *Pseudomonas proteolytica*, *Pseudomonas antarctica*, *Pseudomonas meridiana*, *Arthrobacter gangotriensis*, *Arthrobacter kerguelensis*, *Bacillus cecembensis*, and *Bacillus indicus* [13], while Ahmed et al. used F. oxysporum to reduce silver oxide for preparation of silver nanoparticles [14]. Once *Candida albicans* was used for the synthesis of selenium nanoparticles [15], while Trichoderma viride was tried for the fabrication of silver nanoparticles [16]. Uma Suganya et al. successfully attempted blue-green alga *S. Platensis*-mediated synthesis of gold nanoparticles [17]. Since many years, plant extracts are being used for eco-friendly, green synthesis of metallic nanoparticles. Extracts of all the plant organs like leaves, flowers, barks, and fruits have been tried to fabricate

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metallic nanoparticles. Then, it is anticipated that plant metabolites or phytochemicals are involved in the reduction of metal ions (present in donor compound), formation of their clusters, and then particles of nano size. Further, after the fabrication of nanoparticles, phyto-compounds have also been observed to present on the surface of nanoparticles, i.e., they act as capping and stabilizing agents for metal nanoparticles. These phytochemicals can be primary metabolites like carbohydrates, amino acids-proteins or lipids, or secondary metabolites like flavonoids, anthocyanins, iridoids (also in their glycosidic forms), alkaloids, tannins, resins, terpens, or terpenoids. Nie et al. attempted the synthesis of silver and gold nanoparticles using nucleotides, adenine (A), cytosine (C), guanine (G), and thymine (T) as template [18]. Leaves contain carbohydrates, waxes, alkaloids, and polyphenols like flavonoids. Leaves of family-like verbenaceae, lamiaceae composed of terpenes as well. Barks are rich in tannins and flavonoids, while flowers and fruits contain monosaccharides, anthocyanins. Also, fruits of family Umbelliferae have terpenes in them. Among these, actually involved phytochemicals are depending upon the solvent used for extraction. Mostly, polar solvents like distilled water, methanol, ethanol are used; ultimately polar phytocompounds like carbohydrates, few proteins, flavonoids, anthocyanins, iridoids, and glycosides are likely to be responsible for the entire mechanism. Ethanolic extracts also include resins and terpenoids. Few researchers have tried non-polar petroleum ether extract, indicating involvement of oils, fats, and terpenes in process of nanoparticles synthesis [19].

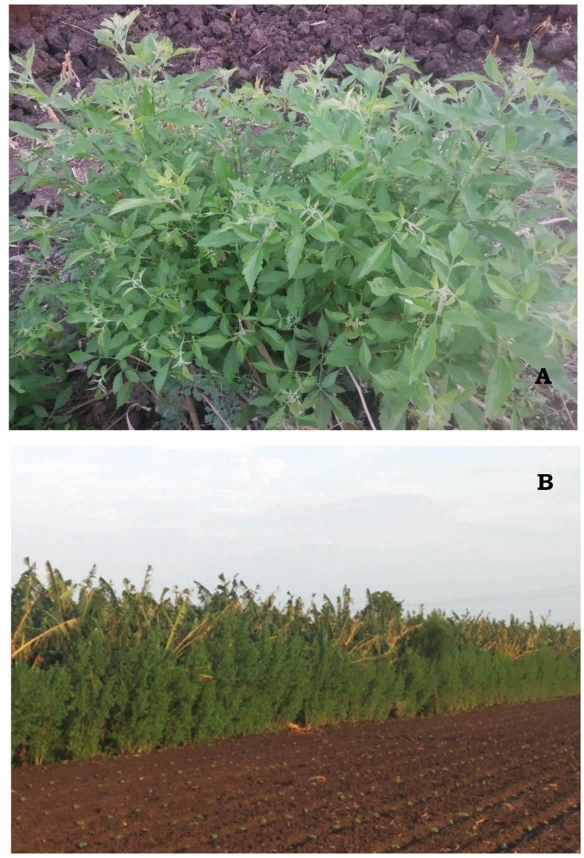

Fig. 1 a *Vitex negundo* plant. **b** Plantation of *V. negundo* at the boundary of banana field

Main text

Vitex negundo Linn. (*VN*) (Fig. 1a), the aromatic and woody, perennial shrub belonging to family Verbenaceae, is widely distributed throughout the Indian subcontinent. Zhang et al. reported that plant also grows on mine waste, indicating its use in phytoremediation [20]. The extract of parts of plant has been reported to have anti-fungal, antibacterial, anticonvulsant, CNS depressant, antiallergic, immunomodulatory, hepatoprotective, anti-hyperglycemic, antinociceptive, anti-inflammatory, antioxidant, anti-HIV, and snake venom neutralization activities [21]. Apart from these, it has been observed that in the Raver region (Dist. Jalgaon) of India, the *VN* plants are planted on the boundary of the banana field, to protect the banana plantations from hot winds running in summer (Fig. 1b). This review focused on applications of *VN* extracts in the fabrication of nanoparticles of different metals, their characterization for determination of visible light absorption maximum, crystalline, functional groups of capping agents, size and shape, and their applications in different domains. Hence, it is worthy to have a look on the morphology of *VN* leaves and phytochemicals present in *VN* leaves, prior to their employment in the synthesis of nanoparticles. For this review, I found various research articles and reviews pertaining to a variety of aspects, most of which are available there on well recognized international databases like the Royal Society of Chemistry (http://www.rsc.org), Elsevier-ScienceDirect (http://www.sciencedirect.com), Springer (http://link.springer.com), MDPI, and PubMed (Error! Hyperlink reference not valid.).

Morphology of *VN* leaves

VN has trifoliate, occasionally pentafoliate leaves with petiole of 2-4 cm. Trifoliate leaves are lanceolate with 5-10 cm long and 2-3.5 cm wide middle leaf. The remaining leaves on either side are sub-sessile. Leaves have a glabrous surface, tomentose bottom, and leathery texture (Fig. 2).

Phytochemistry of *VN* leaves

Several times, preliminary phytochemical studies of *VN* leaves were conducted, which further revealed the presence of polyphenols, terpenoids, and iridoids. Based on preliminary date, researchers have isolated or proved to detect the various phytocompounds, mainly secondary metabolites of different classes (Table 1, Fig. 3).

Fig. 2 *Vitex negundo* leaves

Table 1 Phytochemicals present in *VN* leaves

Class of phytocompounds	Phytocompounds	Reference
Iridoid glycosides	Agnuside	[22]
	2-p-hydroxybenzoyl mussaenosidic acid	[23]
	6′-p-hydroxy benzoyl mussaenosidic acid	
	Nishindaside	
	Negundoside	[24]
Flavonoids and flavonoid glycosides	Vitegnoside	
	7,8 dimethyl herbacetin 3-rhamnoside	
	5,7 dihydroxy-6,4′ dimethoxy flavanone	
	5,3′-dihydroxy—7,8,4′-trimethoxy flavanone	
	5-hydroxy-3,6,7,3′,4′-pentamethoxy flavone	
	5 hydroxy-7,4′ dimethoxy flavone	
	Vitexicarpin	[25]
	Casticin	[26]
	Chryso-spleno	
	Vitexin	
Triterpenoid	Ursolic acid	[27]
	Friedelin	[28]
Hydrocarbons	4,4-dimethoxy-trans-stilbene	

Green synthesis of metallic nanoparticles using *VN* leaves

Zinc oxide nanoparticles

Zinc oxide is thermally and chemically stable, II–VI semiconductor having band gap of 3.37 eV. It has been studied thoroughly and used in solar cells [29], piezoelectric transducers [30], transistors [31], photocatalysts [32], and gas sensors [33]. Considering these applications of zinc oxide, two groups of researchers attempted to develop a facile method for the preparation of high-quality ZnO with uniform morphologies in the form of zinc oxide nanoparticles using *VN* leaves extract. In 2015, Ambika and Sundrarajan, extracted about 5 g of crushed powder of dried *VN* leaves with 50 ml of ethanol for 2 h at 60 °C using soxhlet apparatus [34]. Then, this ethanolic extract was added to the stock solution of zinc nitrate hexahydrate. After 24 h, particles were separated by centrifugation at 6000 rpm for about 15 min. Finally, zinc oxide nanoparticles were obtained on calcinations at 450 °C. This newly obtained powdered material was characterized by UV-Visible, FT-IR spectra, XRD, EDX-Energy Dispersive X-ray, and SEM techniques. UV-Visible spectrum showed the typical excitation absorption peak at 375 nm. Its sharpness may be attributed to the electronic transitions from the valence band to the conduction band. FTIR spectrum exhibiting peaks at 3403.48, 2357.70, 1595.42, 1424.02, 1099, and 533 cm^{-1}. Initial peaks could be assigned to –OH stretching, C-H stretching, and C=C vibrations. The last peak at 533 could be attributed to typical Zn-O-Zn vibrations. XRD pattern of as-synthesized zinc oxide nanoparticles exposed the sharp peaks at 2θ values (100), (002), (101), (102), (110), (103), (112), and (201), indicated that zinc oxide nanoparticles are crystalline in nature. SEM and EDX images of as-synthesized zinc

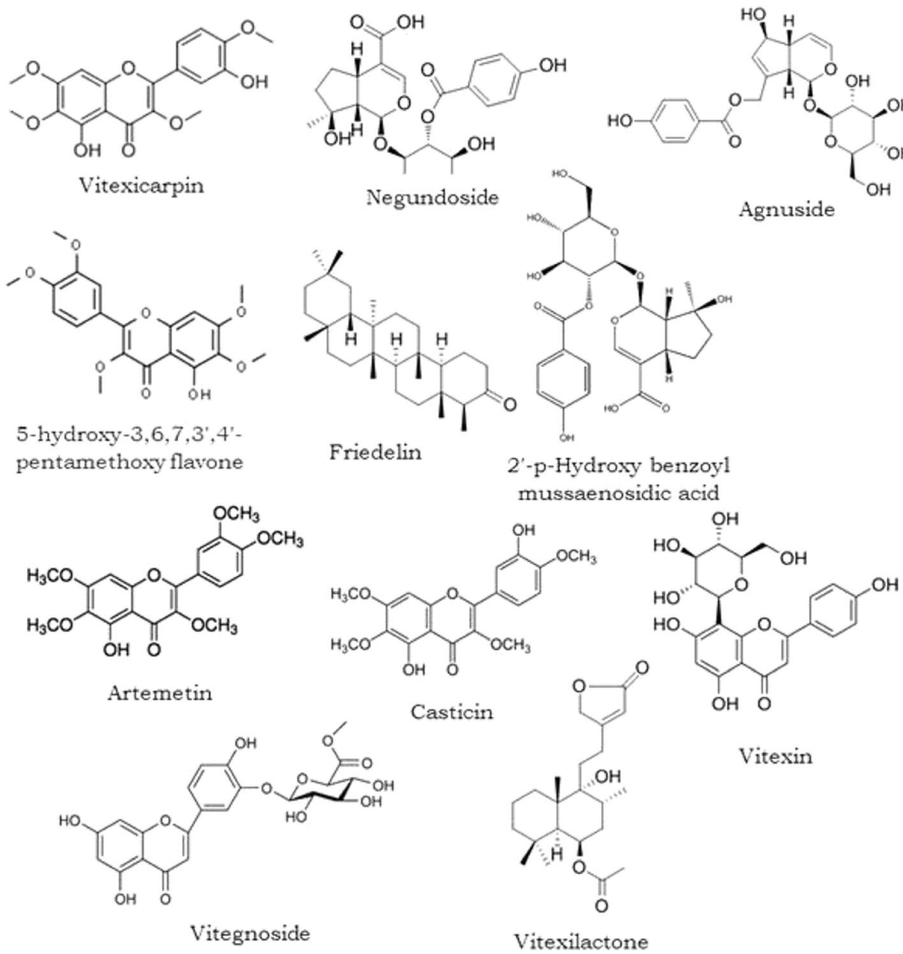

Fig. 3 Phytochemicals present in *V. negundo* leaves

oxide nanoparticles cleared the spherical shape with the particle size approximately 75 to 80 nm and the presence of zinc and oxygen only, respectively. Isoorientin, a flavonoid present in VN extract was considered responsible for the fabrication of zinc oxide nanoparticles. The mechanism involves the formation of zinc-isoorientin complex which on hydrolysis and subsequent calcinations released isoorientin and formed zinc oxide nanoparticles. Then, researchers screened anti-bacterial potential by Kirby-Bauer's agar well diffusion methods against *Escherichia coli* (gram negative) and *Staphylococcus aureus* (gram positive) microbes by measuring zone of inhibition and minimum inhibitory concentration (MIC). The result of anti-bacterial screening was mentioned in Table 2. The MIC was determined by measuring optical density (OD) at 600 nm. The optical densities were found as 0.41 for *E. coli* and 0.51 for *S. aureus*, while that for untreated cultures of both microbes was 0.8.

Then, Anbuvannan et al. 2018 boiled about 20 g of *VN* leave powder with 100 ml of distilled water for 20 min and filtered using Whatman filter paper. Then, they added about 5 g of zinc nitrate to 30, 40, and 50 mL to *VN* leave extracts at the temperature reached 60 °C. The resultant mixtures were then boiled until the dark yellowish paste is converted to ceramic crucible and annealed at 400 °C for 2 h. Finally, obtained light white colored powder was used for characterization and evaluation of antimicrobial potential and photocatalytic activity. Zinc oxide nanoparticles so obtained were then characterized by its UV-Visible (in reflectance mode), photoluminescence, FT-IR spectra, X-ray diffraction, and morphology and size distribution were characterized using FE-SEM and TEM. UV-Visible spectra of zinc nanoparticles prepared using different quantities of VN leave extracts showed absorption at 365, 360, and 355 nm. Based on these values, the band gap energies of three cases were found to be 3.39, 3.44, and 3.49 eV. Here, the blue shift of absorption denotes the quantum confinement effect. In photoluminescence spectroscopy, all the samples have high UV emission at 402 nm [35]. According to Vanheusden et al., this intense UV emission near to band edge emission of ZnO was originated from the recombination of excitons. The sample prepared with a high quantity of

Table 2 Anti-microbial activities (zone of inhibitions in millimeter) of nanoparticles synthesized using *VN* leaves extract

	Zone of inhibition (in mm)								
Nano-particles	*E. coli*	*B. subtilis*	*S. typhimurium*	*P. aeruoginosa*	*S. pyrogens*	*S. aureus*	*S. paratyphi*	*V. cholerae*	Reference
ZnO NPs	16					19			[34]
ZnO NPs	2					8	7	21	[35]
Au NPs	17.7	20	23.7	22	17.3	19.7			[36]
Ag NPs	12					11			[37]
Ag NPs	17					8			[38]

VN extract exhibited a red shift in 432 and 447 nm to 471 and 483 nm, respectively; also a green emission at 530 nm (probably due to oxygen vacancies) [39]. FTIR absorption spectra showed various peaks at 2924, 2353, 1633, 1440, 1382, 1026, 848, and 437 cm^{-1} for zinc oxide nanoparticles, indicating that they have been capped by phytochemicals having acid, amides, and/or hydroxyl functional groups also by aromatic compounds. TEM analysis revealed that zinc oxide nanoparticles are quasi-spherical in shape with the size of 23.81 nm and polycrystalline in nature. This researchers group carried group evaluation of anti-microbial activity by Kelmanl disk diffusion method against the pathogens *Salmonella paratyphi* and *Vibrio cholera* in addition to *S. aureus* and *E. coli*. The results obtained were mentioned in Table 2.

The extend of photodegradation of methylene blue (MB) in aqueous solution under the UV radiation was considered as function of photocatalytic activities of zinc oxide nanoparticles. The dye MB (1×10^{-4} M) with 20 mg of zinc oxide nanoparticles was stirred for 30 min in dark. The reaction was monitored using a UV–Visible spectrophotometer at 665 nm at different time intervals. It was observed that the intensity of the blue color of the mixture decreased gradually, and eventually became colorless. The excited dye deputes an electron to the conduction band of ZnO, and scavenged by pre-adsorbed oxygen, to form reactive oxygen species (ROS) which drove the photodegradation process.

Copper oxide nanoparticles

Many times, it has been proven that nanoparticles have better anti-microbial activity [40]; however, fabrication of copper oxide nanoparticles is mostly preferred due to its cost effectiveness and stability [41]. Copper in involved in redox reaction catalyzed by various enzymes by acting as co-factor. It has been observed that due to the ability to induce oxidative stress, CuO-NPs have anti-cancer potential [42]. Considering these applications, in 2018, Karthikarani and Suresh tried the green synthesis of copper oxide nanoparticles using *VN* leaves extract [43]. They heated 10 g in chopped leaves in 50 ml distilled water at 60 °C for 1 h, with constant stirring and then filtered through Whatman No. 1 filter paper. Extract in different quantities (2, 4, and 6 ml) were added separately to each of 1 M copper nitrate and kept aside overnight. Change in the greenish-brown color of the mixture to dark brown indicated a reduction of copper nitrate to copper oxide. The mixture was then washed with methanol and water, paste was obtained which was finally placed in a ceramic crucible and annealed at 300 °C for 3 h. Lastly, a black colored powder was obtained, which was used for further characterization and photocatalytic degradation of Rhodamine B. Spectral characterization including UV-Visible, FT-IR spectral analysis, and morphological analysis including XRD, SEM, TEM techniques were performed. Copper oxide nanoparticles prepared using different amounts of *VN* leave extracts showed an absorption maximum at 311, 310, and 308 nm, with an energy band gap of around 4 eV. FT-IR analysis revealed the presence of phytochemicals with amine, carboxylic acid, alcohol, aldehydes, and ketones as stabilizing and capping agents. Copper oxide nanoparticles were found crystalline. Further, they evaluate photodegradation activity of copper oxide nanoparticles on dye, rhodamine B (Fig. 4), using a 300-W tungsten halogen lamp equipped Heber Visible Annular Type Photo reactor.

Gold nanoparticles

As such, when gold (Au) is in bulk, it is considered as chemically non-reactive for many reactions, but when gold is fabricated in nanoparticles, it has many unique properties pertaining to localized surface plasmon resonance (LSPR) [38, 44]. The gold nanoparticles with different shapes are associated with diagnosis and therapy including cancer treatment, as anti-angiogenesis, anti-arthritic, and antimalarial agents. Because of their excellent photoelectrochemical and photocatalytic properties that they possess, nanocomposites of Au-graphene or Au-SnO2 which are developed on the electrochemically active biofilms (EABs), are used in various devices like photovoltaic cells, photoelectrodes, sensors, optoelectronic devices, photocatalysis [45–48].

Recently, Veena et al., attempted the green synthesis of gold nanoparticles using *VN* leave aqueous extract prepared by cold maceration and 0.01 M chloroauric acid as gold ions donor [36]. Then, gold nanoparticles were characterized by their UV-Visible and FT-IR spectra and morphology studied by XRD and TEM techniques. UV-Visible spectrum of as-synthesized Au-nanoparticles showed its characteristic highest absorption at 540 nm. The FTIR spectrum showed different peaks at 3550, 1820, 1660, 1450, 1380, 1300, and 401 cm^{-1}, suggesting the presence of phenolic compounds, ketones, and quinones as stabilizing agents. In XRD pattern, peaks like (111), (200), (220), (311), and (222) indicated the crystalline nature of nanoparticles. At last, TEM analysis of Au-nanoparticles revealed the exhibition of their spherical shape with size ranging between 20–40 nm. Anti-oxidant activity was determined by performing DPPH radical scavenging assay and nitric oxide assay. Anti-oxidant activities of gold nanoparticles were found concentration-dependent and IC_{50} values were found to be 62.18 μg (by DPPH radical scavenging assay) and 70.45 μg (by nitric oxide assay). Further, the anti-bacterial activity of gold nanoparticles was screened by widely used agar well diffusion method against various bacterial strains like *E. coli*, *B. subtilis*, *P. aeruginosa*, *S. aureus*, *S. typhimurium*, and *S. pyogenes*, and zone of inhibition were noted (Table 2). The mechanism of antimicrobial activity may be microbial DNA damage, protein synthesis inhibition, or damage of peptidoglycan of microbial cell wall (Fig. 5).

Silver nanoparticles

Silver nanoparticles have been proved to have their use as nanomedicine due to their specific properties and therapeutic potentials in the treatment of AIDS, cancer, hepatitis B, and diabetes [49]. Other non-biological applications of silver particles include use as catalyst in chemical reactions in bio-chemical sensing [50], solar cells, and batteries [51].

Taking this wide range of applications, several attempts have been made for the synthesis of silver nanoparticles using *VN* leave extracts. The first attempt was made by Zargar et al. in 2011 [37]. This group prepared methanolic extract of VN leaves (About 5 g leave powder extracted with 200 ml methanol) and its 0.5 g was dissolved in 100 ml distilled water and finally to synthesis silver nanoparticles, added 100 ml of silver nitrate AgNO3 (1×10^{-1} M). After 48 h, silver nanoparticles were obtained and characterized using UV-Visible spectroscopy, XRD, and TEM techniques. Further, silver nanoparticles were screened for in vitro anti-bacterial activity using Kirby-Bauer method, against *S. aureus* and *E. coli.* Results revealed that silver nanoparticles have exhibited two absorption maximum at 422 and 447 nm: crystalline nature and uneven shapes with 18.2 nm average size. Results of antibacterial screening were mention in Table 2. The mechanism of antimicrobial activity may be microbial DNA damage, protein synthesis inhibition, or damage of peptidoglycan of microbial cell wall (Fig. 5).

Then, in 2013, Prabhu et al. synthesized silver nanoparticles using little concentrated *VN* leave methanolic

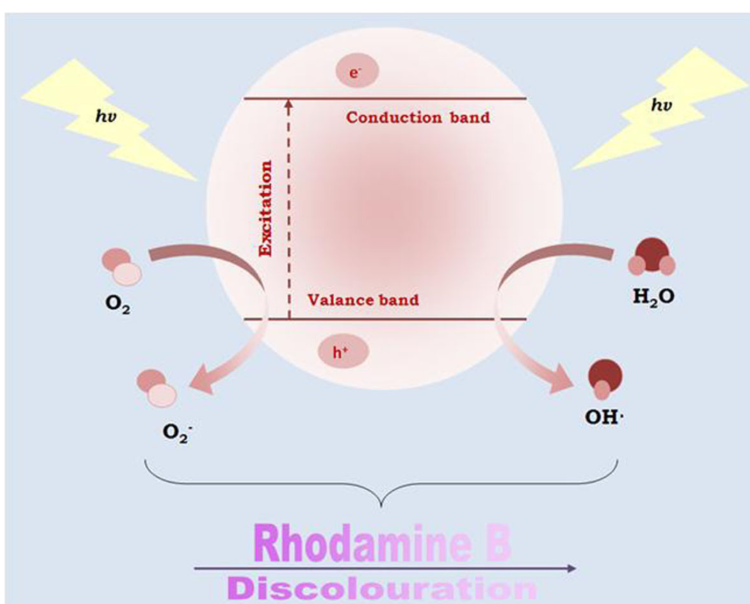

Fig. 4 Photocatalytic degradation of rhodamine B by copper oxide nanoparticles

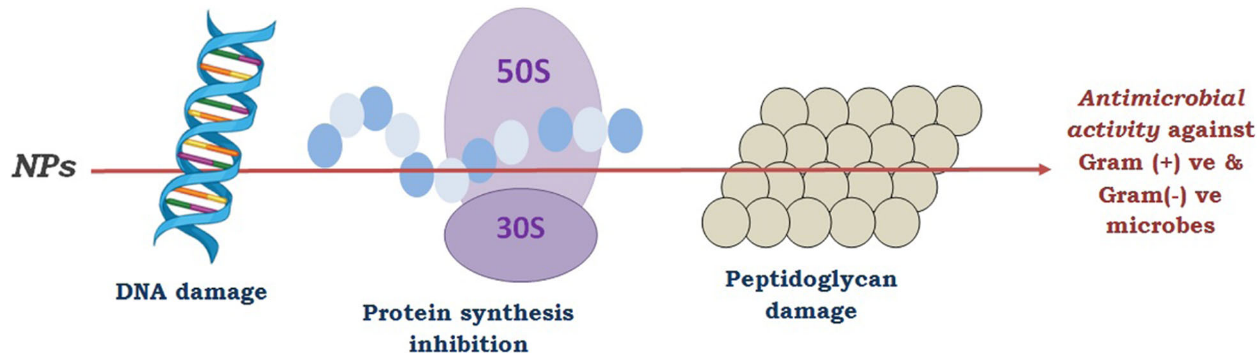

Fig. 5 Mechanism of antimicrobial action of nanoparticles

extract (about 10 g leave powder extracted with 200 ml methanol) and evaluated its growth-inhibitory effect on human colon cancer cell line HCT15 [52]. For the reduction of silver ions, about 5 ml of methanol extract was added to 45 ml of 1 mM silver nitrate solution and incubated for 4 h at 37 °C. Characterization was carried out through UV-Visible; FTIR spectral analysis and morphological studies were performed through field emission scanning electron microscopy (FESEM), TEM, and energy dispersive X-ray (EDX) analysis. The FTIR spectrum of as-synthesized silver nanoparticles showed intensive peaks at 3435, 3331, 2214, 1557, 1416, 1124, and 1051 cm^{-1} indicated that nanoparticles were capped by phenolic compounds present in *VN* leaves. TEM-based determination of the morphology and size showed well dispersed in nature of as-synthesized silver nanoparticles with particle range in size from 5 to 47 nm. The number of Braggs reflections obtained in energy dispersive X-ray (EDX) analysis was found at (111), (200), and (220), which corresponded to the diffraction facets of silver and indexed for the presence of crystalline silver. For determination of effect of silver nanoparticles on human colon cancer cell line HCT 15, nuclear morphological examination and DNA fragmentation were studied using propidium iodide staining and single-cell gel electrophoresis techniques, respectively. The percentage of cell viability was determined by MTT assay. Results showed that silver nanoparticles held HCT15 cells at G0/G1 and G2/M phases with simultaneous decrease in S-phase; after 48 h, silver nanoparticles suppressed proliferation of HCT15 with an IC50 of 20 μg/ml. Hence, it was concluded that silver nanoparticles may exert antiproliferative effects by inducing apoptosis in the colon cancer cell line (Fig. 6).

Kathireswari et al. synthesized silver nanoparticles adding 50 ml of fresh *VN* leaf extract to the aqueous solution of silver nitrate (1 mM); characterized them using UV-Visible, FTIR spectral and SEM, XRD techniques; and evaluated their antibacterial activity against *S. aureus, E. coli*, *P. vulgaris*, and *S. typhi* by agar well diffusion technique [53]. For silver nanoparticles, the highest absorbance of visible light was found at 420 nm. FTIR spectrum showed peaks at 2359, 1683, 1510, 1458, 1238, 1066, 887 cm^{-1}, suggesting the presence of phytocompounds with aromatic ring, alcoholic, ester acid functional groups as capping agents. XRD pattern exhibited peaks which could be indexed to 2θ values of (220), (311), (111), (420), revealing crystalline planes of cubic Ag. SEM studies confirmed the particle size of as-synthesized silver nanoparticles in the range of 40-100 nm. The results of anti-bacterial screening was mentioned in Table 2.

In 2015, Shabanzadeh et al. tried to develop the artificial neural network (ANN) based prediction model, to determine the influence of different variables on the size of silver nanoparticles green synthesized using *VN* extract. An artificial neural network (ANN) is a computational model for simplification of complex input–output relationship, mainly composed of simple processing elements, artificial neuron/nodes (Fig. 7), and their interconnections caring inputs in the form of weights. Neurons are placed in multi-layered system composed of input layer, hidden layer/s, and out layers along with, in some cases bias. The transfer function of all neurons processes all weights placed through all inputs and gives output. In ANN training/optimization process (Fig. 8), set of inputs are taken, weights are systematically adjusted so that network can give proper output. The parameters namely, *VN* extract, stirring time, temperature of reaction, and comcentration of silver nitrate were the four inputs for ANN modeling which had been instructed to give output in the form of the size of silver nanoparticles. Different amount of *VN* extract 0.1, 0.25, 0.5, 0.75, or 1.0 g were stirred for 48, 24, 12, 6, 3, or 1 h with 100 ml silver nitrate solutions of concentration 0.1, 0.2, 0.5, 1.0, 1.5, or 2.0 M, at the temperature 25, 30, 40, 50, 60, or 70 60 °C. The input data was processed through 10 neurons in the hidden

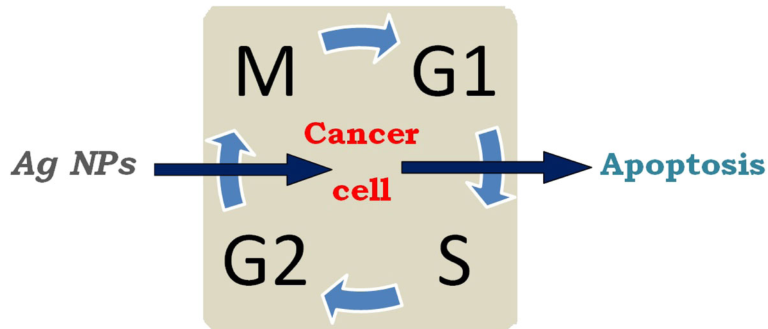

Fig. 6 Silver nanoparticles induced apoptosis in cancer cell

layer and exhibited hyperbolic tangent transfer function. In output, ANN predicted formation of silver nanoparticles with a minimum size of 15.42 nm and maximum size 30.92 nm, exhibited negligible error of −0.05 and 0.05 nm, respectively, representing linear transfer function. Hence, this multilayer perceptron (MLP) system had architecture 4:10:1. Here, the maximum sized AgNPs occurred on stirring about 0.1 g of *VN* extract, and 2 M of $AgNO_3$ solution for 24 h at 60 °C; while the smallest AgNPs were produced on stirring about 1 g of *VN* extract, and 0.2 mol of $AgNO_3$ for 1 h at 25 °C. Hence, it can be concluded that ANN can be an efficient model for computation of accurate and precise production of AgNPs of desired size [54].

In 2018, Janakiraman prepared silver nanoparticles mixing 10 ml of methanolic extract of *VN* leaves to 90 ml of 1 mM silver nitrate; characterized them using UV-Visble, FTIR spectral, and XRD technologies. Further, researcher proved their protective effect in nephrotoxicity induced by anti-cancer drug cisplatin in albino rats. For induction of nephrotoxicity in rats, cisplatin (16 mg/kg/day) was given by intraperitonial route for 15 days. Then, on the 15th day, serum creatinine, uric acid, and urea levels (as biochemical parameters) and malonylaldehyde (MDA) and glutathione reductase (GR) levels (as renal tissue markers) in the different experimental groups were determined. The results showed that silver nanoparticles significantly decreased three biochemical parameters and malonylaldehyde (MDA), while glutathione reductase (GR) levels were restored near to normal, indicating protective effect of silver nanoparticles on cisplatin–induced nephrotoxicity in rats [55].

Recently, Murali et al. synthesized silver nanoparticles using aqueous extract *VN* leaves and 1 mM silver nitrate ($AgNO_3$), and evaluated their anti-larvicidal potential against *Aedes aegypti*, following WHO guidelines. The percentage mortality of larvae was found concentration dependent to silver nanoparticles, increasing from 1 mg/L to 5 mg/L. They also tried their utilities in detection of heavy metals chromium, nickel, lead, mercury based on change in color in addition to solutions, $K_2Cr_2O_7$, $NiSO_4.6H_2O$, $Pb(NO_3)_2$, and $HgCl_2$ respectively [56].

Conclusion

Metal and metal oxide nanoparticles have a very wide range of scientifically proven uses in various fields. To

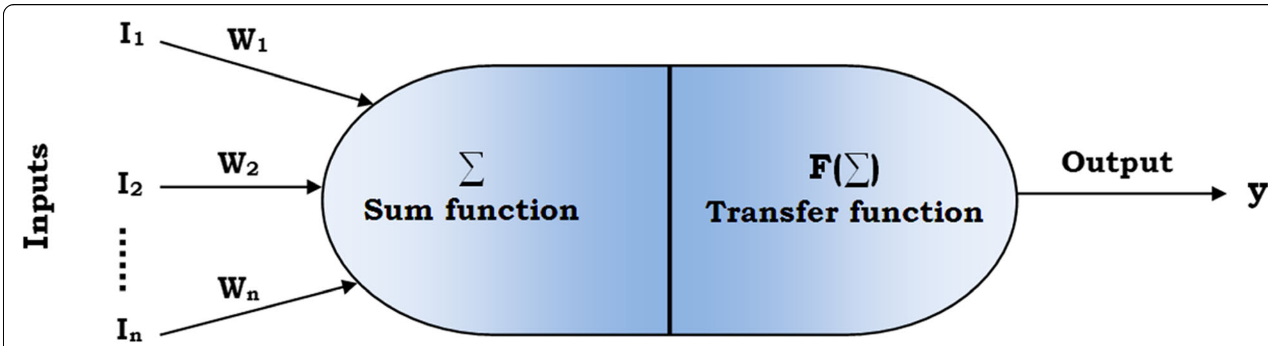

Fig. 7 Architecture of neuron

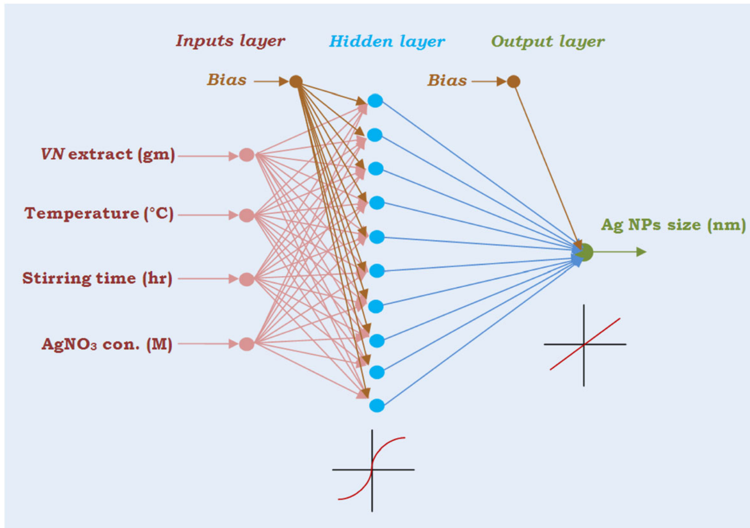

Fig. 8 An artificial neural network (ANN) for synthesis of AgNPs using *V. negundo* leave extract

overcome the environmental challenges posed by chemical methods (where hazardous chemicals are used) and requirement of big, costlier machineries in physical method of fabrication of nanoparticles, an eco-friendly approach has been developed involving the use of plant extracts for green synthesis of various nanoparticles. *Vitex negundo* (Verbenaceae) leaves contain numerous phytochemicals, which are made available for the reduction of donor compound to respective nanoparticles by extraction using appropriate solvent.

Based on this review, it can be concluded that due to the presence of few polar phytoconstituents, *V. negundo* leaf extracts can be used for green synthesis of nanoparticles of different metals (silver and gold) and metal oxides (zinc oxide and copper oxide) having wide range of applications in various scientific domains, including anti-microbial, anti-cancer, and photocatalytic activities.

Abbreviations
VN: *Vitex negundo*; ANN: Artificial neural network; WHO: World Health Organization

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Authors' contributions
SPP initiated the idea of designing this review, and written the review manuscript; read and approved the final manuscript. STK carried out the survey of the available literature and drawn figures and diagrams. All authors have read and approved the manuscript.

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Ethics approval and consent to participate
Not applicable

Consent for publication
Not applicable as our study does not include patients.

Competing interests
The authors declare that they have no competing interests.

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