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Green synthesis of silver nanoparticles: methods, biological applications, delivery and toxicity

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The advent of nanotechnology profoundly transformed the pharmaceutical sciences and greatly enhanced the diagnostics and treatment of various diseases that threaten human life. Several metallic nanoparticles are extensively used as nanomedicines due to their potential therapeutic applications. Among them, silver nanoparticles are remarkable due to their unique chemical and physical properties. This review discusses types of nanoparticles, and green synthesis methods along with their reduction mechanisms, involving economically viable reducing materials like algae, seaweeds and flowers. Apart from environment-friendly methods, several biological activities such as wound healing, antibacterial, antifungal, anti-tumour, anti-viral, *etc.*, are described in detail. Consequently, we have focused on how silver nanoparticles enhance targeted drug delivery and the mechanism of drug release along with their toxic effects.

1. Introduction

The enormous surge in multi-drug resistant pathogens has emerged as a vital challenge before scientists to develop effective therapeutics. Particles with a size range of 1–100 nm are considered nanoparticles (NPs), and silver nanoparticles (AgNPs) have been highly effective antimicrobial agents.[1,2]

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The large surface area of AgNPs is the primary factor that results in better antimicrobial activity due to strong interaction with micro-organisms even at a lower concentration. As AgNPs release silver ions inside pathogens to kill them, many mechanisms have been proposed explaining the actions of AgNPs on bacteria, such as blocking the respiratory chain, protein denaturation due to strong bonding to functional groups, blocking transport of nutrients to the bacterial cell membrane, flowing out cellular contents by disrupting the cell membrane and blocking deoxyribonucleic acid (DNA) replication. Hence, AgNPs act as a potent killing agent against bacteria, including Gram-negative and Gram-positive.[3]

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AgNPs have been synthesized by physical, chemical, photochemical, microemulsion, biological and microwave methods.[4–7] However, the physical methods are costly, and chemical methods generally use reducing agents,[8–11] which are hazardous chemicals. Hence, the research moved toward a new convenient, eco-friendly, high yield and cost-effective method called biological synthesis.[12] In biological synthesis, for the reduction of silver nitrate ($AgNO_3$), some parts of plants[13–22] and microorganisms[23–25] are used as reducing agents. The phytoconstituents responsible for reducing silver ions into AgNPs are glycosides, terpenoids, alkaloids, phenolics, *etc.*[3] This process can be utilised for large scale production of AgNPs without harnessing any high pressure, energy or temperatures. But the drawback of the biological method is that it is a slow process compared to the chemical method.[26,27] Hence, to overcome such problems, the microwave irradiation method has been used, which causes fast and uniform heating of the reaction mixture leading to the synthesis of AgNPs in a small span of time.[28]

Along with AgNPs, noble metals like gold, zinc and iron show an extensive range of material behaviour and their fabulous characteristic feature based on size, morphology and application in many diverse fields.[29] Many capping agents are used to get non-agglomerated and uniform particle sizes, which bind on the surface of NPs and make them soluble in the desired solvent. Stable size of NPs can be used to build 2D and 3D structured materials representing a unique collection phenomenon.[30] They are currently synthesized in many forms to catalyse reactions, protein separation, polymer preparation, sensor technology, optoelectronic recording media and heat propagation in thermal ablation therapy.[31–35] Nowadays, various disease imaging systems like magnetic resonance imaging, positron emission tomography, surface-enhanced Raman spectroscopy (SERS) and optical imaging are in use based on the magnetic property of NPs.[36] Wei *et al.* in 2015 opined that weak interaction with AgNPs causes oscillation of the conduction band electrons of AgNPs, and thereby, photon energy changes into thermal energy so that the SERS effect can be tamed to develop photothermal and thermolytic laser therapies.[37] In a study conducted on the plasmonic properties of AgNPs, Lin *et al.* discussed that spherical AgNPs with a size range of 5–50 nm show yellow colour,[38] and Tao *et al.* have suggested that it can be used to constitute 3D plasmonic crystals.[39]

Apart from the therapeutic role of AgNPs in disease treatment, they could also play a very vital role in developing new diagnostic approaches. Due to their high conductivity, catalytic activity, and plasmonic features, AgNPs are particularly appealing materials for diagnosis and can be used to enhance the performance of biosensors. A key element in detecting an analyte at low concentrations is the sensitivity of the biosensors. The sensitivity of the biosensor has been improved by using AgNPs to increase the electroactive area of the electrodes and, consequently, the electron transfer rate. Cheng *et al.* employed functionalized-AgNPs to develop a highly sensitive electrochemical biosensor for detecting exosomal miRNAs, which helps in the early diagnosis of cancer. In biological samples from humans, this biosensor showed a lower limit of

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0.4 fM for detecting miRNA-21.[40] In another work carried out by Chen *et al.*, AgNPs were used for colorimetric detection of endogenous telomerase based on telomerase-regulated DNA "blunt-dangling" end conversion that causes AgNPs to disperse and change colour. The colour difference allowed the visual distinction between extracts from cancer cells and normal cells, and the detection limit was equal to 1 cell μL^{-1} of telomerase activity.[41]

Over the past decade, many reviews have focused on the green synthesis of AgNPs by various parts of plant extracts such as bark, stem, root, leaves, flower, oil, fruit peels, seed, seaweed and citrus lemon zest. The current review focuses on the green synthesis of AgNPs using extracts from flowers, algae and seaweed, their characterization techniques, and a possible mechanism of reduction of $AgNO_3$ into AgNPs, along with drug delivery, biological application and the toxicity effect as well.

2. Classification of NPs

NPs can be categorized into organic or carbon-based, inorganic and hybrid NPs, as shown in Fig. 1.

2.1. Carbon-based NPs

The carbon atom, being a more versatile element, has received increased attention from researchers towards taming its different types of hybridization states (sp, sp^2 and sp^3) and synthesizing a lot of its allotropes. These are fullerenes (C_{60}), carbon nanotubes, carbon nanofibers, graphene, and carbon onions. Furthermore, single-walled carbon nanotubes, multiple-walled carbon nanotubes, quantum dots, and zero-dimensional dots have also been synthesized.[42] These nanoparticles have biomedical applications like bioimaging, photoacoustic diagnostic, hemofiltration/hemodialysis, X-ray protection, *etc.*[43]

2.2. Inorganic NPs

Inorganic NPs can be classified as metals and metal oxides like aluminosilicates.[44] Various NPs using inorganic metals like silver, gold, silicon, *etc.*, and metal oxide NPs like iron oxide (Fe_3O_4), titanium oxide (TiO_2), copper oxide (CuO), zinc oxide (ZnO), *etc.*, have been synthesized. Other forms of gold NPs, like gold nano shells, have been synthesized[45] and some advanced level synthesis methods of nano diamonds have also been reported.[46]

2.3. Hybrid/organic NPs

Inorganic and carbon-based NPs are combined to synthesize hybrid NPs. The hybrid NPs are synthesized to get multiple carriers and better drug delivery systems, such as lipid–polymer or mesoporous silica hybrid NPs with an inner polymeric core

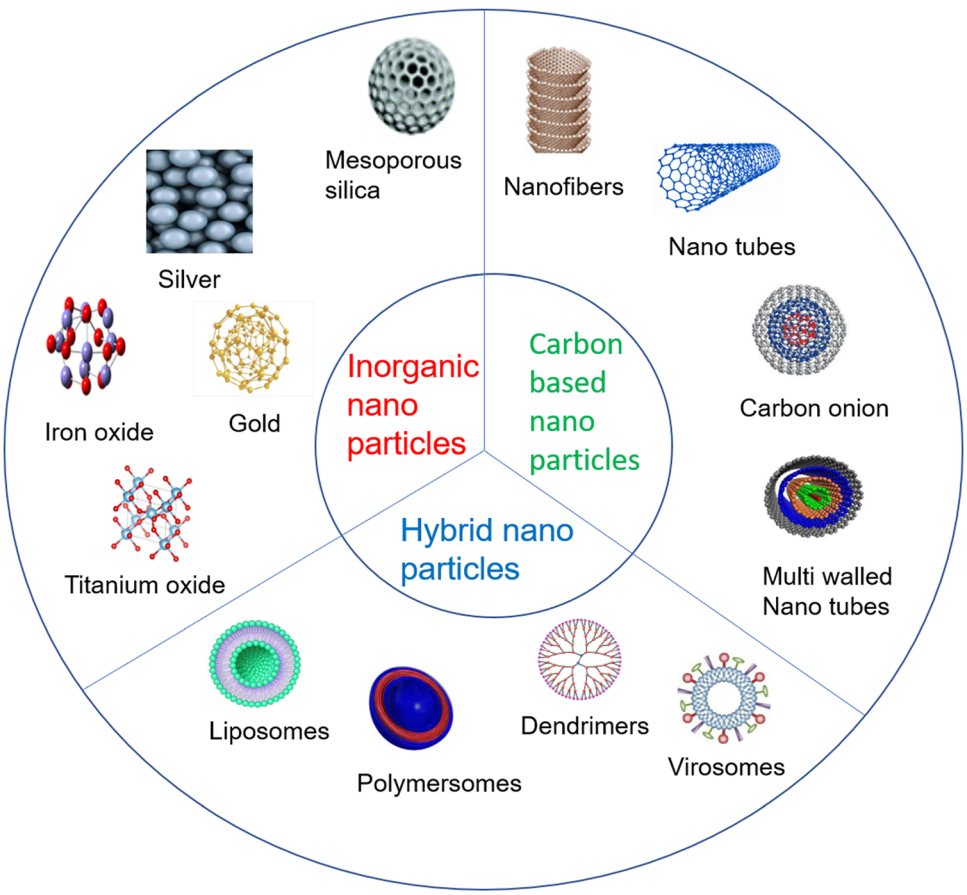

Fig. 1 Types of NPs.

and a lipid shell that are used for a more promising drug carrier system.[47] In addition, the physiochemical properties of hybrid nanoparticles can be harnessed for some medical applications like gene editing, biomedical imaging, dental implants, *etc.*[48]

3. Methods of AgNP preparation

There are many methods of preparation for AgNPs, which are classified into top-down, bottom-up, chemical and biological methods.

3.1. Miscellaneous methods

This section discusses several methods such as top-down, bottom-up, chemical and physical. In the top-down method, bulk materials are used as starting materials and many physical processes are used to fragment large particles into nano size particles (Fig. 2). In this method, we generally discuss the physical method involving mechanical milling, laser ablation, sputtering, *etc.* In mechanical milling, bulk materials are taken into a container and subjected to a high speed rotating ball to break it into a powder/particle form. In laser ablation, the solid material is placed directly under laser radiation to break it into nanoparticles[49] (Fig. 3A). But this approach is not more suitable for synthesizing controlled metal NPs, especially when narrow size distribution or anisotropic morphologies are needed. Therefore, bottom-up methods like ball milling have been used for the size-controlled synthesis of NPs. In this method, some processes such as coalescence, atomic addition and oriented attachment are responsible for the atomic nucleation to synthesize the final NPs[50] (Fig. 2). Whereas in chemical methods as shown in Fig. 3B, some reducing agents like sodium borohydride,[7] hydrazine,[8] ascorbic acid,[9] and trisodium citrate[10] were used for the reduction of $AgNO_3$ into AgNPs. This method gives a high yield of AgNPs but it uses harmful chemicals that threaten living organisms.

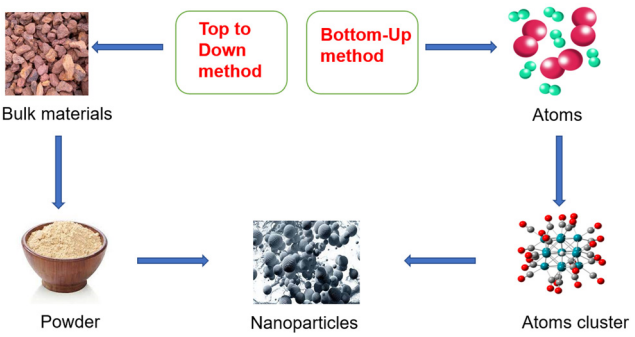

Fig. 2 Top-down and bottom-up methods to synthesize NPs.

3.2. Biological method

The biological method requires plant extracts as a reducing agent instead of chemicals or a high radiation beam. In every biological method (Fig. 3C), plant extracts are used taken from bark, stems, roots, leaves, flowers, oil, fruit peels, seeds, seaweed, citrus lemon zest and microorganisms like fungi, bacteria, and yeast are used as well. In this review, we have mentioned the green synthesis of AgNPs using seaweed and algae extracts as shown in Table 1 and flower extracts in Table 2. So, biological synthesis has very broad methods of preparation of AgNPs. The plant extract is taken in small amounts, added to a high volume of $AgNO_3$ solution, and put on a stirrer to change its colour from yellow to brown.[51]

3.2. (i) Seaweed and algae extract used for biological synthesis of AgNPs. Seaweed *Sargassum wightii* was used for the green synthesis of AgNPs by Shanmugam *et al.* They have reported the synthesized AgNPs' anti-bacterial activity against human pathogens. The UV-Visible spectroscopy (UV-Vis) revealed the optical properties, and the X-ray diffraction (XRD) results revealed the cubic size of AgNPs. Furthermore, scanning electron microscopy (SEM) and high-resolution transmission electron microscopy (HR-TEM) were used for characterizing the morphology and size of the synthesized AgNPs, against human pathogens, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Salmonella typhi*.[52] AgNPs were used against a marine biofilm in 2014 by Vijayan *et al.*, which were synthesized by using an aqueous filtrate of seaweed *Turbinaria conoides* as a reducing agent. The size range was 2–17 nm and it was efficient in controlling the formation of the biofilm. The maximum zone of inhibition was recorded against *Escherichia coli*, followed by *Salmonella* sp.,

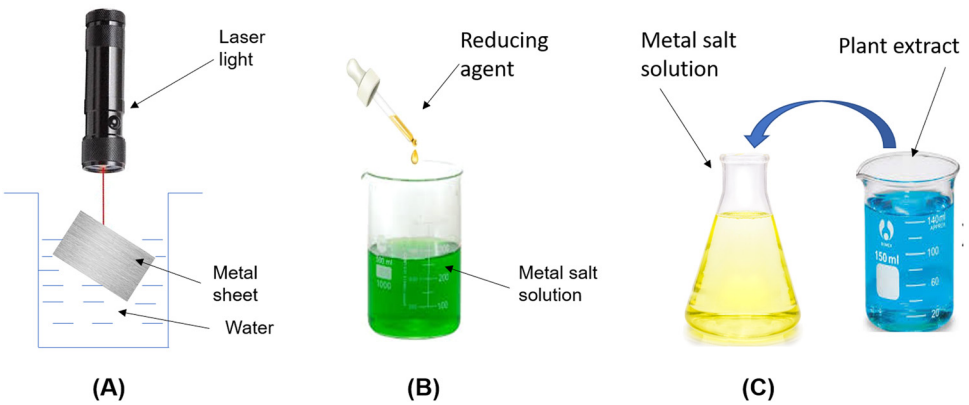

Fig. 3 (A) Physical method, (B) chemical method and (C) biological method.

Table 1 Seaweed and algae used for biological synthesis of AgNPs

S. no.	Reducing agent seaweed (SD), algae (AL)	Operating conditions	Characterization	Particle size (nm)	Author/ref.
1.	Aqueous filtrate of *Sargassum wightii* (SD)	$AgNO_3$ conc. 1 mM, 5 mL/50 mL, incubated at 24 °C, 24 hours	UV-Vis, XRD, FT-IR, HR-TEM, AFM	15–20	52
2.	Aqueous filtrate of *Turbinaria conoides* (SD)	1 mM, Extract/$AgNO_3$: 10 mL/90 mL, incubated at rt	UV-Vis, SPR, XRD, -IR, HR-TEM, FE-SEM	2–17	53
3.	Aqueous filtrate of *Turbinaria ornate* (SD)	1 mM, 12 mL/88 mL, centrifuged at 10 000 rpm, 10 min	UV-Vis, XRD, FT-IR, EDX	20–32	54
4.	Ethanol extract of *Gracilaria birdie* (SD)	1 mM, 10 mL/100 mL, 30 min stirred, centrifuged at 3600 rpm for 15 min, pH= 7	UV-Vis, SPR, TEM, DLS	20.2–94.9	55
5.	Aqueous extract of *Spyridia filamentosa* (SD)	1 mM, 20 mL/80 mL, incubated for 2 hours, centrifuged at 8000 rpm for 10 min	UV-Vis, FT-IR, XRD, EDS, TEM	20–30	21
6.	Aqueous filtrate of *Caulerpa serrulata* (AL)	1 mM, 5–25 mL/95–75 mL	UV-Vis, HR-TEM, XRD	10–100	56
7.	Aqueous filtrate of *Botryococcus braunii* (AL)	1 mM, 5 mL/45 mL, stirred 3 hours	UV-Vis, FT-IR, SEM, XRD	2–100	57
8.	Aqueous filtrate of *Cladophora glomerata* (AL)	5 mM, 5 mL/100 mL, stirred at 500 rpm	UV-Vis, DLS, XRD, TEM, FT-IR	8–11	58
9.	Aqueous filtrate of *Sargassum polycystum* (SD)	0.1 mM, 10 mL/90 mL, incubated 24–48 h, centrifuged at 13 000 rpm for 20 min	UV, FT-IR, XRD, SEM, TEM	—	59
10.	Aqueous extract of *Enteromorpha compressa* (SD)	1 mM, 10/90 mL, incubation 1 hour	UV-Vis, XRD, FT-IR, FE-SEM, HR-TEM	2–24	60
11.	Aqueous extract of *Portieria hornemannii* (SD)	1 mM, 5 mL/45 mL	UV-Vis, XRD, TEM, SEM, FT-IR	60–70	61
12.	Aqueous filtrate of *Halymenia Porphyroides boergesen* (SD)	1 mM, 500 mg dry powder of seaweed in 250 mL of $AgNO_3$, at pH = 5.09	UV-Vis, FT-IR, XRD, HR-TEM, SEM, TGA	34.3–80.5	62
13.	Aqueous extract of *Gelidiella acerosa* (SD)	1 mM, 10 mL/100 mL	UV-Vis, X-ray diffraction, FT-IR, AFM, SPR	20–50	63
14.	Aqueous extract of *Fucus gardneri* (SD)	1 mM, 2 mL/10 mL	UV-Vis, XRD, EDX, FT-IR, HR-TEM, SPR	2–100	64
15.	Polysaccharide of *Caulerpa racemose* (SD)	1 mM, 10 mL/90 mL, stirred 30 min at 50 °C	UV-Vis, SPR, DLS, FT-IR, SEM	88 ± 0.5	65
16.	Aqueous filtrate of *Cystophora moniliformis* (AL)	1 mM, 1 mL/10 mL	UV-Vis, SEM, EDX	50–100	66
17.	Aqueous filtrate of *Chlorella vulgaris* (AL)	1 mM, 10 mL/90 mL, stirred for 3 hours, centrifuged for 20 min	UV-Vis, FT-IR, XRD, SEM	40–90	67

#UV-Vis (UV-Vis spectroscopy), XRD (X-ray diffraction), FT-IR (Fourier-transform infrared spectroscopy), HR-TEM (high-resolution transmission electron microscopy), AFM (atomic force microscopy), SPR (surface plasmon resonance), FE-SEM (field emission scanning electron microscopy), EDX (energy dispersive X-ray), TEM (transmission electron microscopy), DLS (dynamic light scattering), TGA (thermo gravimetric analysis), SEM (scanning electron microscopy).

Serratia liquefaciens and *Aeromonas hydrophila*. Weak adherence and disintegration of marine biofilm formation were confirmed by confocal laser scanning microscopic (CLSM) images when the bacterial strains were treated with AgNPs. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were found to be (20–40 μg mL^{-1}) and (40–60 μg mL^{-1}), respectively. The synthesized colloidal AgNPs showed LC_{50} (lethal concentration) value 88.914 ± 5.04 μg mL^{-1} which was confirmed by Artemia cytotoxicity assay.[53] In 2016, Paramasivam *et al.* reported green synthesis of AgNPs using *Turbinaria ornate*. The size of the AgNPs was confirmed by SEM having a range of 20–32 nm and was used against the fourth instar larvae of three mosquitoes. The lethal concentration values (μg mL^{-1}): LC_{50} of 0.738, 1.134 and 1.494; and LC_{90} of 3.342, 17.982 and 22.475 were used for the three mosquitoes *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*, respectively. The study gave a key route to develop an eco-friendly, low-cost pesticide.[54] Aragão *et al.* synthesized AgNPs at pH 10 and 11 by stirring for 30 min and at temperature 90 °C using seaweed *Gracilaria birdiae.* The Fourier transform infrared (FT-IR) data was used to study the interaction between the NPs and functional biomolecules present in the polysaccharide. The size of the AgNPs synthesized had the range of 20.2–94.9 nm and no agglomeration was found after four months. The antimicrobial activity of the AgNPs was evaluated for MIC ranging from 5.15 μM to 137.5 μM and found to be active against *Escherichia coli*.[55]

Marine seaweed *Spyridia filamentosa* was used by Valarmathi *et al.* in 2019 to synthesize spherical shape AgNPs of size range 20–30 nm. The AgNPs showed anti-bacterial activity as 20 mM concentration of AgNPs inhibited 44.6% and 63.4% growth of *Staphylococcus* sp. and *Klebsiella* sp., respectively. They were also found to have anticancer activity against human breast cancer (MCF-7) cells as the viability of the cells decreased with an increase in the AgNP concentration (25, 50, 75 and 100 μg mL^{-1}) analyzed by MTT assay.[21] Furthermore, stable colloidal AgNPs were synthesized by Aboelfetoh *et al.* using green algae *Caulerpa serrulata*. During synthesis, many factors

Table 2 Flowers used for biological synthesis of AgNPs

S. no.	Reducing agent flower extract (FE)	Operating conditions	Characterization	Particle size (nm)	Author/ref.
1	Aqueous extract of *Plumeria alba*	$AgNO_3$ concentration – 1 mM, FE/$AgNO_3$: 10 mL/70 mL	UV-Vis, Zetasizer, FT-IR, TGA-DSC, XRD, SEM, EDX, DLS	5–100	68
2	Ethanolic extract of *Nyctanthe sarbor-tristis*	1 mM, 5% v/v into 500 μL stirred at 80 °C	UV-Vis, TEM, XRD, TGA, DTA, FT-IR	5–20	69
3	Aqueous extract of *marigold*	1 mM, 6 mL/44 mL, centrifuged at 10 000 rpm for 10 min	UV-Vis, FT-IR, XRD, TEM,	10–90	70
4	Aqueous extract of *Jatropha integerrima*	1 mM, different concentrations, centrifuged at 7000 rpm for 15 min	UV-Vis, FESEM, TEM, XRD, FT-IR	38.48–45.81	71
5	Aqueous extract of *Couroupita guianensis*	1 mM, 5 mL/50 mL	UV-Vis, FT-IR, XRD	—	72
6	Aqueous filtrate of *Caesalpinia pulcherrima*	1 mM, 12 mL/38 mL	UV-Vis, FT-IR, XRD, TEM	3.3–18.28	73
7	Aqueous filtrate of *Madhuca longifolia*	1 mM, 3 mL/30 mL, heated in water bath at 40 °C for 20 min, centrifuged at 11 000 rpm for 25 min	UV-Vis, XRD, FT-IR, TEM, FE-SEM	30–50	74
8	Aqueous filtrate of *Fritillaria*	0.01 M, 10 mL/100 mL, incubated 24 hours	UV-Vis, FT-IR, SEM, TEM, EDX	9.49–30.63	75
9	Aqueous filtrate of *Stachys lavandulifolia*	1 mM, 20 mL/20 mL, centrifuged at 4000 rpm for 20 min	UV-Vis, FT-IR, TEM, EDS, SEM	20–40	76
10	Aqueous filtrate of *Ferulago macrocarpa*	1 mM, FE and $AgNO_3$ ratio 1 : 1, 1 : 2, 1 : 4, 3 : 4 and 3 : 2, temperature 30 °C, 60 °C and 80 °C, at pH 4.5, 7, 9, and 11 respectively, centrifuged at 10 000 rpm for 20 min	UV-Vis, FT-IR, EDX, SEM, XRF	14–25	77
11	Aqueous filtrate of *Moringa oleifera*	1 mM, different concentrations of FE and $AgNO_3$, stirred for 30 min	UV-Vis, FT-IR, XRD, TEM	11–16	78
12	Aqueous filtrate of *Calendula Officinalis*	1 mM, 5 mL/95 mL, shaken for 48 hours	UV-Vis, FT-IR	2–20	79
13	Ethanol extract of *Lantana camara*	1 mM, 2 mL/18 mL	UV-Vis, DLS, XRD, TEM, SAED	16–40	80
14	Aqueous filtrate of *Cassia auriculata*	1 mM, 10 mL/40 mL	UV-Vis, XRD, FT-IR, HR-TEM	10–28	81
15	Aqueous extract of *Bauhinia purpurea*	1 mM, 4 mL/96 mL, centrifuged at 12 000 rpm for 15 min	UV-Vis, FT-IR, SEM, EDS, XRD, TEM	5–50	82
16	Aqueous filtrate of *Thunbergia grandiflora*	1 mM, 10 mL/90 mL, heated at 80 °C for 10 min	UV-Vis, XRD, FT-IR TEM, EDX, DLS	20–50	83
17	Aqueous filtrate of *Mangifera indica*	1 mM, 4 mL/96 mL, stirred for 30 min, centrifuged at 3000 rpm for 15 min	UV-Vis, XRD, FT-IR, SEM, TEM	10–20	84
18	Aqueous filtrate of *Felty germander*	1–45 mM, different concentrations of FE and $AgNO_3$	UV-Vis, XRD, FT-IR, DLS, FE-SEM, SEM, TEM	10–100	85
19	Aqueous filtrate of *Calotropis gigantea*	2 mM, 5 mM, and 9 mM, 10 mL/90 mL, stirred for 48 h	UV-Vis, XRD, FT-IR, SPR-EDS, TEM	87.85–227.65	86
20	Aqueous filtrate of *Clitoria ternatea*	3 mM, 20 mL/4 mL, at pH 10, heated at 50 °C, centrifuged at 15 000 rpm for 15 min	UV-Vis, TEM, zeta potential, FT-IR, XRD, EDX	10–30	87
21	Aqueous filtrate of *Aerva lanata*	—	UV-Vis, TEM, AFM, EDX	90	88
22	Aqueous filtrate of *Catharanthus roseus*	1 mL, 1 mL/9 mL, kept for 3 days	UV-Vis, SEM	1–30	89

#UV-Vis (UV-Vis spectroscopy), XRD (X-ray diffraction), FT-IR (Fourier-transform infrared spectroscopy), HR-TEM (high-resolution transmission electron microscopy), AFM (atomic force microscopy), SPR (surface plasmon resonance), FE-SEM (field emission scanning electron microscopy), EDX (energy dispersive X-ray), TEM (transmission electron microscopy), DLS (dynamic light scattering), TGA (thermo gravimetric analysis), DTA (differential thermal analysis), SAED (selected area electron diffraction), SEM (scanning electron microscopy).

were considered, like algae extract concentration, contact time, temperature and pH value. Higher temperature leads to the formation of spherical AgNPs having an average size of 10 ± 2 nm. The AgNPs were used to study the catalytic reduction activity of congo red dye from aqueous solutions. The higher temperature showed higher catalytic activity and the reaction was found to be pseudo first order with respect to the dye concentration.[56]

Further on, Arya *et al.* used green algae *Botryococcus braunii* to synthesize AgNPs and study their anti-bacterial property. The X-ray diffraction technique revealed that the shape of AgNPs was face centred cubic. It was found to be highly toxic against pathogenic bacterial strains such as *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* as well as a fungal strain *Fusarium oxysporum* at a concentration of 500 μg mL^{-1}.[57] The effect of AgNPs in human colon cancer cells was reported by Acharya *et al.* in 2020, who synthesized AgNPs using green algae *Cladophora glomerata* with a size range of 8–11 nm. The AgNPs displayed specific cytotoxicity to human colon cancer cells (HCT116) with IC_{50} value 142 ± 0.45 μM at 72 hours, whereas nil or minimal effect was observed in the control human colon epithelial cell line cells.

They have also demonstrated the role of AgNPs in inducing the p53-dependent apoptosis of human colon cancer cells.[58]

3.2. (ii) Various types of flower extract used for biological synthesis of AgNPs. Flower extracts are also used as a reducing agent for the green synthesis of AgNPs. *Plumeria alba* flowers were used by Mata *et al.* in 2014 for the synthesis of AgNPs that had a face-centred cubic structure. The synthesized AgNPs were used for the reduction of 4-nitrophenol to 4-aminophenol within 8 min and biological activities are evaluated by means of anti-oxidant, anti-bacterial and cytotoxic effect. Two different pathogenic bacterial strains are used for the anti-bacterial effect and a growth kinetic study in *Escherichia coli* confirmed their bacteriostatic effect. The cytotoxic effect of AgNPs in COLO 205 was seen by MTT assay and the IC_{50} concentration was found to be 5.5 and 4 μg mL^{-1} after 24 and 48 hours, respectively, on incubation.[68] A flower extract of *Nyctanthes arbour-tristis* was used by Gogoi *et al.* for AgNP synthesis and they were found to have anti-bacterial activity against the pathogenic strain of *E. coli* MTCC 443 with MIC value of 220.05 μg mL^{-1}. A mouse fibroblastic cell line (1929) was used for cytotoxicity analysis of the synthesized AgNPs and the results showed non-toxic nature clearing it for biocompatibility with 83% cell viability at a concentration of 250 μg mL^{-1} after 24 hours of treatment.[69] Padalia *et al.* synthesized AgNPs from marigold flower where TEM analysis revealed the particles as spherical, hexagonal and irregular having size range 10–90 nm. The antimicrobial activity of the AgNPs was analysed with different commercial antibiotics against Gram positive (*Staphylococcus aureus* and *Bacillus cereus*) and Gram negative (*Escherichia coli* and *Pseudomonas*) bacteria, and fungi (*Candida glabrata*, *Candida albicans* and *Cryptococcus neoformans*).[70]

A flower extract of *Jatropha integerrima* was used to synthesis AgNPs and anti-dengue activity was analysed by cytotoxicity assessment by Verma *et al*. in 2022. The synthesised AgNPs was tested against aquatic larval stages of *Aedes aegypti* which revealed maximum mortality with AgNPs in combination with leaf and flower extract of used plant.[71] Singh *et al*. synthesised AgNPs using aqueous extract of flower *Couroupita guianensis* Aubl and reported its free radical scavenging activity through a DPPH.[72] AgNPs synthesized by the flower extract of *Caesalpinia pulcherrima* gave 12 nm particle sizes as reported by Moteriya *et al.* They investigated the AgNPs for their antimicrobial activity against *Bacillus subtilis* and *Corallium rubrum* and the MIC value was found to be 10 mg mL^{-1}. AgNPs were also tested for anti-oxidant and cytotoxic effects and further genotoxic study cleared their non-toxic nature at lower concentration.[73]

Flowers of *Madhuca longifolia* were used by Patil *et al.* to synthesize AgNPs, which gave a size range of 30–50 nm. Analysis of the antimicrobial activity of the AgNPs against Gram-negative bacteria (*Escherichia coli*, *Salmonella typhimurium*) and Gram-positive bacteria (*Bacillus cereus*, *Staphylococcus saprophyticus*) was done by collecting pathogenic bacterial cultures from the Korean Culture of Microorganisms (KCCM).[74] The MIC value was found to be 60, 40, 90 and 80 μg mL^{-1} for *Bacillus cereus* ATCC13061, *Staphylococcus saprophyticus* KCTC3345, *Escherichia coli* KCTCI1682 and *Salmonella typhimurium* KCCM11862, respectively. *Fritillaria* flowers were used by Hemmati *et al.* to synthesize spherical shaped AgNPs and agar disk and agar well diffusion methods were used to determine the anti-bacterial properties of the AgNPs synthesized. Furthermore, the antimicrobial activity was analysed by a broth dilution assay. In this analysis, distilled water was used as a negative control whereas difloxacin, chloramphenicol, streptomycin, gentamicin, oxytetracycline, ampicillin and amikacin were used as positive controls. AgNPs at concentrations 1, 2, 4, and 8 mg mL^{-1} inhibited the growth of several bacteria including *Bacillus subtilis*, *Escherichia faecalis*, and *Pseudomonas aeruginosa*.[75] Cutaneous wound-healing along with other properties like cytotoxicity, anti-oxidant and anti-bacterial were shown by AgNPs synthesized by Zangeneh *et al.* using an aqueous filtrate of *Stachys lavandulifolia* flowers in 2019. In anti-oxidant activity tests, the DPPH (1,1-diphenyl-2-picrylhydrazyl) free radical scavenging of effect of *Stachys lavandulifolia* and AgNPs indicated impressive prevention compared to that of butylated hydroxytoluene. For anti-bacterial analysis, several bacterial species were taken like *Proteus mirabilis*, *Streptococcus pneumonia*, *Salmonella pneumonia*, *Shigella flexneri*, *Listeria monocytogenes*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *etc.*, from the Iranian Research Organisation for Science and Technology, which gave excellent results. The widest zone of inhibition was seen at 64 mg mL^{-1} through the disc diffusion method on an agar plate.[76]

A *Ferulago macrocarpa* flower extract was used by Azarbani *et al.* for green synthesis of AgNPs, and they analysed their anti-oxidant and anti-bacterial properties. The anti-oxidant activity was analysed by DPPH radical scavenging activity, and anti-bacterial activity was assayed against *Escherichia coli*, *Bacillus cereus*, *Klebsiella pneumonia* and *Staphylococcus aureus* by the disc diffusion method. The broth micro dilution method was used to evaluate MIC and it was found to be 62.5, 62.5, 250 and 250 μg mL^{-1} against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* and *Klebsiella pneumonia*, respectively.[77] Another group, Bindhu *et al.*, studied the effect of AgNPs synthesized from flower extracts of *Moringa oleifera* against infection caused by *Salmonella*, *Rhizopus* and *Escherichia coli* bacteria.[78]

4. Mechanism of $AgNO_3$ reduction

A plant extract has many molecules, like polyphenols, terpene derivatives, saccharides, alkaloids, *etc.*, which cause the reduction of $AgNO_3$ into Ag. The possible mechanism of such chemical reactions is shown in Fig. 4. Generally, these organic molecules' functional groups (–OH, –COOH groups) interact with $AgNO_3$. Since $AgNO_3$ is a salt, it breaks up to give two ions, first Ag^+ and second NO_3^- ions when dissolved into water. Since OH and COOH groups of phytoconstituents are acidic in nature, they furnish H^+ and acquire a negative charge. The negative functional groups, such as O^- in phenols and COO^- in acids present in plant extracts form electrostatic linkage with Ag^+. During the formation of such types of linkage, Ag^+ ions get

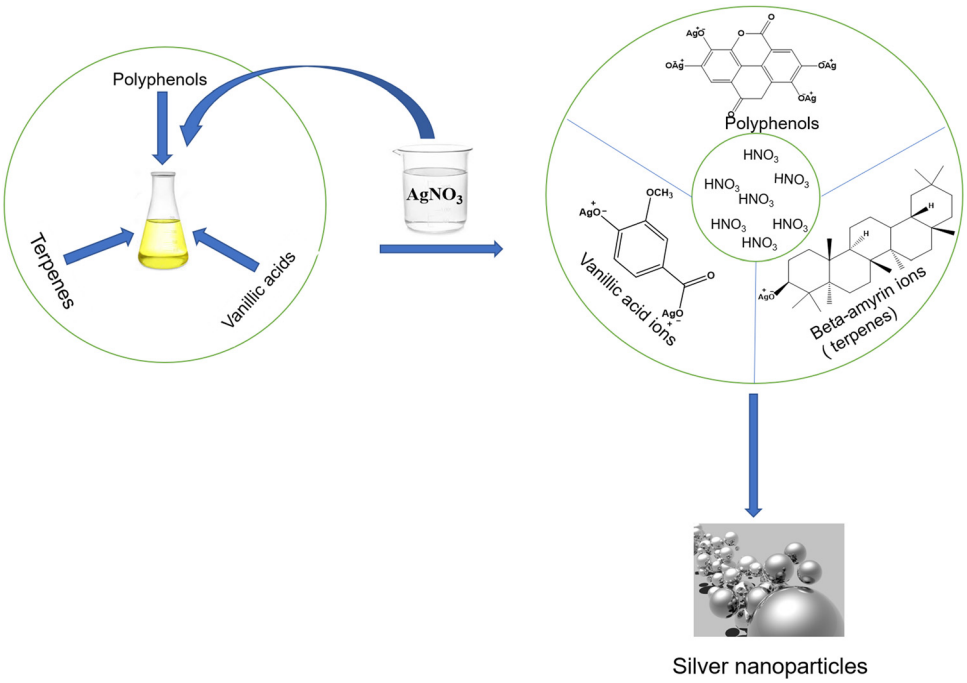

Fig. 4 Mechanism of $AgNO_3$ reduction into AgNPs.

reduced. The second ion, NO_3^-, accepts H^+ from OH of phenol or from COOH of acids of phytoconstituents to form HNO_3. Since HNO_3 is water soluble, this remains in the aqueous phase, whereas Ag survives in a free metallic state (Ag^0) to form AgNPs.

5. Biological applications

People have employed silver and its compounds for thousands of years as anti-bacterial and medicinal agents. Hippocrates utilized silver remedies to treat ulcers and speed up the healing of wounds. For the treatment of burns and wound infections, silver preparations were used at the start of the 19th century. Since the 1940s, when antibiotics were first developed, they have been abused, leading to bacterial resistance that has become a global issue, especially since the 1980s. With the advent of nanotechnology at the beginning of this century, silver has gained attention once more.[90] Due to their distinctive physicochemical features, AgNPs have been one of the most appealing nanomaterials in biomedicine. AgNPs are well known for their powerful, broad-spectrum anti-bacterial, anti-cancer and other properties as shown in Fig. 5. AgNPs have also been studied for their potential biological effects against diabetes, bone healing, and wound healing.[91] In addition, they could improve vaccination immunogenicity.[92]

According to studies, AgNPs are effective against a wide range of pathogens, including bacteria, fungi, and viruses. Additionally, nematodes and worms can be successfully killed by AgNPs. Numerous researchers have tested hypotheses, albeit the precise processes behind AgNPs' anti-bacterial and anti-cancer effects are still unknown.[93] By causing membrane

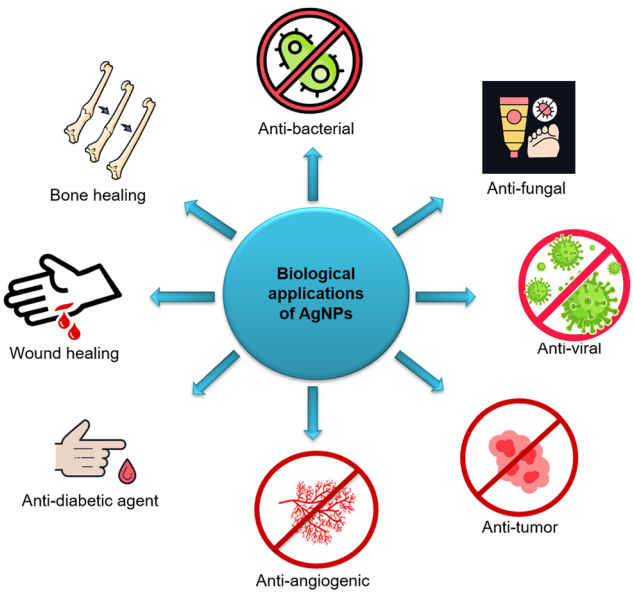

Fig. 5 Various biological applications of AgNPs.

deterioration, reactive oxygen species (ROS) production, DNA damage, enzyme inactivation, and protein denaturation, AgNPs can either slow or stop the development of bacteria.[94]

5.1. Anti-bacterial activity

Resistance of bacteria from the genera *Streptococcus*, *Salmonella*, *Escherichia*, *Pseudomonas*, *etc.*, to numerous common antibiotics is a severe medical issue that requires immediate attention. AgNPs have been discovered to be a promising field

in the fight against diseases in searching for novel bio medicines. The vast majority of studies concur that the potential of AgNPs can prevent growth and cause the death of harmful bacteria that cause many forms of common human diseases. Due to their high surface-to-volume ratios and crystallographic surface structure, AgNPs are promising anti-bacterial agents. The ground-breaking study published by Sondi and co-workers illustrated the anti-bacterial action of AgNPs against *Escherichia coli*. AgNPs accumulated in the bacterial cell wall and formed ''pits'' in the treated *Escherichia coli* cells.[95] Plant extracts are now an endless source of AgNP manufacturing. Plants are the main focus of research in this field since they frequently possess unique medicinal capabilities and generate AgNPs in a particular fashion. Despite most often using plant extracts to synthesize AgNPs, bacteria themselves also function as ''biofactories'' for creating AgNPs. *Brevibacterium casei*,[96] *Streptomyces albogriseolus*,[97] *Salmonella typhimurium*,[98] *Acinetobacter calcoaceticus*,[99] *Sporosarcina koreensis*,[100] and *Aeromonas* sp.[101] are among the bacteria that serve as a bacterial ''plant'' for AgNPs with an inhibitory effect against pathogenic pathogens. In experimental medicine, AgNPs are used in conjunction with various antibiotics as anti-bacterial agents. However, not all antibiotics have this synergistic effect.[102]

5.2. Anti-fungal activity

Immunosuppressed patients are more likely to contract fungi, and treating fungi-mediated illnesses can be difficult due to the scarcity of anti-fungal medications on the market right now.[103] Hence, there is an unavoidable and urgent need to produce anti-fungal medicines that are biocompatible, non-toxic, and environmentally friendly. AgNPs currently serve a significant role as anti-fungal agents against many diseases caused by fungi. The anti-fungal properties of AgNPs and their mode of action were examined in the work carried out by Kim and colleagues. They elucidated the anti-fungal mode of action of the AgNPs by assessing the change in membrane dynamics of *Candida albicans* using 1,6-diphenyl-1,3,5-hexatriene (DPH) as a probe and employing techniques such as flow cytometry analysis, and transmission electron microscopy and a glucose-release test. The findings imply that AgNPs may operate as an anti-fungal agent by altering the composition of the cell membrane and preventing proper budding because the integrity of the membrane is compromised.[104]

5.3. Anti-viral activity

Diseases caused by viruses have become the most difficult and challenging task to overcome. Despite their structural simplicity, viruses pose a significant threat in the form of deadly diseases like human immunodeficiency virus (HIV), Ebola, the Spanish flu, and finally the COVID-19 virus that caused the pandemic in 2020 resulting in the death of millions of people all over the world. This demonstrates how little we understand about combating viruses. Although AgNPs have been shown to be effective against viruses, the precise mechanism by which they do this is still unknown.[105] While establishing infection, viral surface components interact with ligands and proteins on the cell membrane, allowing the virus to attach itself to host cells and enter into it. The greatest approach in formulating new anti-viral agents is to disrupt the interaction between the virus and cell membrane, preventing the virus from adhering and entering the cells. Data available based on previous research suggests that the possible mechanisms of anti-viral activity of AgNPs could be due to (i) binding of AgNPs to the outer coat of the virus resulting in the inhibition of viral attachment on the cell surface receptors or (ii) binding of AgNPs to the viral DNA or RNA and suppressing its replication inside the host cell.[106] Speshock *et al.* evaluated the interaction of AgNPs with Tacaribe virus and found a significant reduction in the viral RNA production due to inhibition of the replication process.[107] Furthermore, Xiang *et al.* investigated the interaction of AgNPs with H1N1 influenza A virus and demonstrated the anti-H1N1 influenza A virus activity of AgNPs.[108] Galdiero *et al.* showed that herpes simplex virus types 1 and 2 and type 3 of the human parainfluenza virus interact with AgNPs in a size-dependent manner. They demonstrated that it is possible to produce AgNPs from several fungi, and that the manufacturing method affects the anti-viral activity of these particles.[109]

5.4. Anti-tumor activity

Cancer is a life threatening disease and leads to many deaths worldwide. The World Health Organization (WHO) projects that there will be 22 million new cases of cancer by 2032, up from 14 million in 2012.[110] Consequently, for many years, researchers have been working to develop new anticancer medications and successful clinical techniques for the treatment of cancer. AgNPs are widely used as possible cancer diagnostic and therapeutic agents. In a work carried out by Gopinath and his team, the molecular mechanism of AgNP-mediated cytotoxicity was investigated and it was revealed that the programmed cell death in both cancer and non-cancer cells depends on the concentration of AgNPs. They also studied the synergistic effect of AgNPs on the uracil phosphoribosyl transferase expression system and found that the cells treated with 5-fluorouracil became more sensitised.[111] AgNPs could also inhibit the growth of acute myeloid leukemia (AML) cells. Guo *et al.* investigated the cytotoxic effect of AgNPs on AML cells and found that DNA damage, ROS production, and loss of mitochondrial membrane potential (MMP) results in the apoptosis of AML cells.[112] Al-Sheddi *et al.* used the *Nepeta deflersiana* plant to reduce silver ions in a single step, demonstrating for the first time the biosynthesis of AgNPs and their anticancer potential against human cervical carcinoma (HeLa) cells. Their findings demonstrated that HeLA cells were cytotoxically affected by biosynthesized AgNPs (NDAgNPs) in a concentration-dependent manner.[113]

5.5. Anti-angiogenic activity

Angiogenesis is a complicated process that involves several gene products expressed by various cell types, all of which contribute to a coordinated series of events. However, an imbalance of the growth factors involved in this process leads to the acceleration of several diseases, such as inflammatory,

neoplastic, and ophthalmic conditions. A possible approach to slow the spread of these disorders is to inhibit angiogenesis by interfering with its mechanism.[114] AgNPs are involved in angiogenesis, but the mechanism is still unknown. Various studies have shown the anti-angiogenic and anticancer characteristics of AgNPs employing both *in vitro* and *in vivo* models.

Kemp *et al.* developed AgNPs reduced with diaminopyridinyl (DAP)-derivatized heparin (HP) polysaccharides that effectively inhibited angiogenesis. The synthesized AgNPs had a higher anti-angiogenesis efficacy when conjugated with DAPHP.[115] It is known that nitric oxide synthase (NOS) upregulation encourages the production of several angiogenic factors, including vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF2). In rat models, suppression of inducible nitric oxide synthase (iNOS) was reported to stop angiogenesis.[116] Kitimu *et al.* showed that biogenic AgNPs made from neem plant (*Azadirachta indica*) blocked the VEGF-NO and VEGF/VEGF-R pathways and further obstructed cell migration and metastasis, hence reducing angiogenesis.[117]

5.6. Anti-diabetic activity

Nearly 422 million people worldwide have diabetes; the majority of them reside in low and middle-income countries. Diabetes also causes 1.6 million fatalities globally each year.[118] In recent years, diabetes diagnosis and treatment have benefited greatly from nanotechnology. There is a long history of using medicinal plants to treat various diseases. Plant extracts have been utilised in the development of AgNPs and drawn great attention over the past decade as they are eco-friendly and cost effective. Certain bioactive compounds such as flavonoids, antioxidants, and phenolic chemicals, are abundant in medicinal plants and are recognised as a crucial source in the development of medications against Type II diabetes mellitus.[119] Bagyalakshmi and Haritha synthesized AgNPs using *Pterocarpus marsupium* bark and wood extract and found them to be effective for *in vitro* anti-diabetic activity.[120] The metabolism of carbohydrate involves two main enzymes, α-amylase and α-glucosidase that are responsible for the breakdown of carbohydrates into monosaccharides resulting in elevated blood sugar levels. Thus, inhibition of these enzymes is one of the most important strategies for diabetes therapy.[16] Perumalsamy and Krishnad have synthesized AgNPs and tested their anti-diabetic abilities using a hydroethanolic extract of *Myristica fragrans* seeds (MFHE). The α-amylase and α-glucosidase enzymes were significantly inhibited by MFHENP. Additionally, MFHENP delayed the transport of glucose across the membrane, which was measured by glucose diffusion and glucose uptake assays.[121]

5.7. Wound repair

The body's largest organ and primary barrier against viruses, poisons, and injuries is the skin.[122] A wound is formed when the skin's structural integrity is compromised; a disease, an unintentional injury, or a deliberate act may cause this disruption.[123] The hemostasis/inflammatory phase, proliferative phase, and remodelling phase are three overlapping phases of the wound healing process that focus on restoring tissue integrity and functionality. The care of chronic wounds must include the control of infections.[124] Even though wounds and skin flora naturally include bacteria, these bacteria have been

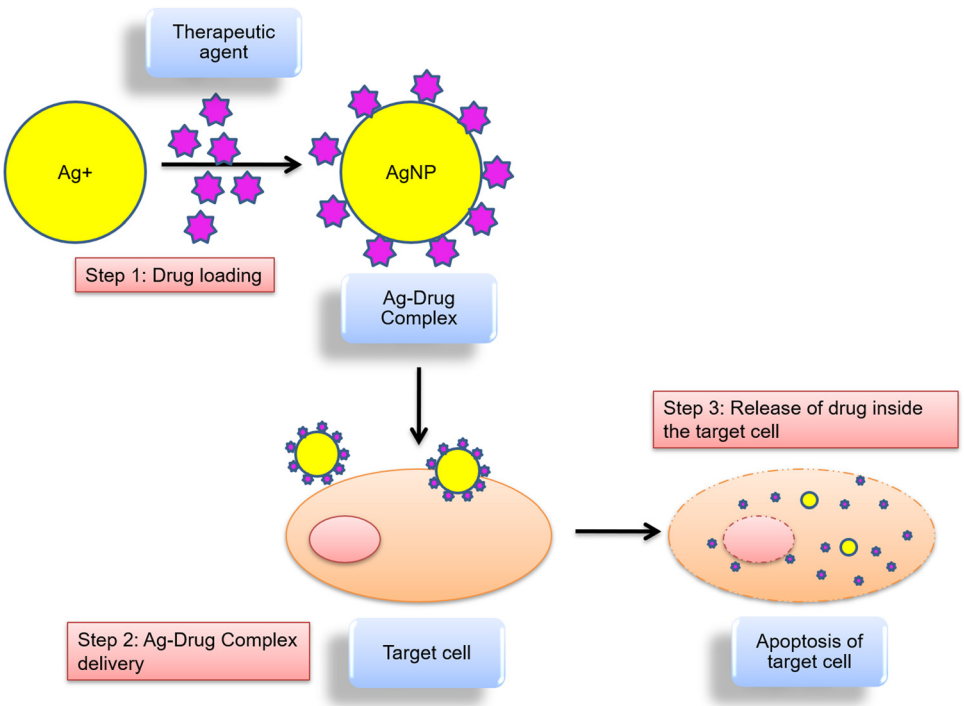

Fig. 6 Systemic drug delivery in the target cell.

proposed as the crucial threshold between colonisation and clinically meaningful illness. In skin that is already injured, bacteria can inflame the tissues beneath it, releasing proteases and ROS from inflammatory cells. Increased bacterial endotoxins raise pro-inflammatory cytokine levels, which slows down and delays collagen deposition in wounds and growth factor production. Therefore, many absorbent dressings are impregnated with silver ions or particles, the most popular substance to obtain antimicrobial effects and to reduce bacteria and the risk of infection.[125] Mariam *et al.* investigated the combined effect of mint and AgNP hydrogel films as wound-healing agents in diabetic rats. They discovered that it significantly increased the rate at which the wounds healed.[126]

5.8. Bone healing

Bone is a living tissue with the capacity for regeneration and restoration. Infectious diseases, genetic disorders, degenerative diseases, malignancies, and fractures are a few of the varied and complex pathologies impacting millions of individuals each year.[127] Bacterial infection in bone defects typically compromises the bone's capacity to heal. However, significant defects typically caused by severe trauma, tumour removal, or genetic abnormality are frequently replaced or restored with the help of bone grafts.[128] AgNPs have intrinsic anti-bacterial action with a larger spectrum than standard antibiotics. AgNPs can suppress or impede the development of mature biofilms or mature biofilms in the case of antibiotic-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus*.[129] For artificial bone scaffolds, AgNPs can be utilised as doping agents. Strong anti-bacterial activity against both Gram-positive and Gram-negative bacterial strains is demonstrated by AgNP-implanted crystalline hydroxyapatite (HA) or titanium scaffolds.[130] A study conducted by Zhang *et al.* revealed that AgNPs could enhance osteogenesis and mesenchymal stem cell (MSC) proliferation to speed up the healing of bone fractures.[131]

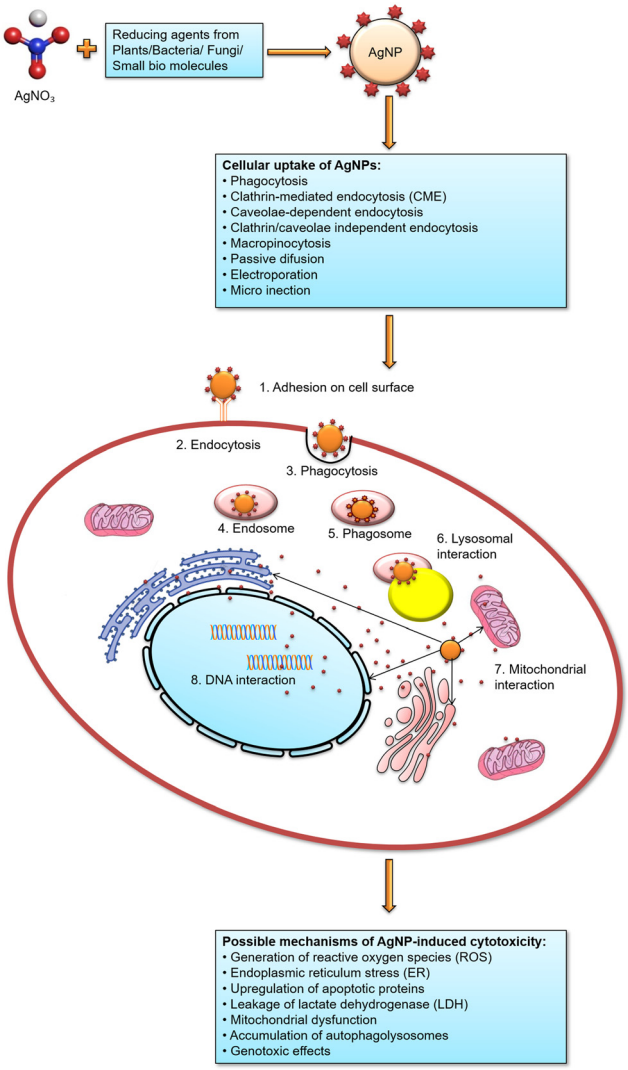

Fig. 7 Cellular uptake of AgNPs and hypothesized mechanism of AgNP-induced cytotoxic effects resulting in apoptosis of the target cell.

6. Drug delivery *via* AgNPs

The majority of medicinal drugs have poor solubility, quick blood clearance, poor targeting, and frequently inadequate ability to cross cell membranes. However, drug delivery systems (DDSs) are able to get around some of these obstacles and improve drug delivery to the intended target, like inside cancer cells, as shown in Fig. 6.

The delivery of NPs can be done either through an active or passive process. In passive delivery systems, NPs are transported across the leaky tumor capillary to tumor cells and the interstitium through passive diffusion. Whereas an active delivery system is based on molecular recognition, that delivers the NPs to a specific site. The cellular uptake of drugs can be aided by receptor-mediated endocytosis.[132] For example, coupling of NPs to a ligand, such as peptides, lectins or monoclonal antibodies, allows it to interact with its receptor at the target cell site and increases the rate of cellular internalization.[133] Our understanding of the mechanism of action of NPs and their underlying interactions with medicines, biomembranes, and other biological molecules has improved as a result of complementary experimental and computational studies.

Based on numerous published literatures, AgNPs are a suitable and promising drug to stop the development of cancer cells using several mechanistic methods. Fig. 7 displays the possible mechanisms of uptake and cytotoxic effects of AgNPs.

7. Toxicity

AgNPs have several benefits that make them ideal for biomedical applications, although it has some harmful effects, as mentioned in Fig. 8. AgNPs are generally advertised as extremely efficient anti-bacterial agents with minimal adverse side effects on healthy mammalian cells. However, several *in vitro* investigations in rat hepatocytes, neuronal cells, murine stem

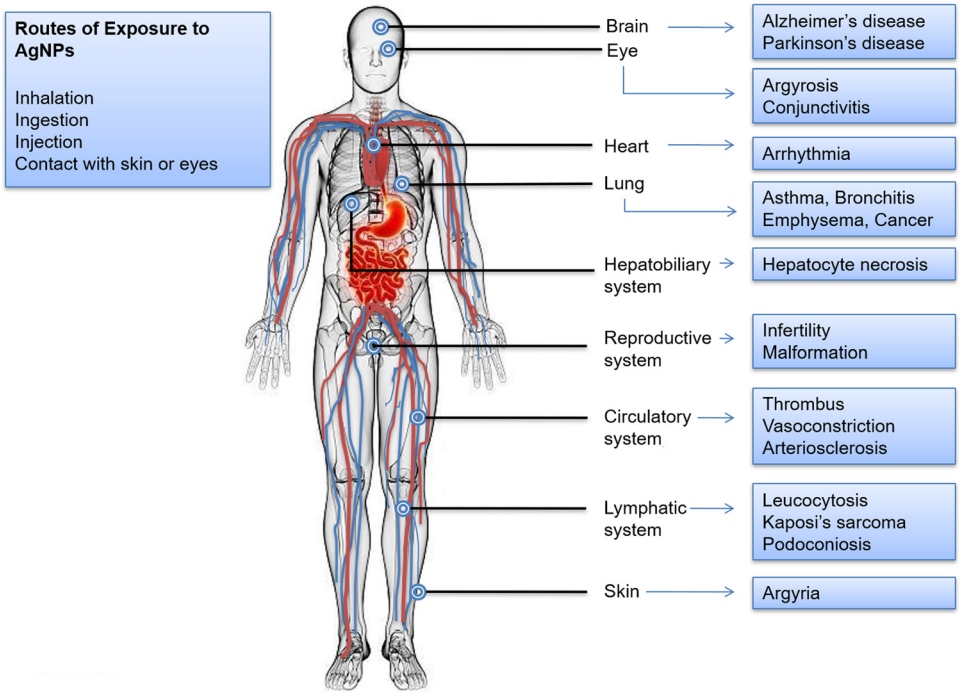

Fig. 8 An illustration of AgNPs' possible toxicities in the human body. AgNPs can be exposed through skin contact, intravenous injection, oral ingestion, and pulmonary inhalation. Eye, brain, skin, nerves, respiratory, immunological, hepatobiliary, and reproductive systems are among the organs that are impacted. AgNP-induced illnesses or pathological alterations are listed.

cells, and human lung epithelial cells showed AgNP-related harmful effects. Roda *et al.* assessed the effect of AgNPs in rat liver and lungs. Intratracheal instillation of AgNPs (50 μg per rat) resulted in lung parenchyma injury and diffuse hepatocyte injury accompanied by inflammation.[134] Xu *et al.* examined the toxic effects of AgNPs (20 nm) on rat cortical cells. They reported inhibition of neurite outgrowth and reduced cell viability of glial and neuron cells at a concentration of 50 μg mL^{-1}.[135] In an interesting work done by Foldbjerg and colleagues, the toxic effects of AgNPs on human lung epithelial cell line A549 were investigated through gene expression profiling. They observed alteration in the regulation of more than 1000 genes following the exposure of cell lines to 12.1 μg mL^{-1} of AgNPs.[136] The effect of AgNPs on the proliferation and self-renewal ability of mouse embryonic stem cells (mESCs) has also been evaluated. It was reported that at a 50 μg mL^{-1} concentration, AgNPs could induce cell cycle arrest at G1 and S phase in mESCs.[137] Pinzaru *et al.* investigated the *in vitro* toxicological profile of AgNPs on human keratinocytes – HaCat cells at different concentrations. They found no effect on the number of viable cells at lower concentrations, *i.e.* 0.1, 0.3, 1 and 3 μM; however, at a concentration of 10 and 50 μM, significant cytotoxic effects were observed.[138]

Humans consume between 0.4 to 30 g of silver daily from natural sources in food and drink.[139] Studies on AgNPs harmful effect on biological systems, including bacteria, viruses, and human cells, are currently accessible, although they produce conflicting and inconsistent findings.[140] The blood–brain and blood–testis barriers, for example, are easily crossed by the small-sized AgNPs, which may then cause potential cytotoxicity once within the body. AgNPs may also be delivered to several organs through blood circulation in addition to the directly exposed tissues. The absorbed AgNPs are dispersed throughout many systems, including the dermis, respiratory, spleen, digestive, urinary, nervous, immune, and reproductive systems. The primary distribution sites are the spleen, liver, kidneys, and lungs, with little AgNP deposition seen in the teeth and bones. In a study conducted by Huo *et al.*, endoplasmic reticulum (ER) stress was employed as a sensitive and early biomarker to assess AgNPs potential for toxicity in three different human cell lines, both *in vitro* and *in vivo* in mice. According to mouse investigations, different tissues responded differently to intratracheal instillation exposure to AgNPs. Only the lungs and kidneys revealed evidence of apoptosis by the terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay, but the liver and kidneys both significantly showed significant ER stress responses.[141] According to the toxicity experiments carried out in a rat ear model, AgNP exposure caused severe mitochondrial dysfunction and, depending on the inoculation dose, either temporary or permanent hearing loss. In addition, AgNPs were absorbed by retinal cells at even lower concentrations, and the increased number of cells that experienced oxidative stress led to significant structural damage.[142]

Numerous studies demonstrated that exposure to AgNPs can cause a reduction in cell viability *via* various biological pathways. The activation of the apoptosis mechanism and the expression of genes associated with apoptosis are examples of one of these mechanisms. Additionally, it has been

demonstrated that AgNPs can alter the permeability of the mitochondrial membrane, produce ROS and accumulate inside cells, and damage DNA.[143,144] AgNPs can potentially cause severe oxidative damage to cellular membranes and organelles such as the nucleus, mitochondria, and lysosomes, directly causing necrotic or apoptotic events[145] as shown in Fig. 7. AgNP-induced oxidative stress can trigger inflammatory reactions, such as the activation of innate immunity and an increase in endothelial cell permeability.[146]

8. Conclusion and future outlook

In all facets of human existence, recent developments in nanoscience and nanotechnology have fundamentally altered how we identify, treat, and prevent different diseases. The unique qualities of AgNPs, their size and shape-dependent biomedical applications, have made them one of the most analysed nanostructures created from nanotechnology during the past several years. Various applications of green synthesized AgNPs and their improved antimicrobial properties have attracted a lot of attention of researchers worldwide. The plant extract has been proven to be highly efficient among various kinds of natural extract from biocomponents like plants, yeast, fungi, *etc.*, used for synthesizing AgNPs. This method has decreased the use of hazardous chemicals to synthesize the AgNPs. The applications of AgNPs are broader than those of other NPs as they have displayed immense and dynamic roles in the medical field, demonstrating anti-fungal, anti-bacterial, anti-diabetic, anti-cancer effects, *etc.* Excellent biological activity with low toxicity to healthy cells and significant toxicity to cancer cells has been achieved by plant-based AgNPs.

Additionally, targeted drug delivery systems using AgNPs are a possible alternative for cancer treatment in the future. Their physicochemical characteristics have been studied for developing biosensors, particularly for biomedical applications that will aid in diagnosing several ailments. In conclusion, future research and development of the potential green synthesis of nanoparticles should focus on scaling up laboratory-based work to an industrial scale while taking into account current challenges, particularly the consequences on human health and the environment.

Author contributions

VS and RRP performed the literature survey and writing of the manuscript. The compilation of the manuscript was carried out by VS, RRP and SKS. MS designed and conceptualized the work. SKS and MS did the final editing of the manuscript.

Abbreviations

NPs	Nanoparticles
AgNPs	Silver nanoparticles
$AgNO_3$	Silver nitrate
AL	Algae
SD	Seaweed
FE	Flower extract

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare that they have no conflicts of interest.

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