



Bio-inspired silver nanoparticles from *Artocarpus lakoocha* fruit extract and evaluation of their antibacterial activity and anticancer activity on human prostate cancer cell line

Meghashyama Prabhakara Bhat¹ · Raju Suresh Kumar² · Muthuraj Rudrappa¹ · Dhanyakumara Shivapoojar Basavarajappa¹ · Pallavi Sathyanarayana Swamy¹ · Abdulrahman I. Almansour² · Karthikeyan Perumal³ · Sreenivasa Nayaka¹

Received: 16 November 2021 / Accepted: 16 January 2022 / Published online: 11 February 2022
© King Abdulaziz City for Science and Technology 2022

Abstract

The growing multi-drug resistance in human disease causing pathogens is an issue of great concern, and there is a need for broad-spectrum antibiotic to fight severe diseases. As silver is toxic to microbes like fungi, bacteria and yeast, the use of silver nanoparticles as antimicrobial agent may help control the resistant pathogenic microbes. During this study, the bio-fabrication of silver nanoparticles was done from *Artocarpus lakoocha* fruit extract and characterized using various morphological and structural analysis. The agar well diffusion technique was performed to determine the bactericidal potential of nanoparticles against human disease causing pathogenic bacteria; finally, the anticancer activity was assessed by employing 96-well plate MTT assay and flow cytometry-assisted apoptosis on human prostate adenocarcinoma (PC-3) cells. The primary indication on nanoparticles synthesis was given by colour change from slight yellow to brown; further, reaffirmed by the peak obtained at 415 nm for absorption maximum in UV–vis. analysis. Meanwhile, the smooth surface and spherical shapes were determined by AFM and SEM analyses. Similarly, poly-dispersed distribution, size range of 6.59–25 nm and FCC crystalline nature were confirmed by TEM and XRD analyses. The silver nanoparticles displayed higher antibacterial activity by forming clear zones of inhibition and exhibited increased anticancer activity on PC-3 cells. The IC_{50} value obtained was 30.62 $\mu\text{g/ml}$ and 48.11 \pm 0.7%, 24.92 \pm 0.5%, and 1.19 \pm 0.4% of early, late apoptosis and necrosis was observed in flow cytometry-assisted Annexin V/PI study. The results obtained encourage the idea of using green AgNPs to cure microbial and cancer-related diseases in near future.

Keywords Silver nanoparticles · Green synthesis · Antibacterial activity · PC-3 cell line · Anticancer activity · Flow cytometry

Introduction

In recent years, nanoscience has emerged as an important multidisciplinary section that deals with research and advancement in material sciences. Nanotechnology deals with the production and utilization of nanomaterial from 1 to 100 nm size range (Akintelu et al. 2020). In present day, nanotechnology is an important tool for manufacturing various kinds of biologically active pharmaceuticals and materials in the nano-range using metallic or alloy-based nanoparticles that have novel optical, chemical, and physical traits (Ijaz et al. 2021; Kumar et al. 2018).

Metallic nanoparticles can be produced by several approaches comprising physical, chemical and biological systems, but the biological or ‘green chemistry’ oriented

✉ Raju Suresh Kumar
sraju@ksu.edu.sa

✉ Sreenivasa Nayaka
sreenivasanayaka06@gmail.com

¹ P.G. Department of Studies in Botany, Karnatak University, Dharwad, Karnataka 580001, India

² Department of Chemistry, College of Science, King Saud University, Riyadh 11451, Saudi Arabia

³ Department of Chemistry and Biochemistry, The Ohio State University, 151 W. Woodruff Ave, Columbus, OH 43210, USA

synthesis technique is the most fascinating synthesis process. The biological synthesis methods have unique features and advantages as compared to other conventional synthesis methods which involve various parameters, such as high pressure, inert gases, high temperature, laser radiation and toxic by-products that cause harmful effects to environment and human health (Garg et al. 2020; Chung et al. 2016).

Silver (Ag) is the basic element and used as an effective antimicrobial agent from early medical practice by humans in contrast to other metals and their large surface area to volume ratio that furnishes greater contact with target microorganisms. Silver nanoparticles (AgNPs) are the metallic nanoparticles with unique and distinctive properties, including high conductivity, high stability and flexibility that makes them the most desired one's to be used in divergent fields, such as optics, telecommunications, electronics, textiles, pharmaceuticals, biosensors, waste water treatment, agriculture and food processing and other industries (Garg et al. 2020; Velidandi et al. 2020). Apart from these, AgNPs are extensively used as antifungals, antivirals, anti-inflammatory, antioxidant, anti-angiogenesis, anti-platelet and anticancer agents in the field of medicine and biomedical sciences (Tadele et al. 2021; Thirumal, 2021).

Biogenic synthesis of AgNPs can be accomplished by utilizing various life forms such as bacteria (Javaid et al. 2018; Singh et al. 2015), fungi (Khan et al. 2018; Zhao et al. 2017), actinomycetes (Kumari et al. 2020a, b; Manivasagan et al. 2014), algae (Al-Nadhari et al. 2021; Sharma et al. 2016), and plants (Tarannum and Gautam 2019; Rajeshkumar and Bharath 2017), which contain enough metabolites to effectively reduce and stabilize AgNPs. However, plants contain numerous bioactive secondary metabolites like alkaloids, flavonoids, terpenoids, carbohydrates, proteins, glycosides and saponins that naturally reduce AgNPs during the synthesis (Ahmed et al. 2016). The plant-mediated metallic nanoparticles synthesis is more advantageous as the characters of nanoparticles are majorly regulated by the physical conditions, adsorption process of stabilizing agent, and the rate at which metal ions interact with reducing agents (Ahmad et al. 2019; Restrepo and Villa 2021).

The need for a broad-spectrum antibiotic is increasing at an immense pace as many of the human pathogenic bacteria are acquiring multi-drug resistance. The age old knowledge of silver or silver-coated antimicrobials can come in handy for the preparation of such clinical antibiotic to fight severe diseases (Ahmad et al. 2019). As silver is toxic to bacteria, fungi and yeast, the use of AgNPs as an antimicrobial agent may help control the resistant pathogenic microbes. Cancer is considered as a deadly disease taking countless lives every year with the prostate cancer being the third most dangerous, contributing to 1,414,259 (7.3%) of incidence and 375,304 (3.8%) of mortality worldwide in 2020 (Sung et al. 2021). There is an immediate need to cure cancer in a lesser painful

and adverse manner; AgNPs are the promising alternatives to replace chemotherapy to achieve that need.

Artocarpus lakoocha belongs to *Moraceae* family and the fruits have been proven to be used for antibacterial, antifungal, antiviral, antitubercular, antiplatelet, antiarthritic and other medicinal purposes. Therefore, the current research was focused on the biological synthesis, characterization and potential antibacterial and anticancer activity of *Artocarpus lakoocha* fruit extract-mediated AgNPs.

Materials and methods

Collection of materials

Artocarpus lakoocha Roxb. (*A. lakoocha*) fruit was collected from local market near Dharwad, Karnataka, India and validated by referring literature and herbarium collection at Plants and Animals museum, Karnatak University Dharwad (Fig. 1A). Silver nitrate was acquired from Sigma-Aldrich laboratories and microbial pathogens were obtained from National Collection for Industrial Microorganisms (NCIM), Pune, India.

Preparation of fruit extract

The collected fruits were washed thoroughly to remove adhered unwanted materials and cut into smaller pieces. The dried pieces were ground into a powder (Fig. 1B) and 10 g of dried *A. lakoocha* fruit powder loaded into the thimble placed inside the soxhlet extractor; methanol was added to the round bottom flask. Once the process was finished methanol was evaporated using rotary evaporator leaving extracted plant material in the round bottom flask and that was stored in separate vial.

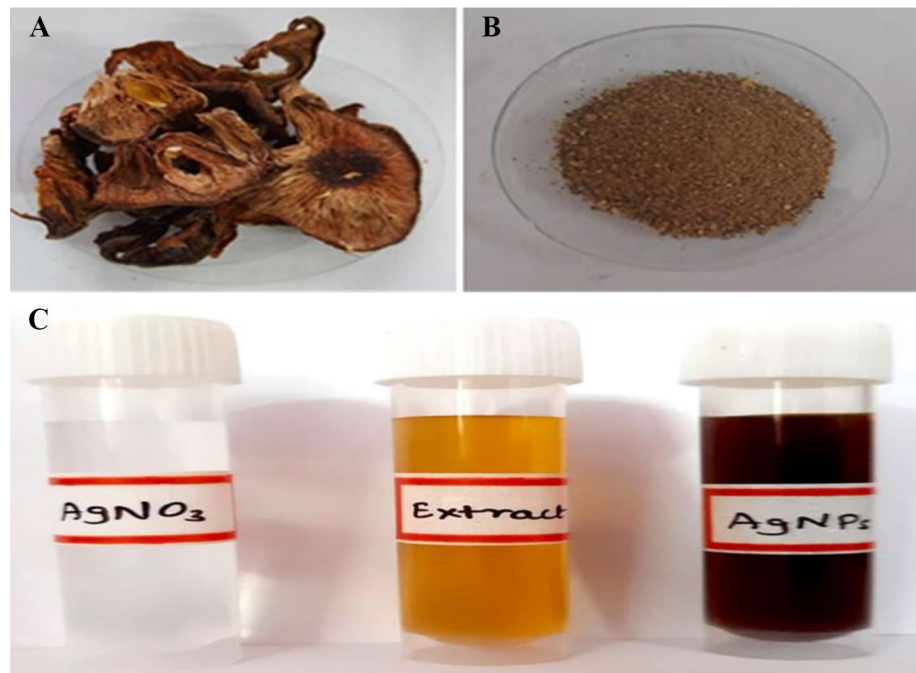
Synthesis of AgNPs

About 1.0 mM AgNO₃ solution was prepared by solvating 0.0169 g of AgNO₃ in 100 ml of distilled water. 25 ml of *A. lakoocha* fruit methanol extract was mixed with 75 ml of AgNO₃ solution in the ratio of 1:3, and the pH was adjusted to 9.0. Thus prepared solution was incubated for 24 h in dark and then subjected to centrifugation for 10 min at 10,000 rpm. The residue was air dried and the AgNPs were collected and stored in Eppendorff tubes to carry out further analysis.

Characterization of AgNPs

The spectrophotometric study of biosynthesized AgNPs was analysed in the wavelength range of 200–700 nm by using double beam UV–visible spectrophotometer (UV-9600A,

Fig. 1 Visual observations; **A** *A. lakoocha* fruit, **B** dried fruit powder, **C** colour change from light yellow to dark brown after AgNO_3 addition



Metash Instruments Co. Ltd., Shanghai, China). The functional groups/biomolecules accountable for the bio reduction and capping of AgNPs was studied from FTIR analysis (Nicolet 6700, Thermo Fisher Scientific, Waltham, Massachusetts, USA) by scanning the KBr mixed sample pellet from 400 to 4000 cm^{-1} . A thin film of dried AgNPs powder was prepared on a clean glass slide and scanned with atomic force microscope (Nanosurf Flex-AFM, Liestal, Switzerland) to ascertain the surface topology and distribution of the AgNPs. The morphological details and the elemental compositions of the AgNPs were investigated by subjecting the sample to SEM with EDS analysis (JEOL JSM-IT 500LA, USA). The atomic arrangements at interfaces and the crystalline structure of synthesized AgNPs were determined by XRD analysis (Rigaku SmartLab SE, Japan). The determination of shape, size and distribution nature of the synthesized AgNPs was done by TEM analysis (FEI, TECNAI G2, F30, China).

Antibacterial activity of AgNPs

The antibacterial potential of the synthesized AgNPs was verified against pathogenic bacteria, such as *Streptococcus pneumoniae* (MTCC1935), *Staphylococcus aureus* (MTCC6908), *Klebsiella pneumoniae* (MTCC9238), *Bacillus subtilis* (MTCC6633), *Shigella flexneri* (MTCC1457), and *Escherichia coli* (MTCC40) using agar well diffusion method by making 6 mm diameter wells with the help of cork borer on nutrient agar (NA) media plates. The stock AgNPs solution of 1 mg/ml concentration was prepared and 25, 50, 75 and 100 μl (1 $\mu\text{g}/\mu\text{l}$ each) of solutions were

filled into corresponding wells; for positive and negative controls, streptomycin and sterile distilled water were used, respectively. The plates were incubated overnight at 37 °C and the clear zone formed around each well was measured as diameter in mm.

Determination of MTT cytotoxic activity of AgNPs

To determine the anticancer potential of AgNPs, human prostate adenocarcinoma (PC-3) cell lines were procured from NCCS, Pune, India and sub-cultured on DMEM-High Glucose (#AL111, Himedia) medium. During analysis, medium with cells but without the AgNPs/anticancer drug was taken as negative control and medium with cells and 12.5 $\mu\text{g}/\text{ml}$ of cisplatin (#PHR1624, Sigma) was taken as positive control; AgNPs solution with concentrations of 6.25–100 $\mu\text{g}/\text{ml}$ was filled into respective wells. The plates were incubated in a humidified 5% CO_2 atmosphere (Heal-force, China) for 24 h at 37 °C to allow cells to grow. After incubation, MTT reagent (# 4060 Himedia) was added by removing the used-up media; again after 3 h of incubation, 100 μl of DMSO (#PHR1309, Sigma) was added and MTT reagent was removed. Finally, the absorbance at 570 nm was read on an ELISA reader by taking 630 nm as reference wavelength and the IC_{50} value was calculated.

Evaluation of apoptosis using flow cytometry analysis

The apoptosis/necrosis study of the synthesized AgNPs was done by employing FITC Annexin V (Annexin V)/

Propidium Iodide (PI) expression assay. Annexin V (Cat No: 51-65874X, BD Biosciences) was used to discover the percentage of cells undergoing apoptosis, whereas PI (Cat No. 51-66211E, BD Biosciences) was used to differentiate viable from nonviable cells. During this study, 6-well plate (Biolite-ThermoNunc) was used to culture PC-3 cells and kept for overnight incubation at 37 °C in a humidified CO₂ incubator. The cells were treated with 30.62 µg/ml (IC₅₀) concentration of AgNPs. The flow cytometry analysis was done by following the standard protocol suggested by manufacturers of FITC Annexin-V apoptosis detection kit (BD FACS calibur, Biosciences, USA). Finally, the preparation was analysed using flow cytometer immediately after the addition of PI (5 µl) and 1× binding buffer (400 µl) to each tube. The images were assessed by using BD Cell Quest Pro Ver.6.0 software.

Statistical analysis

All the analysis were performed in triplicates and the data are represented as mean ± standard deviation. The statistical analysis was performed by using Graph Pad Prism 4.0 software (San Diego, CA, USA).

Results

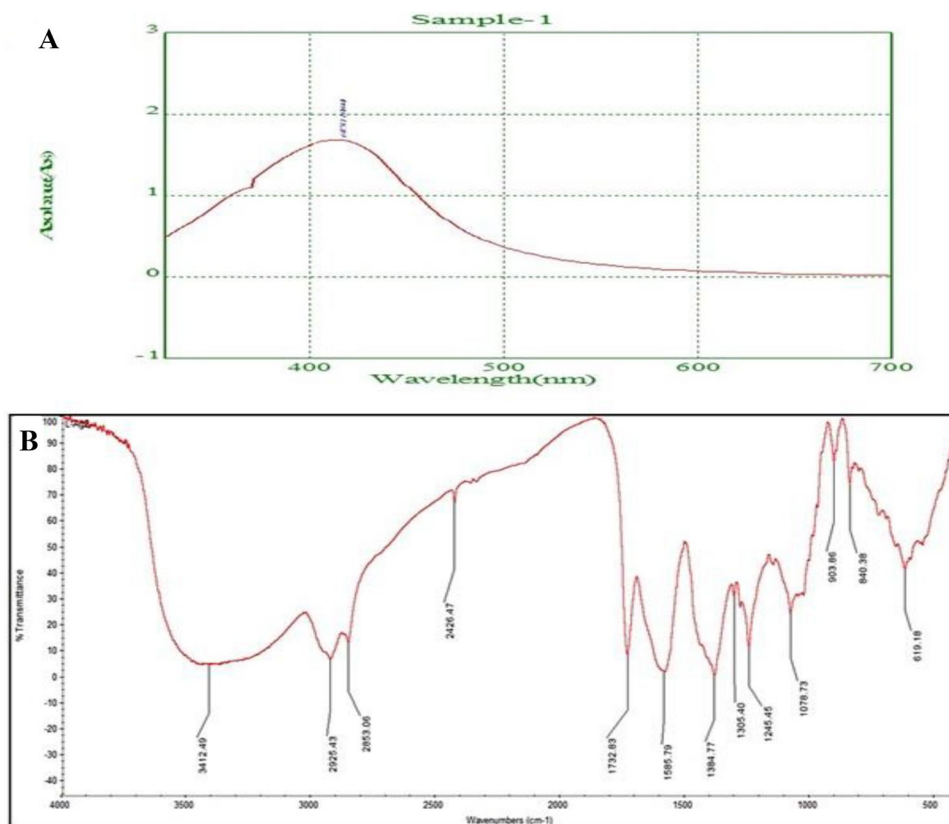
Synthesis of AgNPs

The initial indication on formation of AgNPs was evidenced by colour change in the reaction mixture (Fig. 1C). The AgNPs synthesized by using *A. lakoocha* fruit methanol extract was slightly yellow in colour; when the extract was added with AgNO₃ the observed colour change was from light yellow to dark brown. The colour change was due to the bio-reduction of ionic silver (Ag⁺) to elemental silver (Ag⁰) by the combined action of biomolecules present in the *A. lakoocha* fruit extract.

Characterizations of AgNPs

The bio-reduction of Ag⁺ ion was recorded with the use of UV–visible spectroscopy by recording the absorption spectral wavelength between 200 and 700 nm. UV–visible spectral analysis showed that maximum absorption was at 415 nm (Fig. 2A), that reasserted the synthesis of AgNPs in the solution. The single characteristic absorption peak was obtained due to the surface plasmon resonance of excited particles. The FTIR analysis exhibited several bands/peaks at around 3412, 2925, 2853, 2426,

Fig. 2 Characterization of *A. lakoocha* fruit extract AgNPs; **A** UV–vis. analysis, and **B** FTIR analysis



1732, 1585, 1384, 1305, 1245, 1078, 903, 840, and 619 cm^{-1} wave numbers (Fig. 2B). The broad absorption band observed at 3412 cm^{-1} was correlated to O–H stretching alcohol and the absorption bands at 2925 and 2853 cm^{-1} corresponded to the symmetrical and asymmetrical stretching of alkane molecules respectively. The band at 1732 cm^{-1} is for stretching of aldehyde molecules and band at 1585 cm^{-1} attributed to N–H bending amine. The bands at 1384 cm^{-1} and 1245 cm^{-1} showed the S=O stretching of sulphate and C–N stretching amine. The bands at 1078, 903 and 619 cm^{-1} corresponded to C–O stretching primary alcohol, C=C bending alkane and C–Br stretching halo compounds, respectively. The peaks at 2426 and 1305 cm^{-1} were due to the absorbed atmospheric CO_2 .

Morphological characterization

AFM analysis gave an insight to the surface morphology, distribution and distance between AgNPs by displaying two and three dimensional topographical views (Fig. 3A–C). AFM data revealed that the synthesized AgNPs were poly-dispersed with less or no agglomeration, spherical and diameter ranging from 10 to 30 nm. SEM image displayed relatively spherical-shaped AgNPs formed with polydispersed nature (Fig. 3D). The EDS spectrum exhibited peaks for various elements, such as C, O, Na, and Al along with the typical peak for elemental silver (Ag^0) at 3 keV (Fig. 3E). The peaks for C, O and Na were emerged due to the surface bound biomolecules, whereas peak for Al was due to sample grid holder.

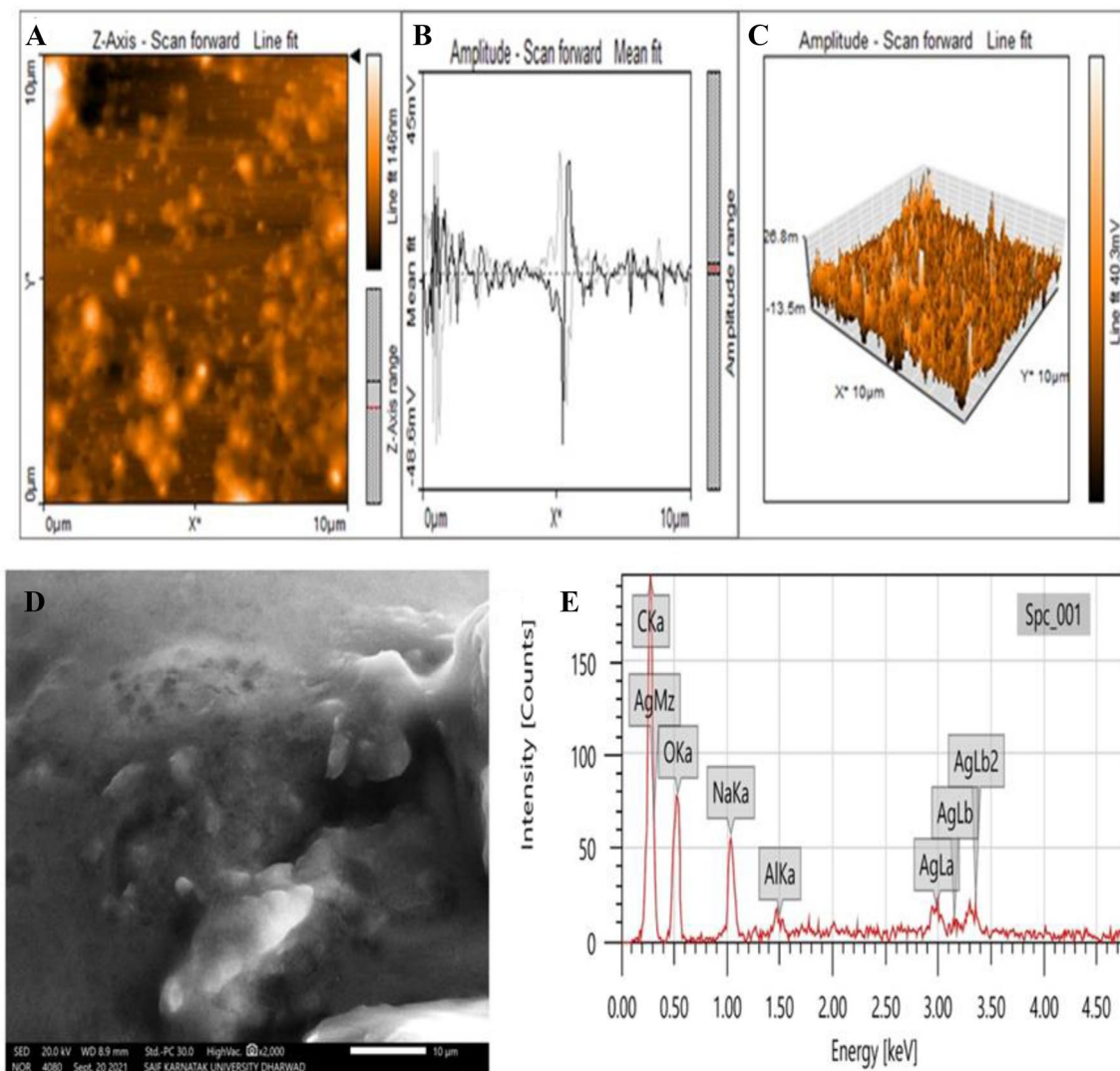


Fig. 3 Morphological characterization of *A. lakoocha* fruit extract AgNPs; **A** 2-D AFM view, **B** particle size distribution, **C** 3-D AFM view, **D** SEM micrograph, and **E** EDS spectrum

Structural characterization

The XRD patterns of *A. lakoocha* AgNPs showed the synthesis of crystalline structured nanoparticles and the XRD peaks were obtained at 38.13° , 44.11° , 63.82° , 77.48° , and 81.49° . The obtained diffraction intensities can be assigned to the (111), (200), (220), (311), and (222) Bragg's diffraction planes of the metallic silver having face-centered cubic (FCC) crystalline structure (Fig. 4A).

The image obtained from HR-TEM analysis illustrated the morphological details of the synthesized AgNPs along with accurate size range of the particles. The micrograph displayed the spherical, polydispersed AgNPs ranging from 6.59 to 25 nm in size (Fig. 4B), and the smallest size of the particle was found out to be 6.59 nm (Fig. 4C).

Antibacterial activity of AgNPs

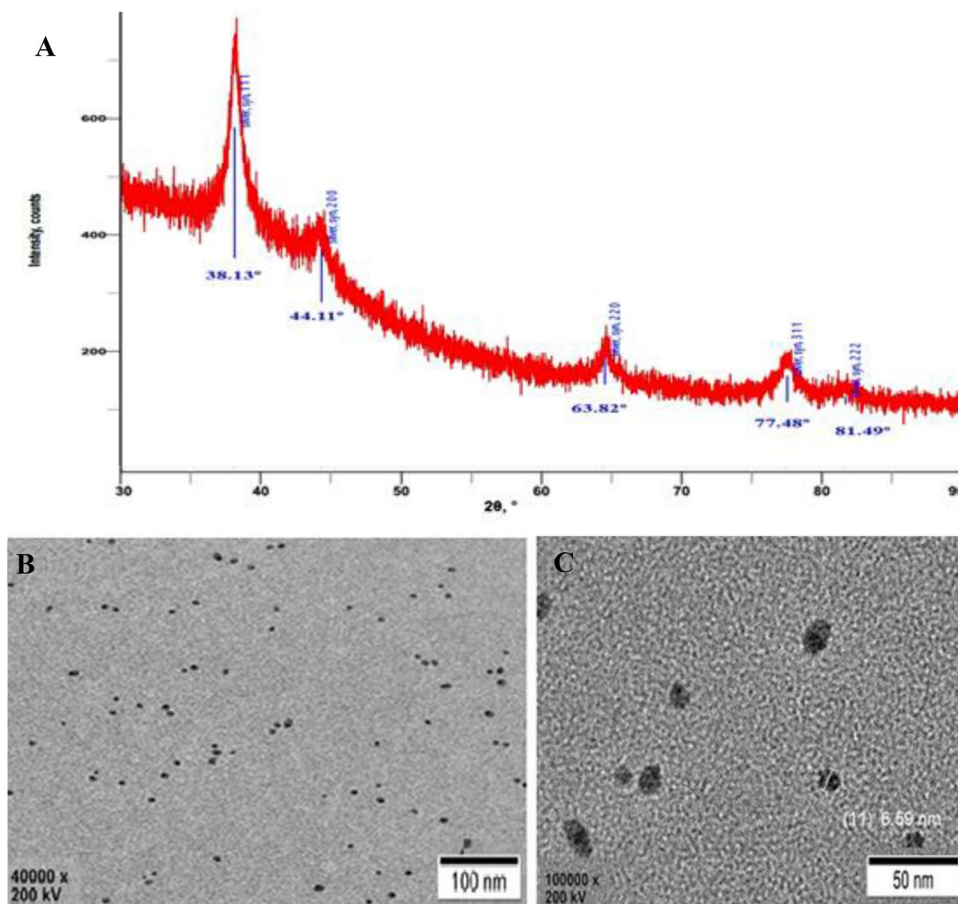
The potential of synthesized AgNPs to inhibit bacterial growth was analysed against human pathogenic bacteria; among the tested pathogens, *S. pneumoniae* was the most sensitive with measured inhibition zones of 14 ± 0.6 , 16 ± 0.5 , 17 ± 0.5 , and 20 ± 0.4 mm at 25, 50, 75, and 100 μ l of AgNPs treatment. Similarly, *S. aureus*

was observed to be the least sensitive with inhibition zones of 13 ± 0.5 , 14 ± 0.4 , 14 ± 0.5 , and 15 ± 0.6 mm at 25, 50, 75, and 100 μ l of AgNPs solutions. The AgNPs displayed antibacterial activity by increased zones of inhibition with increased AgNPs volume. All the other pathogenic bacteria like *K. pneumoniae*, *B. subtilis*, *E. coli* and *S. flexneri* exhibited moderate zones of inhibition at different concentrations of AgNPs (Fig. 5A–G).

Determination of MTT cytotoxic activity of AgNPs

The bio-fabricated AgNPs exhibited increased cytotoxic activity with increase in concentration to prevent the growth of cancer cells by inducing apoptosis; that is marked by the difference in cell shape, size, and other morphological details (Fig. 6A–G). The AgNPs effectively inhibited PC-3 cells by displaying decreased % cell viability of $96.34 \pm 0.5\%$, $84.06 \pm 0.6\%$, $57.90 \pm 0.6\%$, $32.43 \pm 0.5\%$, and $11.07 \pm 0.4\%$ at 6.25, 12.5, 25, 50, and 100 μ g/ml of AgNPs concentrations indicating the dose-dependent activity (Fig. 6H). The IC_{50} value of 30.62 μ g/ml against PC-3 cell line indicated the higher potential of *A. lakoocha* AgNPs to inhibit the proliferation of tumour cells.

Fig. 4 Structural characterization of *A. lakoocha* fruit extract AgNPs; **A** XRD pattern, **B** TEM micrograph, and **C** TEM image showing smallest particle



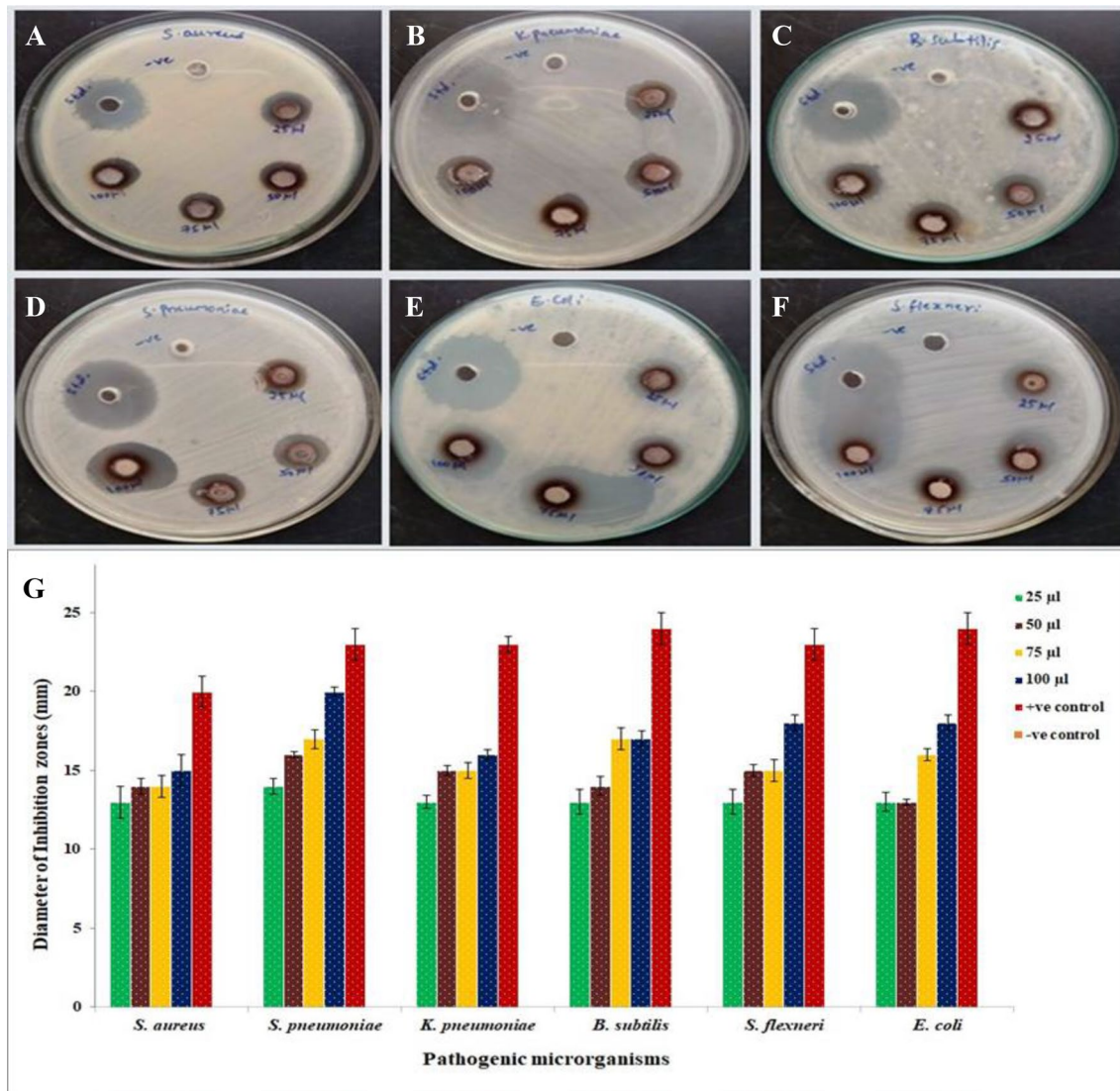


Fig. 5 Antibacterial activity of *A. lakoocha* fruit extract AgNPs against pathogens; **A** *S. aureus*, **B** *K. pneumoniae*, **C** *B. subtilis*, **D** *S. pneumoniae*, **E** *E. coli*, **F** *S. flexneri*, and **G** Graph showing zones of inhibition formed against pathogenic bacteria

Evaluation of apoptosis using flow cytometry analysis

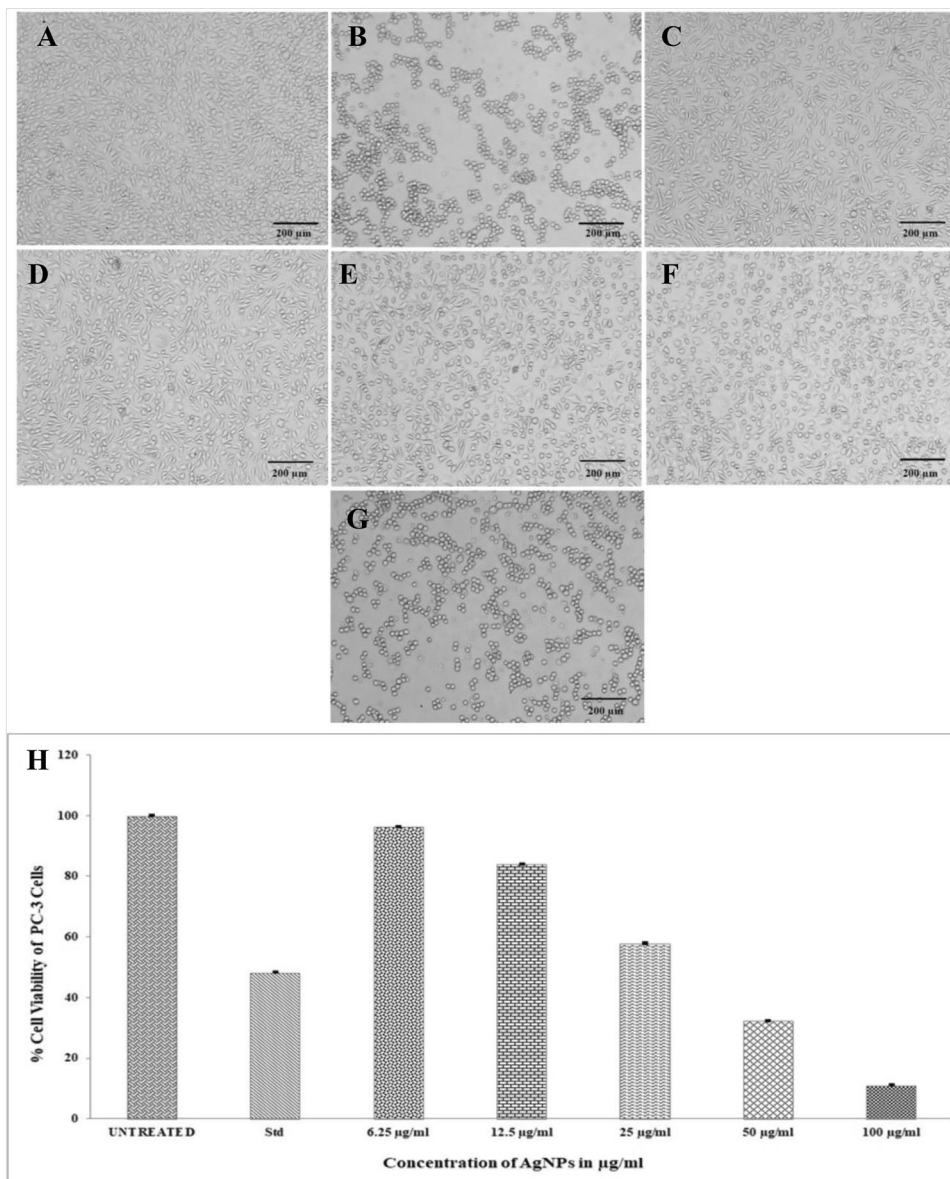
In Annexin V/PI expression study, the cells in early apoptosis stained positive for Annexin V and negative for PI, while the cells positively stained for both Annexin V and PI were in late apoptosis or already dead. The viable cells or cells with no measurable apoptosis were stained negatively for both Annexin V and PI after 24 h of treatment with AgNPs. The flow cytometer analysis unveiled 48.11 ± 0.7% of early apoptosis (lower right), 24.92 ± 0.5% of late apoptosis (upper right), 25.78 ± 0.6% of viable cells (lower left) and 1.19 ± 0.4% of necrotic cells (upper left) as depicted in the quadrangular plot for both control (Fig. 7A) and treated cells (Fig. 7B). The obtained results specified that AgNPs

can prevent proliferation of cancer cells by increasing apoptosis and the possible mechanism of action of AgNPs on cancer cells leading to cell death is shown in Fig. 7C.

Discussion

The change in colour after adding AgNO₃ to extract indicates about initiation of AgNPs synthesis; the dark brown colour was attributed to the intense absorption of light in the specific wavelength range leading to surface plasmon resonance effect from the combined oscillation of induced free electrons (Hemmati et al. 2018). The previous studies regarding UV–vis. analysis of green AgNPs also reported the similar results, where absorption spectra of AgNPs

Fig. 6 MTT cytotoxic activity of *A. lakoocha* AgNPs against PC-3 cell line; **A** untreated, **B** standard, **C** 6.25 $\mu\text{g/ml}$, **D** 12.5 $\mu\text{g/ml}$, **E** 25 $\mu\text{g/ml}$, **F** 50 $\mu\text{g/ml}$, **G** 100 $\mu\text{g/ml}$, and **H** graph showing % cell viability of PC-3 cells at different concentrations of AgNPs

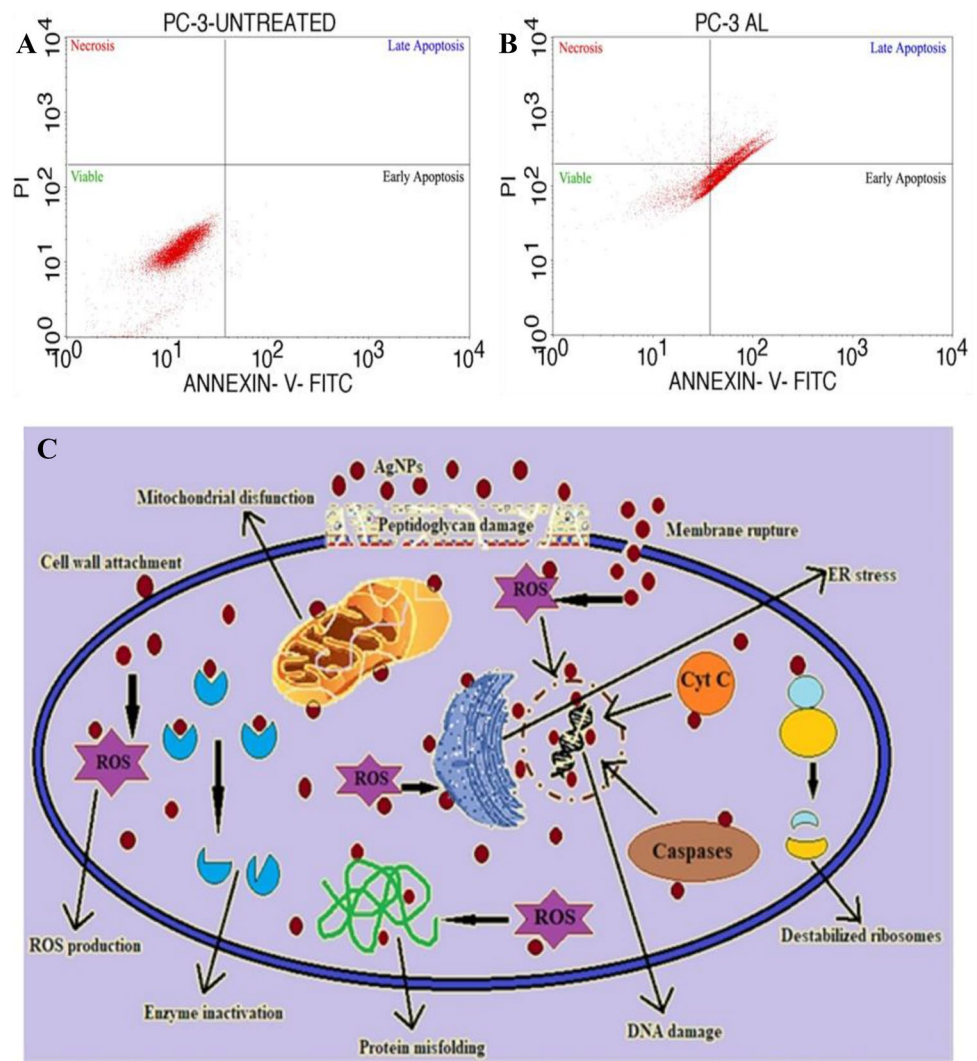


present in the aqueous solution displayed absorbance peak around 400–440 nm and with an increase in the reaction time a swift increase in the synthesis of AgNPs was observed (Hemmati et al. 2018; Salayova et al. 2021). The formation of stabilized AgNPs was because of the presence of biochemical functional groups and the role of plant extract that contain biomolecules namely phenolics, terpenoids, flavonoids, polysaccharides, alkaloids, enzymes, amino acids, proteins and alcoholic compounds, which were accountable for the synthesis of stable AgNPs (Salayova et al. 2021; Arumugam et al. 2017). The AFM analysis for *A. lakoocha* AgNPs depicted the spherical shape, polydispersion of AgNPs; and the obtained results were well supported by the earlier studies on biosynthesized AgNPs investigated using AFM analysis, where the biosynthesized AgNPs were

spherical, polydispersed with less evidence of agglomeration (Bhat et al. 2021). The EDX spectrum of *A. lakoocha* AgNPs exhibited various peaks corresponding to various elements; however, a strong absorption peak was obtained at 3 keV depicting silver. The earlier findings suggested that metallic silver exhibits typical absorption peak at 3 keV because of surface plasmon effect. According to them, AgNPs synthesized using plant extracts were stable in solution several months after synthesis due to the encircled biomolecules (Bhat et al. 2021; Umoren et al. 2014).

The XRD pattern of *A. lakoocha* AgNPs displayed five diffraction planes specific for metallic silver at five different 2θ angles and was compared with the International Center for Diffraction Data (ICDD) of silver to confirm the FCC structure; the result was also supported by findings of the

Fig. 7 Flow cytometry analysis of *A. lakoocha* AgNPs against PC-3 cell line; **A** untreated PC-3 cells, **B** treated PC-3 cells, and **C** possible mechanism of action of AgNPs against PC-3 cell line



earlier studies, where biosynthesized AgNPs exhibited same pattern of Bragg's diffraction peaks characteristic for metallic silver at similar range of 2θ angles (Acharya et al. 2020; Nayaka et al. 2020a). In TEM analysis, the AgNPs showed spherical shape, small size and less agglomeration. Similarly, earlier studies using TEM analysis of AgNPs suggested similar results regarding shape, size and distribution of AgNPs; the results suggested the synthesis of spherical AgNPs of 10–50 nm in size with demonstrating some amount of agglomeration and mostly dispersed nanoparticles (Bhat et al. 2021; Nayak et al. 2020). The green AgNPs from *A. lakoocha* fruit methanol extract exhibited increased antimicrobial activity with increase in concentration. The previous reports about the antimicrobial activity of green AgNPs suggested that, cell membranes of microorganisms are negatively charged because of the presence of amino acids, phosphates, and carboxyl groups. The slightly positively charged AgNPs were attracted towards cell membrane and attach to bacterial cell wall. The AgNPs migrate through

membranes and cell walls, alter the permeability of plasma membrane and affect cellular homeostasis of the microorganism to induce the chain of events that cause cell death (Nayaka et al. 2020a; b).

The synthesized AgNPs demonstrated dose-dependent anticancer activity in vitro against PC-3 cell line indicating the potential of AgNPs to inhibit the tumour growth by altering the structure and function of cancer cells. Similar observations displayed dissembled gaps between neighbouring cells and deformation of cells were reported in the previous studies involving MTT assay; where, the AgNPs prepared by *Hyptis suaveolens* callus, Asafoetida, and *Pinus roxburghii* extracts showed notable anticancer activity against PC-3, MDA-MB-231, HepG2 and A549 cell lines (Botcha and Prattipati 2020; Satsangi, 2020; Kumari et al. 2020a, b). According to previous findings, the AgNPs attach to an end consisting of thiol groups of enzymes and bring about the unfolding, aggregations and deformation of proteins inside the cancer cells and lead to

induction of apoptosis. The flow cytometry-assisted apoptosis studies were reported indicating the % of early apoptosis, late apoptosis, necrosis and viable cells, when cancer cell lines were treated with bio-fabricated AgNPs. These results suggested that AgNPs can induce apoptosis and prevent cellular multiplication by generating reactive oxygen species (ROS) leading to cellular DNA damage. The increased level of ROS induces oxidative stress causing early apoptosis; meanwhile, the ROS generation increases due to the reduced membrane potential of mitochondria that acts as a secondary messenger simultaneously in many signaling pathways. The cascade of events play predominant role in apoptosis by controlling the activity of specific enzymes concerned in the apoptotic pathways (Vasanth et al. 2014; Almalki and Khalifa 2020; Amini et al. 2021).

Conclusion

As awareness increasing towards green nanotechnology, use of green route for metal nanoparticles synthesis is leading to a desire to establish eco-friendly technique; AgNPs synthesis from plant extract is beneficiary over other sources as the former is energy efficient, cost effective, and less affective to human health and environment. Biosynthesized AgNPs from *A. lakoocha* exhibited high antibacterial activity against human pathogenic bacteria indicating its possible use as an alternative to antibiotics in coming years after successful clinical trials. The AgNPs displayed dose-dependent anticancer activity on PC-3 cells suggesting the possible use as an anticancer agent to cure prostate cancer. Therefore, the findings of the present study conclude that, the green AgNPs can replace the clinical or biomedical agents to cure microbial and cancer-related diseases in near future.

Acknowledgements The authors are thankful to the P.G. Department of Studies in Botany for extending laboratory facility and SAIF (USIC), Karnatak University, Dharwad for providing instrumentation facilities.

Funding This project was supported by seed grant for research program (2021-22/62), Karnatak University, Dharwad, Karnataka, India. This project was also supported by Researchers Supporting Project number RSP-2021/142, King Saud University, Riyadh, Saudi Arabia.

Declarations

Conflict of interest The authors declare that there are no competing interests.

Ethical approval Not applicable, the research does not involve either human participants and/or animals.

References

- Acharya D, Satapathy S, Somu P, Parida UK, Mishra G (2020) Apoptotic effect and anticancer activity of bio-synthesized silver nanoparticles from marine algae *Chaetomorpha linum* extract against human colon cancer cell HCT-116. *Biol Trace Elem Res*. <https://doi.org/10.1007/s12011-020-02304-7>
- Ahmad S, Munir S, Zeb N, Ullah A, Khan B, Ali J et al (2019) Green nanotechnology: a review on green synthesis of silver nanoparticles—an eco-friendly approach. *Int J Nanomed* 14:5087–5107. <https://doi.org/10.2147/IJN.S200254>
- Ahmed S, Ahmad M, Swami BL, Ikram S (2016) A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: a green expertise. *J Adv Res* 7:17–28. <https://doi.org/10.1016/j.jare.2015.02.007>
- Akintelu SA, Bo Y, Folorunso AS (2020) A review on synthesis, optimization, mechanism, characterization, and antibacterial application of silver nanoparticles synthesized from plants. *J Chem*. <https://doi.org/10.1155/2020/3189043>
- Almalki MA, Khalifa AYZ (2020) Silver nanoparticles synthesis from *Bacillus* sp. KFU36 and its anticancer effect in human breast cancer MCF-7 cells via induction of apoptotic mechanism. *J Photochem Photobiol B* 204:111786. <https://doi.org/10.1016/j.jphotobiol.2020.111786>
- Al-Nadhari S, Al-Enazi NM, Alshehrei F, Ameen F (2021) A review on biogenic synthesis of metal nanoparticles using marine algae and its applications. *Environ Res* 194:110672. <https://doi.org/10.1016/j.envres.2020.110672>
- Amini SM, Pour MSS, Vahidi R, Kouhbananejad SM, Bardsiri MS, Farsinejad A et al (2021) Green synthesis of stable silver nanoparticles using *Teucrium polium* extract: in-vitro anticancer activity on NALM-6. *Nanomed Res J* 6(2):170–178. <https://doi.org/10.22034/nmrj.2021.02.008>
- Arumugam N, Thulasinathan B, Pasubathi R, Thangavel K, Muthuramalingam JB, Arunachalam A (2017) Biogenesis of silver nanoparticles using selected plant leaf extract; characterization and comparative analysis of their antimicrobial activity. *Nanomed J* 4(4):208–217. <https://doi.org/10.22038/nmj.2017.04.002>
- Bhat M, Chakraborty B, Kumar RS, Almansour AI, Arumugam N, Kotresha D et al (2021) Biogenic synthesis, characterization and antimicrobial activity of *Ixora brachypoda* (DC) leaf extract mediated silver nanoparticles. *J King Saud Univ Sci* 33:101296. <https://doi.org/10.1016/j.jksus.2020.101296>
- Botcha S, Prattipati SD (2020) Callus extract mediated green synthesis of silver nanoparticles, their characterization and cytotoxicity evaluation against MDA-MB-231 and PC-3 cells. *BioNanoSci* 10:11–22. <https://doi.org/10.1007/s12668-019-00683-3>
- Chung IM, Park I, Seung-Hyun K, Thiruvengadam M, Rajakumar G (2016) Plant-mediated synthesis of silver nanoparticles: their characteristic properties and therapeutic applications. *Nanoscale Res Lett* 11:40. <https://doi.org/10.1186/s11671-016-1257-4>
- Garg D, Sarkar A, Chand P, Bansal P, Gola D, Sharma S et al (2020) Synthesis of silver nanoparticles utilizing various biological systems: mechanisms and applications—a review. *Prog Biomater*. <https://doi.org/10.1007/s40204-020-00135-2>
- Hemmati S, Rashtiani A, Zangeneh MM, Mohammadi P, Zangeneh A, Veisi H (2018) Green synthesis and characterization of silver nanoparticles using *Fritillaria* flower extract and their antibacterial activity against some human pathogens. *Polyhedron*. <https://doi.org/10.1016/j.poly.2018.10.049>
- Ijaz M, Zafar M, Iqbal T (2021) Green synthesis of silver nanoparticles by using various extracts: a review. *Inorg Nano-Metal Chem* 51(5):744–755. <https://doi.org/10.1080/24701556.2020.1808680>

- Javadi A, Oloketuyi SF, Khan MM, Khan F (2018) Diversity of bacterial synthesis of silver nanoparticles. *Bio Nano Sci* 8:43–59. <https://doi.org/10.1007/s12668-017-0496-x>
- Khan AU, Malik N, Khan M, Cho MH, Khan MM (2018) Fungi-assisted silver nanoparticle synthesis and their applications. *Bioprocess Biosyst Eng* 41:1–20. <https://doi.org/10.1007/s00449-017-1846-3>
- Kumar HK, Venkatesh N, Bhowmik H, Kuila A (2018) Metallic nanoparticle: a review. *Biomed J Sci Tech Res* 4(2):3765–3775. <https://doi.org/10.26717/BJSTR.2018.04.001011>
- Kumari R, Saini AK, Kumar A, Saini RV (2020a) Apoptosis induction in lung and prostate cancer cells through silver nanoparticles synthesized from *Pinus roxburghii* bioactive fraction. *J Biol Inorg Chem* 25:23–37. <https://doi.org/10.1007/s00775-019-01729-3>
- Kumari S, Tehri N, Gahlaut A, Hooda V (2020b) Actinomycetes mediated synthesis, characterization, and applications of metallic nanoparticles. *Inorg Nano-Metal Chem*. <https://doi.org/10.1080/24701556.2020.1835978>
- Manivasagan P, Venkatesan J, Sivakumar K, Kim SK (2014) Actinobacteria mediated synthesis of nanoparticles and their biological properties: a review. *Crit Rev Microbiol*. <https://doi.org/10.3109/1040841X.2014.917069>
- Nayak S, Bhat MP, Udayashankar AC, Lakshmeesha TR, Geetha N, Jogaiah S (2020) Biosynthesis and characterization of *Dillenia indica* mediated silver nanoparticles and their biological activity. *Appl Organometal Chem*. <https://doi.org/10.1002/aoc.5567>
- Nayaka S, Bhat MP, Chakraborty B, Pallavi SS, Airodagi D, Muthuraj R et al (2020) Seed extract-mediated synthesis of silver nanoparticles from *Putranjiva roxburghii* Wall., phytochemical characterization, antibacterial activity and anticancer activity against MCF-7 cell line. *Indian J Pharm Sci* 82(2):260–269. <https://doi.org/10.36468/pharmaceutical-sciences.646>
- Nayaka S, Chakraborty B, Bhat MP, Shashiraj KN, Airodagi D, Pallavi SS et al (2020) Biosynthesis, characterization, and in vitro assessment on cytotoxicity of actinomycete-synthesized silver nanoparticles on *Allium cepa* root tip cells. *Beni-Suef Univ J Basic Appl Sci* 9:51. <https://doi.org/10.1186/s43088-020-00074-8>
- Rajeshkumar S, Bharath LV (2017) Mechanism of plant-mediated synthesis of silver nanoparticles—a review on biomolecules involved, characterisation and antibacterial activity. *Chem Biol Interact*. <https://doi.org/10.1016/j.cbi.2017.06.019>
- Restrepo CV, Villa CC (2021) Synthesis of silver nanoparticles, influence of capping agents, and dependence on size and shape: a review. *Environ Nanotechnol Monit Manag* 15:100428. <https://doi.org/10.1016/j.enmm.2021.100428>
- Salayova A, Bedlovicova Z, Daneu N, Balaz M, Bujnakova ZL, Balazova L et al (2021) Green synthesis of silver nanoparticles with antibacterial activity using various medicinal plant extracts: morphology and antibacterial efficacy. *Nanomaterials* 11:1005. <https://doi.org/10.3390/nano11041005>
- Satsangi N (2020) Synthesis and characterization of biocompatible silver nanoparticles for anticancer application. *J Inorg Organomet Polym Mater* 30:1907–1914. <https://doi.org/10.1007/s10904-019-01372-0>
- Sharma A, Sharma S, Sharma K, Chetri SPK, Vashishtha A, Singh P et al (2016) Algae as crucial organisms in advancing nanotechnology: a systematic review. *J Appl Phycol* 28:1759–1774. <https://doi.org/10.1007/s10811-015-0715-1>
- Singh R, Shedbalkar UU, Wadhvani SA, Chopade BA (2015) Bacteriogenic silver nanoparticles: synthesis, mechanism, and applications. *Appl Microbiol Biotechnol* 99:4579–4593. <https://doi.org/10.1007/s00253-015-6622-1>
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A et al (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 71:209–249. <https://doi.org/10.3322/caac.21660>
- Tadele KT, Abire TO, Feyisa TY (2021) Green synthesized silver nanoparticles using plant extracts as promising prospect for cancer therapy: a review of recent findings. *J Nanomed* 4(1):1040
- Tarannum N, Gautam YK (2019) Facile green synthesis and applications of silver nanoparticles: a state-of-the-art review. *RSC Adv* 9:34926. <https://doi.org/10.1039/c9ra04164h>
- Thirumal S (2021) A modern review of silver nanoparticles mediated plant extracts and its potential bio-applications. *Int J Bot Stud* 6(3):170–175
- Umoren SA, Obot IB, Gasem ZM (2014) Green synthesis and characterization of silver nanoparticle using red apple (*Malus domestica*) fruit extract at room temperature. *J Mater Environ Sci* 5(3):907–914. www.researchgate.net/publication/2617111017
- Vasanth K, Ilango K, Mohankumar R, Agrawal A, Dubey GP (2014) Anticancer activity of *Moringa oleifera* mediated silver nanoparticles on human cervical carcinoma cells by apoptosis induction. *Colloids Surf B* 117:354–359. <https://doi.org/10.1016/j.colsurfb.2014.02.052>
- Velidandi A, Dahariya S, Pabbathi NPP, Kalivarathan D, Baadhe RR (2020) A review on synthesis, application, toxicity, risk assessment and limitation of plant extract synthesized silver nanoparticles. *Nano World J* 6(3):35–60. <https://doi.org/10.17756/nwj.2020-079>
- Zhao X, Zhou L, Rajoka MSR, Yan L, Jiang C, Shao D et al (2017) Fungal silver nanoparticles: synthesis, application and challenges. *Crit Rev Biotechnol*. <https://doi.org/10.1080/07388551.2017.1414141>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.