



# Bio prospecting of *Aloe barbadensis miller* (Aloe vera) for silver nanoparticles against breast cancer: A review

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## ABSTRACT

Silver nanoparticles (AgNPs) are gaining substantial importance in the fields of biotechnology and medicine. Its composites are metal oxides, silicates, polymers, graphene, fibers, dendrimers, etc. The green synthesized AgNPs possess advantages over conventional AgNPs in the form of fewer chemical reagents and a low temperature and pressure for synthesis. The anticancer efficacy of AgNPs is attributed to a number of variables, including size, shape, surface-to-volume ratio, etc. There are several ways to make SNPs, but the green synthesis of AgNPs, which uses harmless chemicals and natural reagents, has gained significant interest and value. In this review, a comprehensive range of topics related to silver nanoparticles, the environmentally friendly method of producing them from plants such as *Aloe barbadensis miller* (aloe vera), which have a vast medicinal uses, and their anticancer effectiveness against breast cancer cells are discussed. The synthesized AgNPs are characterized via a range of methods, for instance, Fourier Transform Infrared Spectroscopy (FTIR), UV-visible spectroscopy, Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), and X-ray Diffraction (XRD). This review study includes an investigation into the stability of produced nanoparticles, the wide range of nanoparticle forms, the many techniques used in the conglomeration of nanoparticles, and comparison methods emphasizing the benefits of green synthesis relative to traditional techniques. Furthermore, the discussion explores the chemical and structural makeup of nanoparticles.

## 1. Introduction

Antimicrobial and anticancer therapies are two areas in which **silver nanoparticles (AgNPs)** find extensive use. Additionally, they are being used as biosensors, vaccine adjuvants, and anti-diabetic agents, as well as to promote bone mending and wound healing. The amalgamation methods of AgNPs include biological, chemical and physical routes (Xu et al., 2020). Silver nanoparticles are known for their high anticancer effects. Polymer coating on nanoparticles improves the stability of the suspension against aggregation. However, for biologically synthesized silver nanoparticles, coating is not required, as the plant extract designed for the synthesis of nanoparticles itself functions as a calibration and reduction agent. During the process of chemical binding of

silver nanoparticles, coating substances have been designed to alleviate silver nanoparticles, which allow the maintenance of specific sizes and reduce the amount of silver ions that take part in the reaction. These are the crucial factors that determine the toxicity of the silver nanoparticles. Presently, silver nanoparticles have wide applications in the arena of medicine, especially in cancer treatment. Metal nanoparticles will be generated through various ways (Fahmy et al., 2019, Marins et al., 2018, Shah et al., 2015).

The procedure of manufacturing AgNPs by employing plant or leaf extract as a reducing agent is better than other methods since it does not require the laborious task of sustaining cell culture. *Aloe barbadensis miller* gel is utilized in many cosmetic and skincare products. It is also considered a medicinal plant for the medication of burns and lesions. It

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is now being explored for the amalgamation of silver nanoparticles. Several researchers have indicated that silver nanoparticles can also be obtained from *Jasminum officinale*, *Centella asiatica*, bacteria, fungi, yeast, etc. (Kaviya et al., 2012, Tippayawat et al., 2016, Rahman et al., 2017, Surjushe et al., 2008, Kumar and Yadav, 2009, Kulothungan et al., 2022, Sahu et al., 2022). Pioneering attempts were made to give a comprehensive review studies of *Aloe barbadensis miller* plants in detail. Among the various diseases that cause mortality, cancer is a noteworthy issue that needs more attention. One of the main causes of death for individuals in 172 countries worldwide is cancer (Mehrotra and Yadav, 2022). Among the cancers, breast cancer accounts for over 2 million cases in women globally, leading to 60,000 deaths per year. Breast cancer has the ability to extend when cancer cells put on the blood or lymphatic system and move to different body parts. The fourth common cancer that prevailed in India in the year 1990 occupies the first position in the last decade (McMillan et al., 2011). Number of cancer cases and cancer-related deaths as per reports is shown in Fig. 1 (Prakash Sharma et al., 2014, Chávez-Rodríguez et al., 2021).

Breast cancer stands the prominent cause of mortality among cancer-related diseases. The biological manufacture of AgNPs utilizing *Aloe barbadensis miller*, as well as their anticancer efficacy against breast cancer cells, are the main topics of this review study for the first time. This review article discusses a variety of compounds from these plant extracts and their significant biological activities, the biosynthesis of AgNPs from various plant extracts and their application to cancer cell lines, the various techniques for synthesizing AgNPs, the various capping agents used in the process, the characterization of AgNPs, and

the applications of AgNPs.

## 2. Categories of nanoparticles

The nanoparticles are broadly tabulated into three types based on their origin and chief constituents: inorganic, organic nanoparticles, and carbon-based nanoparticles. Organic nanoparticles such as macromolecules, lipid vesicles, microstructure and ferritin are widely used in the medical field as a drug delivery system as they operate well and can be instilled into distinct parts of the body to target cancer cells selectively without destroying normal cells (Khan et al., 2022). Inorganic nanoparticles are generally defined as those that are based on metal or metal oxide. Metal based includes Al, Ag, Cd, Co, Cu, Au, Fe, Pb, Zn and metal-oxide includes Al<sub>2</sub>O<sub>3</sub>, CeO<sub>2</sub>, Fe<sub>2</sub>O<sub>3</sub>, SiO<sub>2</sub>, TiO<sub>2</sub>, ZnO. Nanoparticles created entirely based on carbon are called carbon-based nanoparticles, which include fullerenes, graphene, carbon nanotubes (CNT), carbon nanofibers, carbon black, etc. (Fritea et al., 2021, Baig et al., 2021, Pal et al., 2020).

## 3. Synthesis of nanoparticles

Top down and bottom-up approaches are the two main categories into which nanoparticle synthesis techniques fall. To create nanoparticles, the former method reduces the size of a suitable starting material. The top-down methodology uses a number of chemical and physical processes, including sputtering, laser ablation, and ball milling. Top-down methods are straightforward because they divide or minimize

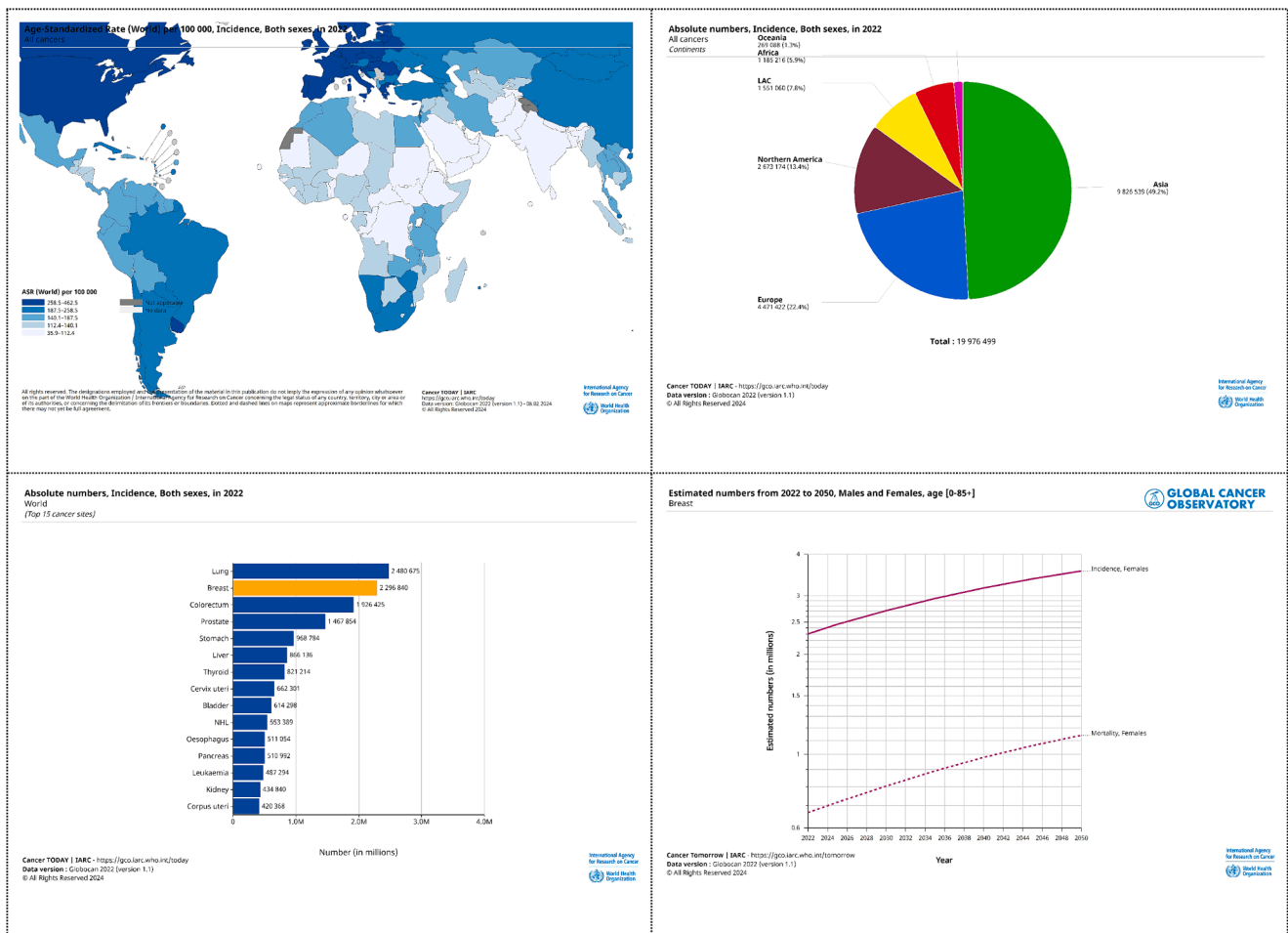


Fig. 1. Estimated number of cancer-related deaths in 2022 among both sexes around the world. Graph production. Global Cancer Observatory (<http://gco.iarc.fr>) Data source. GLOBOCAN2022.

bulk material to produce the desired nanoparticle structure and properties. However, the main pitfall in this approach is the deformity of the surface structure of the produced nanoparticle (Das et al., 2022, Patekari et al., 2011, Khan et al., 2019). Because of their superior ordering and more uniform chemical composition, bottom-up methodologies are primarily used in the coalescence of nanoparticles rather than top-down methods. Sol-gel synthesis, hydrothermal synthesis, colloidal precipitation, etc. are the most commonly used bottom-up approaches to producing nanoparticles.

The creation of nanoparticles via chemical and physical means is exorbitant and uses hazardous chemicals that can have negative biological and environmental effects. Nanoparticles obtained from chemical processes are not appropriate for medical applications, as many toxic substances might be involved in the production of nanoparticle synthesis (Samuel et al., 2022, Gautam et al., 2021, Ray et al., 2009, Zhang et al., 2020). Thus, a surrogate method is essential for the production of nanoparticles to reduce the cost and toxicity of the material and minimize environmental and biological problems. This led to the investigation and progress of the biological synthesis of nanoparticles, which is cost-effective and associated with less or no toxicity. Researchers found that the molecules produced from living organisms such as plants, fungi, bacteria, algae, etc. can be used as calibration agents to produce nanoparticles (Sharma et al., 2019, Shah et al., 2015, Khandel et al., 2018).

#### 4. Biological synthesis of silver nano particle

In the biological synthesis/green chemistry approach, highly stable and well-characterized AgNPs can be obtained. The appearance and morphology of the silver nanoparticle can be controlled by altering certain parameters such as light, pH, temperature, biomass, etc. (Pandit et al., 2022, Rónavári et al., 2021, Raza et al., 2016). An important factor in a nanoparticle's application is its size and shape. It appears that smaller nanoparticles are more effective than larger ones (Hoshyar et al., 2016, Albanese et al., 2012, Vega-Baudrit et al., 2019). The primary benefit of employing biological methods is the ease of access to microorganisms like bacteria, fungus, and others, as well as the abundance of plants. These are used as calibration agents in the production of AgNPs, which impart more stability and less toxicity to the produced nanoparticles (Garg et al., 2020).

As compared with microbial synthesis from bacteria or fungi or synthesis from algae, the synthesis of AgNPs from plant extract is advantageous due to its vast availability and lower toxicity (Chugh et al., 2021, Mukaratirwa-Muchanyereyi et al., 2022). A wide range of phytochemical extracts can be rapidly used to reduce silver ions. The process of biological synthesis of AgNPs uses blending or combining silver nitrate solution with a suitable plant extract (Ahmed et al., 2016, Song and Kim, 2009). A typical reaction can be finished in a few minutes or hours. Table 1 list the *Aloe barbadensis miller* plant extracts that are utilized to create AgNPs.

The green synthesis process is the method used to create nanoparticles from plant extract. Here, an aqueous extract derived from the leaves, stem, seed, or root is combined with the liquid solution of silver salt. Plant extracts are applied as steadying and reducing agents in the

**Table 1**  
Synthesis of silver nanoparticles from *Aloe barbadensis miller* plant extract.

Plant part	Method of preparation	Characteristics	Ref.
Leaf	5 ml of 10 mM AgNO <sub>3</sub> solution was mixed with 5 ml of aloe vera plant extract diluted with 1 % of ammonium solution and kept at room temperature for 48 hrs	It was observed that the maximum absorbance occurs at 430 nm	(Begum et al., 2020)

synthesis of AgNPs. Many different phytochemicals have the ability to produce AgNPs (Singh et al., 2018, Habeeb Rahuman et al., 2022, Nallamuthu et al., 2012). Silver ions can be minimized by the functional groups of phytochemicals, such as amino groups and aldehydes.

#### 5. Characterization of silver nanoparticle

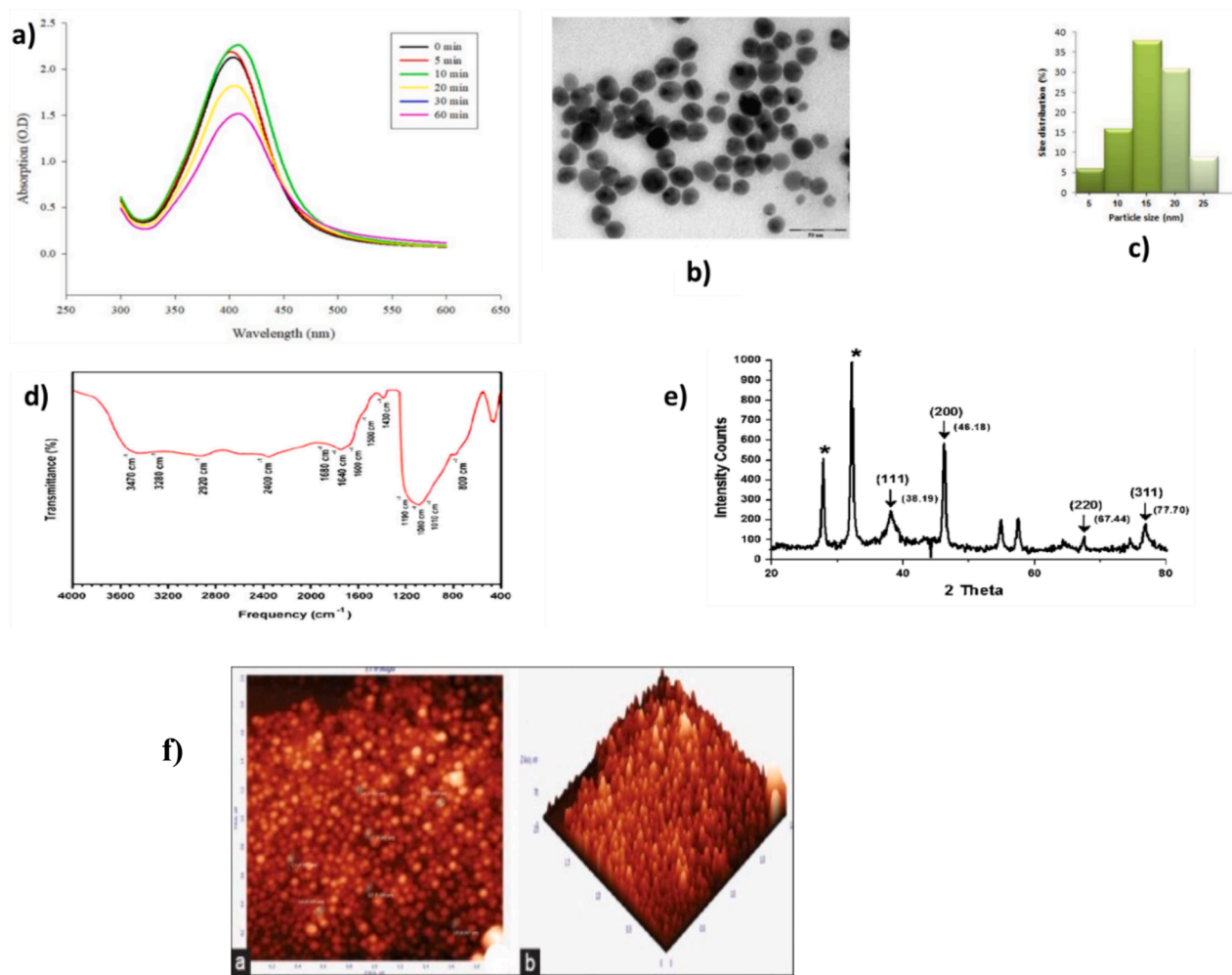
AgNPs are commonly characterized using heterogeneous techniques including Energy Dispersive Spectroscopy (EDS), FTIR, XRD, SEM, TEM, AFM, and UV-Vis spectroscopy. The analysis of AgNP's UV-Vis spectra is displayed in Fig. 2a (Fu et al., 2021). Through optical spectrum measurement, the creation of AgNPs can also be ascertained. It measures the light's absorbance or transmittance, which goes through a specific medium that acts as a function of its wavelength. The AgNPs size and shape aspect ratio are key variables influencing the wavelength of light absorbed. The location of the Surface Plasmon Resonance (SPR) band in UV-Vis spectra is reliant on the size and shape of the particles. Fig. 2b shows the TEM characterization of the structure and morphology of the silver nanoparticle. The TEM method allows observation at the molecular or atomic level. The particle size distribution shown in Fig. 2c and it gives a mean size of 16 nm (David et al., 2020). The functional group present on the silver nanoparticle can be obtained by using the FTIR technique. The FTIR analysis provides an illustration of the agents that function as a stabiliser and minimiser during the biosynthesis of AgNPs. An essential factor in the stability of AgNPs is the capping agent. Each peak in an FTIR analysis corresponds to a particular functional group (Fig. 2d). Mainly three peaks 1010 cm<sup>-1</sup>, 1190 cm<sup>-1</sup> and 1080 cm<sup>-1</sup> correspond to C-O stretching from alcohol, carboxylic acid, ester and ether; all due to functional groups of proteins and metabolites covering the AgNPs. The crystal structure of the nanoparticle is examined using XRD. Fig. 2e displays a typical XRD spectrum of AgNPs. XRD provides sample data about the lattice parameters. The dimensions and form of the unit cell of the crystalline phase can be determined from the location of the diffraction peak. Peak can be described using the miller index since it symbolizes a lattice plane. Fig. 2f displays typical AFM images of the AgNPs, and 2 μm resolution shows the 25–57 nm size, spherical shaped, polydisperse particles.

#### 6. Stability of silver nanoparticle

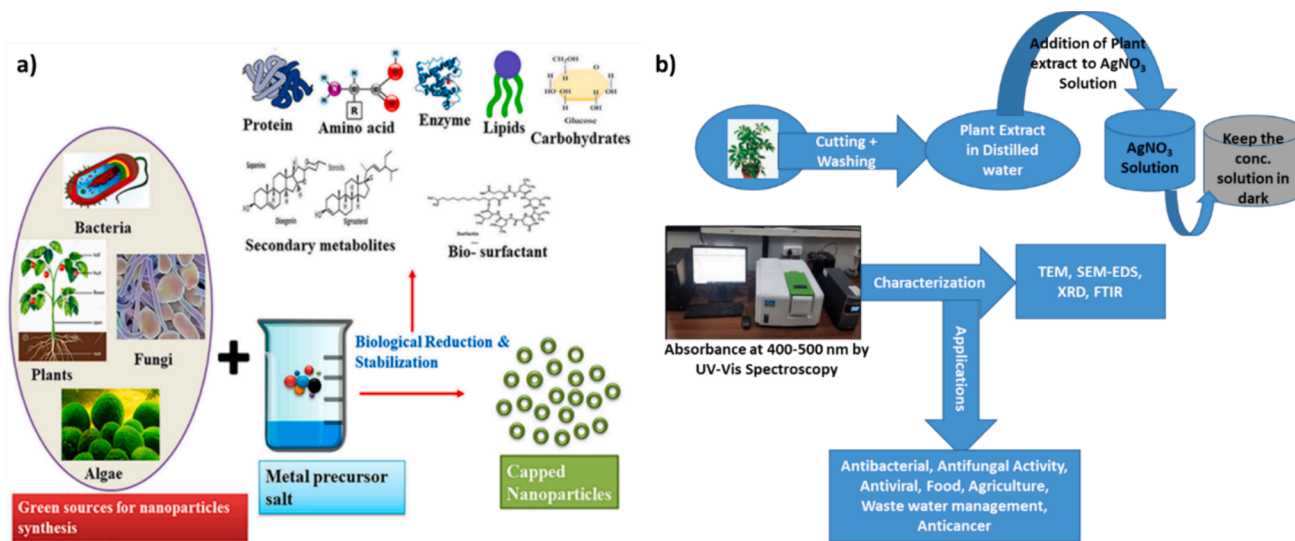
The resilience of nanoparticles is crucial for their utilization in the field of biomedicine. If the synthesized AgNPs are unstable, they would react with other substances, which may result in the worst outcome. Thus, the calibration agent plays a significant role in the union of AgNPs as it prevents the agglomeration and overgrowth of nanoparticles (Burdusel et al., 2018, Gomes et al., 2021, Sidhu et al., 2022, Archana et al., 2023). Generally, natural polysaccharides such as starch, heparin, chitosan, cellulose, glucose, etc. are used as capping agents (Fig. 3a) (Sidhu et al., 2022). The advantages of using a biogenic capping agent over AgNPs are that these:

- 1) Prevent agglomeration
- 2) Provide functional group for the attachment of biomolecules or medicines
- 3) Control the size of the nanoparticle
- 4) Impart more storage and stability properties

Capping agents modify the property of nanoparticles thereby making it amenable for the medical field, especially towards cancer treatment (Fig. 3b, Table 2) (Zafar et al., 2019). In chemical synthesis of nanoparticle PEG, Polyvinyl alcohol etc. are added as capping agents during the time of synthesis to improve the stability (Zafar et al., 2019, Javed et al., 2020). The disadvantage of adding a capping agent is that the addition of chemicals will affect the property of the nanoparticle and is sometimes not suitable for application to the health sector/ medical field. In biological synthesis, addition of chemicals as capping agents is



**Fig. 2.** a) UV-Vis absorption spectra of AgNPs (Creative Commons CC-BY license (Fu et al., 2021), © by Lung-Ming Fu et. al., MDPI); b) TEM image of AgNPs; c) histogram of obtained AgNPs (Creative Commons CC-BY license (David et al., 2020), © by David L. et. al, Nanomaterials, MDPI); d) FTIR spectra of the silver nanoparticle (reproduced from (Thirunavoukkarasu et al., 2013) after permission, © Elsevier); e) XRD pattern of AgNPs (Creative Commons CC-BY license (Vanaja et al., 2013), © by Vanaja, M et. al, Appl Nanosci, Springer Nature); f) Atomic force microscopy micrograph of synthesized silver nanoparticles (AgNPs) (Creative Commons CC-BY license (Kumar CMK et al., 2016), © by Kumar CMK et. al, J Intercult Ethnopharmacol, SAGEYA).



**Fig. 3.** a) Schematic representation of biosynthesis of nanoparticles and capping by various molecules (reproduced from (Sidhu et al., 2022) after permission. © American Chemical Society); b) Illustration of green synthesis of AgNPs from plants (Zafar et al., 2019).



**Table 2**  
List of various balancing agents used for the fusion.

S. no	Capping agent	Nanoparticle synthesized	Size of the particle	Ref.
1	Triethanolamine (TEA)	ZnO	20–30 nm	(Chugh et al., 2021)
2	Oleic acid	ZnO	4–5 nm	
3	Thioglycerol	ZnO	3 nm	
4	Oleic acid	Ag	13.5 nm	(Singh et al., 2009)
5	Polyacrylic acid	Ag	122.4 nm	(Li et al., 2013)
6	Hexadecyl amine	Au	4.5–12 nm	
7	β-Glucose	Au	5–13 nm	
8	Tyrosine	Au	45 nm	
9	4-Hexadecylaniline	Au	4.2 nm	
10	Ethylene diamine tetra acetic acid	ZnO	20–25 nm	(Dumur et al., 2011)
11	Triethanolamine	ZnO	25–30 nm	
12	Tetraethylammonium Bromide	ZnO	20–25 nm	
13	Ethylene diamine tetra acetic acid	CdTiO <sub>3</sub>	35–50 nm	(Dobbelstein, 1975)
14	Polyvinylpyrrolidone	CdTiO <sub>3</sub>	35–50 nm	
15	Diethanolamine	CdTiO <sub>3</sub>	35–50 nm	
16	sodium dodecyl sulphate	CdTiO <sub>3</sub>	35–50 nm	
17	Ethyl cellulose	NdVO <sub>4</sub>	50–80 nm	
18	Starch	NdVO <sub>4</sub>	<30 nm	(Rahimi-Nasrabadi et al., 2016)
19	Tween 80	NdVO <sub>4</sub>	>30 nm	

not required as the extract of plants or the microorganism itself contains amino acids and other organic substances which act as calibrator (Pedroso-Santana and Fleitas-Salazar 2022, Nguyen et al., 2022, Chugh et al., 2021).

Capping agents or stabilizers modify the surface property of colloidal nanoparticles and make them perfect for application in the biomedical field such as drug delivery and chemotherapy in cancer.

### 7. Uses of silver nanoparticles

Silver nanoparticles are used in textiles, electronics, coatings, medical devices, food preservation, and other industries as antibacterial agents. AgNPs are frequently used for a number of purposes, such as sterilizing sewage treatment and surgical instruments. Silver nanoparticles show definite improvement in modern commercial applications as coatings for cardiovascular implants, central venous catheters, and neurosurgical catheters. Additionally, they have been applied to latex films used as biomaterials for skin regeneration treatments and to monitor the release rate of nanoparticle films. AgNPs are employed in biosensors, which use the content of AgNPs as biological markers to enable quantitative detection. AgNPs are also utilized in other products, such as clothes and shoes. Additionally, AgNPs are used in plastics, paints, cosmetics, appliances, treatments for cuts and scrapes, and clothing.

Composite systems contain AgNPs, that are utilised to increase conductivity in conductive tinting. AgNPs are used in optical applications for improved metal fluorescence (MEF), better optical spectroscopy, and effective data collection. They also provide superficial raman dispersion (SERS). They are also used in innovative technology in the fields of optoelectronics, nanoengineering, and nanoelectronics. The main applications of silver nanoparticles are shown in Fig. 4 (Mondal, M.S., et al 2023).

### 8. Aloe barbadensis miller

The *Aloe barbadensis miller* leaf can be partitioned as shown below (Fig. 5).

- Outer layer that encompasses the vascular bundles
- Interior translucent parenchyma containing the aloe gel

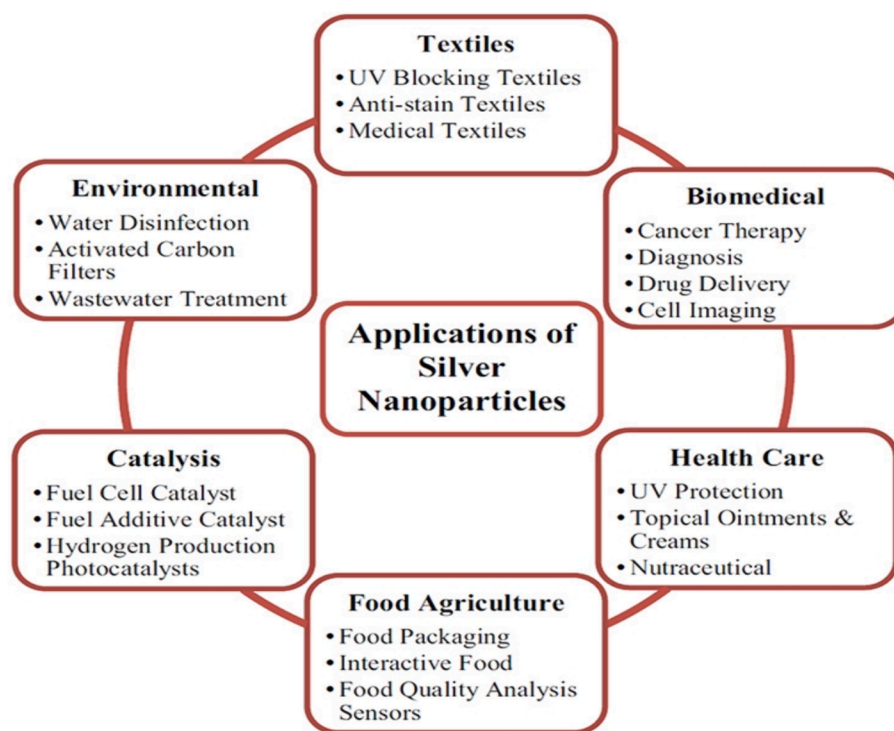


Fig. 4. Various applications of Silver nanoparticles.



Fig. 5. *Aloe barbadensis miller* (Aloe vera) leaves.

The three components of the *Aloe barbadensis miller* pulp are.

- Cell wall
- Deteriorated organelles
- Viscous fluid contained within the cells

The inner gel contains 99 % water, and the remaining part is made of glucomannans, amino acids, steroids, etc. The intermediate layer consists of anthraquinones and glycosides, and the outer layer is composed of carbohydrates and proteins (Hosseinpour-Mashkani and Sobhani-Nasab, 2017). It has components in the form of the chemical composition of crude fiber, crude fat, and ascorbic acid. *Aloe barbadensis miller* has gained significant attention for minimizing the side effects caused by conventional chemotherapy. The most important substances that are responsible for the effects are cinnamic acid, barbalonia, calcium, aloe, etc. (Surjushe et al., 2008, Vega-Gálvez et al., 2014). Aloin, a main ingredient in aloe, has been effective in therapeutic applications in cancer. The US Food and Drug Administration legalized the developmental study of *Aloe barbadensis miller* for HIV/AIDS. *Aloe barbadensis miller*, combined with cisplatin, has been shown to have antineoplastic effects on cervical and breast cancer cells (Guo et al., 2016). The potential anticancer activity of *Aloe barbadensis miller* leaf extract is owing to the occurrence of anthraquinones. Numerous compounds present in *Aloe barbadensis miller* that contribute to diverse biological activities are listed in Table 3.

These compounds are included in different classes such as Anthraquinones/anthrones, Carbohydrates, Chromones, Enzymes, Inorganic compounds, Vitamins, Saccharides, Proteins etc. Table 4 gives the recent research that uses the Aloe vera leaves to produce AgNPs with their biological activity (fungi, virus, and bacteria).

### 9. Biosynthesis of silver nanoparticle and anticancer activity

The biological synthesis of AgNPs displays significant anticancer activity against certain cancer cell lines. Nanoparticles are safe at lower doses and cause extremely toxic effects in higher doses. The synthesised silver nanoparticle can selectively kill the cancer cell lines and enable cytotoxicity. In conventional therapy of cancer treatment, the normal cells may also die due to the over dose of medicine, unpredictable side effects, toxicity of the medicine etc. The application of biologically

Table 3  
Compounds and biological activity.

S. no	Name of compound	Biological activity	Ref.
1	1-Heptanol, 2-propyl-	Antimicrobial	(Hussain et al., 2015, Hamman 2008, Radha and Laxmipriya, 2015)
2	(4,7-Dinitronaphthalen-1-yl) –(4-methoxyphenyl) diazene	Antimicrobial	
3	Tetra decanoic acid	Cancer preventive	
4	Hexadecenoic acid, methyl ester	Antioxidant	
5	1,2-Benzenedicarboxylic acid, butyl octyl ester	Antimicrobial	
6	n-Hexadecenoic acid	Antioxidant	
7	11,14-Eicosadienoic acid, methyl ester	Hypocholesterolaemia	
8	Oleic Acid	Anti-inflammatory and cancer preventive	
9	1,2-Benzenedicarboxylic acid, diisooctyl ester	Antifouling	
10	Squalene	Anti-bacterial and cancer preventive	

Table 4  
Aloe vera leaves used to produce AgNPs with their biological activity.

Aloe vera leaves AgNPs	Biological activity	Analysis	Ref.
	Anti-fungal activity	This study demonstrated that the high antifungal activity of the synthesised AgNPs was evaluated against to <i>Aspergillus flavus</i> and <i>Aspergillus terreus</i> strains (excellent antifungal activity).	(Ahmadi et al., 2019)
	Anti-cancer activity	This study highlights the production of an excellent SERS substrate featuring octahedron-shaped AgNPs, synthesised through microwave heating with Aloe vera gel, which serves as an effective agent for controlling size and shape.	(Logaranjan et al., 2016)
	Anti-bacterial activity	The antibacterial activity of the synthesised AgNPs was tested using <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> bacteria and the obtained results indicated their significant inhibitory effects against these two Gram-negative and Gram-positive bacteria.	(Ahmadi et al., 2018)

synthesised AgNPs may overcome the disadvantages of conventional therapy in cancer treatment. Thus, different plant species are used as steadying agents and reducing agents to produce AgNPs, and the synthesised nanoparticle can be successfully applied to different cancer cells.

The tiny size and multiple modes of cell death of AgNPs make them special candidates for cancer treatment. AgNPs cause chromosomal instability, oxidative stress, and double-stranded DNA disruption, all of which lead to cell death. AgNPs of smaller sizes (10 nm) generate cellular toxicity at higher levels because they enter the cell more easily and localize inside the nucleus, while larger AgNPs (100 nm) more efficiently produce these outcomes than smaller AgNPs. According to reports, AgNPs cause cytotoxicity in mammalian cells through a number of different mechanisms, including (a) The absorption of free silver ions causes suspension to energy-dependent cellular processes and DNA replication, which results in compromised cellular functions; (b) production of reactive oxygen species (ROS) and free radicals; (c) cell membrane impairment resultant due to direct interaction with AgNPs (Mei et al., 2020). Cell death is caused by ROS which are created when

green-synthesis AgNPs are present. ROS production is detrimental to the pathways that cause cell apoptosis. Hydrogen peroxide production alters the membrane potential of mitochondria resulting in the uncoupling of respiration (Avalos et al., 2016).

AgNPs activate nuclear factor kB (NF-kB), produce ROS, lower glutathione (SGH) levels, and produce tumor necrosis factor-alpha (TNF-alpha) when they enter the cell. The increased levels of superoxide radicals change the potential of the mitochondrial transmembrane and disrupt the signaling system, which leads to apoptosis and cell death (Fani et al., 2016, Nishanth et al., 2011). Biological components are harmed by increased ROS generation and decreased GSH, which results in lipid membrane peroxidation, protein carbonylation (a harmful oxidation of proteins), and DNA breakage. Moreover, altered mitochondrial membrane potential triggers the activation of caspases 3 and 9, which kill cells. It triggers the activation of the enzyme c-Jun NH<sub>2</sub> terminal kinase (JNK), which results in the production of apoptotic bodies, and breaks DNA, causing cell cycle arrest (Verano-Braga et al., 2014).

Folkman's theory states that angiogenesis, or the creation of new blood vessels, is what leads to the development of tumors. According to this theory, a tumor's blood supply affects how easily it can grow and spread. These newly formed blood vessels give cancer cells oxygen and nourishment, which allows them to spread to surrounding tissues. Biologically synthesized AgNPs showed effectiveness against a condition similar to retinal neovascularization (RNV). AgNPs inhibited the activation of extracellular signal-related kinase (ERK1/2) and decreased the RNV convinced by vascular endothelial progress factor by regulating the phosphorylation of receptor 2. AgNPs have been used in the treatment of cancer because of their anti-angiogenic characteristics (Ratan et al., 2020).

Proposed mechanisms for the anticancer action of green synthesized AgNPs include the upregulation of caspase 3 and activation of the p53 protein, pH-dependent relief of silver ions, discerning assassination of cancerous cells, and inhibition of Vascular endothelial growth factor (VEGF) induced activities. Apoptosis is induced by caspase-dependent and mitochondrial-dependent pathways, cell cycle arrest in the sub-G1 phase, the generation of ROS, and disruption of cellular equilibrium (Halawani et al., 2020, Lee et al., 2019). AgNPs that are produced sustainably emit silver ions, which can be used as a visual cue that cancer cells are dying. Consequently, the amount of silver ions released within the cells directly leads to the destruction of malignant cells, one by one.

Normal cell lines release silver ions differently from cancer cell lines because of pH differences. The release of silver ions is also influenced by the electrostatic contact between healthy and malignant cells (Gurunathan et al., 2015). Due to their anti-angiogenic effectiveness, green-synthesised AgNPs have been proposed as a novel avenue for the treatment of cancer. AgNPs' anticancer potential has been explained by yet another theory. This process includes the breakdown of cells brought on by autophagy, which ends in cell death. Additionally, because autophagolysosomes accumulate in cancer cells and are more prevalent there, greenly produced AgNPs encourage autophagy, which ultimately results in cell death (Shi et al., 2017). A possible mechanism of action of AgNPs in cancer cells is shown schematically in Fig. 6 (Khan et al., 2018).

## 10. Green synthesized AgNPs using *Aloe barbadensis miller* and its activity against MCF-7 breast cancer cell lines

The aqueous leaf extract of Aloe vera leaves and 1 mM aqueous solution of AgNO<sub>3</sub> solution were used to synthesize AgNPs, which appears to be brownish colour and the UV-Vis spectral analysis confirmed the production of AgNPs by showing a peak at 420 nm (Alwhibi et al., 2021). FTIR Spectroscopy of synthesised silver nanoparticle using Aloe vera leaf extract shows peak at 1386.4 cm<sup>-1</sup> (geminal methyls), 1587.6 cm<sup>-1</sup> (C = C groups or from aromatic rings), and 1076 cm<sup>-1</sup> (ether linkages) all point to the potential existence of terpenoids or flavanones on the surface of synthesised AgNPs (Logaranjan et al., 2016). The size, shape and surface morphology of the synthesised AgNPs can be found out by SEM and TEM. Reports suggest that the size of the nanoparticle is about 20–40 nm (Mustafa H. N and S. mohammed, 2023). Biogenic silver nanoparticles were synthesized using the extract of aloe vera as a potent bio-reducer. Spherical shaped nanoparticles were observed and they exhibit anticancer activity against MCF- human breast cancer cell lines. Further in vivo investigations and clinical trials are required to address the formulation of biogenic silver nanoparticles as an environmentally friendly and biocompatible alternative to conventional anticancer medications. It induced detrimental impacts of the numerous cellular components in the malignant cells (Basak et al., 2018).

Aloe-emodin, an anthraquinone present in *Aloe barbadensis miller*, is recognized for triggering apoptosis (programmed cell death) in cancer cells. It curtails the growth of these cells by disrupting the cell cycle and promoting apoptosis through the activation of caspases, which are

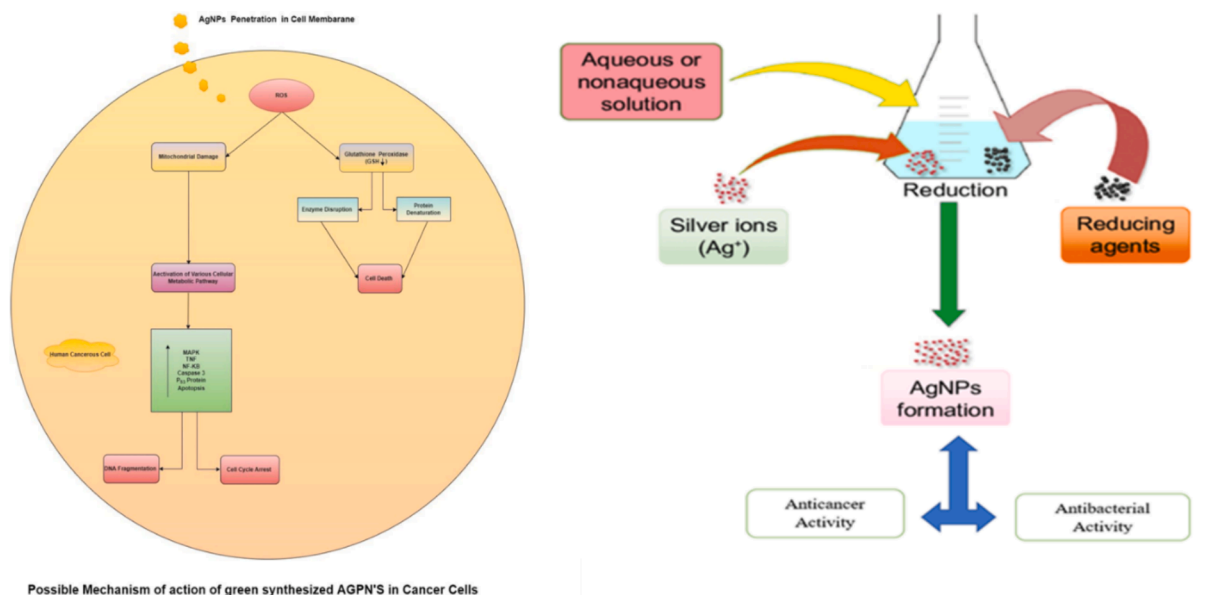


Fig. 6. Possible mechanism of action of AgNPs in cancer cells (Creative Commons CC-BY license (Khan et al., 2018), © by Shahid Ullah Khan et. al, Dove press, UK).



enzymes crucial for programmed cell death (Shalabi et al., 2015). Acemannan, a polysaccharide derived from *Aloe barbadensis miller* leaves, boosts the immune system by increasing the activity of macrophages and the production of cytokines, both of which are vital for the body's defense against cancer cells (Liu et al., 2019). *Aloe barbadensis miller* gel is rich in bioactive compounds, including vitamins, minerals, enzymes, and amino acids, which together enhance its therapeutic benefits. It has antioxidant properties that protect cells from oxidative stress and DNA damage, both of which are associated with cancer development (Tong et al., 2021).

Lab studies on cell cultures have shown that *Aloe barbadensis miller* can potentially inhibit the growth of different cancer cell lines, including breast, liver, lung, and colon cancer cells. Few clinical trials have been conducted on humans. Some studies have reported that *Aloe barbadensis miller*, when used as a complementary treatment, can improve the quality of life and reduce tumor-related symptoms in cancer patients. However, more extensive clinical trials are necessary to validate these results. *Aloe barbadensis miller* appears promising as a complementary cancer therapy because it can boost immune function, trigger apoptosis, and guard against oxidative stress. Although preclinical studies are promising, more extensive clinical trials are needed to confirm its effectiveness and safety for cancer patients.

## 11. Conclusion

There are numerous uses for AgNPs in the industrial and biological domains. This review article examined and emphasized the significance of the following:

- 1) The biological synthesis of AgNPs.
- 2) AgNP synthesis using plant extract.
- 3) AgNPs application in breast cancer cells.

A number of successful research studies on AgNPs show their effective anticancer activity. Nonetheless, given that AgNPs are extremely toxic and should be used with caution in the medical field, there are some fundamental worries about their toxicity. The biological synthesis of AgNPs lowers the material's toxicity, allowing for its potential use in the biomedical field. Various studies prove that it can also be used as a drug carrier in therapy for different cancers. With an emphasis on extraction, this review article discussed the green production of AgNPs utilizing *Aloe barbadensis miller* leaves. Lastly, a great deal of research is needed to analyze the toxicity and anticancer effects of nanoparticles in order to prepare clinical trials and cancer drugs.

Future research ideas or directions on AgNPs show exceptional promise but need to be pursued actively if they are to be successful. The creation of AgNPs with single, dual, or multiple functions is the initial direction. Consequently, this type of drug delivery system will be more effective in treating cancer due to its multifunctional actions. Clinical translation will benefit more from the use of multifunctional nanoparticles with one or more targeting, imaging, sensing, and therapeutic applications.

## CRediT authorship contribution statement

**S. Sudhimon:** Writing – original draft, Methodology, Formal analysis, Conceptualization. **M. Mukesh Kumar:** Visualization, Resources, Data curation. **S. Yamini:** Writing – original draft, Resources, Methodology. **T. Anjana Devi:** Visualization, Validation, Supervision. **S. Sumathi:** Supervision, Software. **J. Sudagar:** Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization.

## Declaration of competing 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.

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## Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jksus.2024.103317>.

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