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Nature's Nano Toolbox: Leveraging Plant Extracts and Silver Nanoparticles for Innovative Biological Applications: A Review

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Abstracts:

The progress in medical science has been significantly propelled by the advancements in nanotechnology, offering ground breaking solutions to combat life-threatening diseases. Nanotechnology represents a significant milestone with diverse applications across various sectors such as electronics, textiles, and particularly in healthcare. Nanotechnology is pivotal in healthcare due to its significant contributions in precision medicine applications such as targeted therapy, diagnostic techniques, therapeutic interventions and biomedical sensing all of which enhance human well-being. Nanoparticles serve as an extremely promising framework for a wide range of biomedical uses, showcasing their immense potential in revolutionizing medical treatments and interventions. The emergence of eco-friendly technologies for the biosynthesis of nanoparticles represents a significant stride within the realm of nanotechnology. This development intersects with the broader domain of materials science, particularly in the manipulation of atomic structures to confer distinct properties and facilitate diverse bio-applications. Among metal nanoparticles, silver nanoparticles stand out due to their remarkable physical, chemical and biological attributes. In this context, green chemistry has surfaced as a viable alternative to conventional synthesis methods for nanoparticles. Among the array of green approaches, leveraging plant extracts for nanoparticle synthesis garners particular attention. This preference stems from the rich diversity of biomolecules inherent in plants, which serve not only to reduce nanoparticles but also to act as stabilizing and capping agents, thereby expediting reaction kinetics. In contrast to microbial cultures, plants offer ease of handling, wide distribution and ready availability. The present review delves into the varied plant species suitable for rapid, one-step protocols in silver nanoparticle synthesis. Additionally, it delineates the multifaceted bioactivities exhibited by these nanoparticles, encompassing antibacterial, antifungal, antioxidant, antiviral, anticancer and anti-diabetic properties.

Keywords: silver, nanoparticles, antioxidant, antiviral, anticancer, diabetes

Highlights:

1. The review explores the green approach to synthesizing silver nanoparticles using phytoconstituents.
2. The review emphasizes the potential of plant-based silver nanoparticles in combating, cancer, viral infections, autooxidising properties, in treatment of diabetes and detailing their mode of action.
4. It summarizes the therapeutic prospects and future challenges associated with these nanoparticles.

Introduction:

Nano science and nanotechnology are interdisciplinary domains dedicated to investigating and controlling matter at the nanoscale, typically ranging from 1 nm to 100 nano meters. These fields are pivotal in scientific exploration and technological innovation. In his ground-breaking 1959 speech to the American Physical Society, physicist Richard Feynman underscored the vast possibilities of manipulating matter at the atomic level [1]. Subsequently, Professor Norio Taniguchi coined the term "Nanotechnology" in the pursuit of ultra-precise fabrication. Historical significance of Silver dates back thousands of years, with civilizations like the Egyptians, Persians, Greeks and Romans utilizing it in various forms for food storage. Its antimicrobial properties led to widespread use in daily life, documented as far back as 300 BC. Even today, Hindu rituals involve the use of silverware for preparations such as "Panchamrit." The ancient Indian text Charak Samhita also mentions the therapeutic properties of metals [2]. Nanotechnology has emerged as a transformative force across various sectors including electronics, textiles and healthcare. In the medical field, nanotechnology offers ground breaking solutions such as targeted drug delivery, diagnostics and bio sensing, particularly crucial in combating life-threatening diseases like cancer and viral infections [3].

The advent of nanoparticles has sparked a paradigm shift across various scientific domains, particularly in biomedical engineering, attributable to their remarkable properties [4]. Unlike their macroscopic counterparts, nanoparticles possess an exceptionally high surface-to-volume ratio and exhibit distinct optical [5], electronic and magnetic properties [6]. This characteristic renders them amenable to precise surface modifications, thereby enhancing pharmacokinetic properties, prolonging vascular circulation lifetime and augmenting bioavailability particularly in drug delivery systems. In the realm of drug delivery, nanoparticles offer unparalleled advantages, including heightened efficacy and reduced dosage requirements. Their capacity for surface modifications facilitates targeted drug administration and enables monitoring of drug release rate in real time. Furthermore, nanoparticles' size-dependent properties, such as optical, electronic and magnetic features, find extensive utility in biomedical applications [7, 8]. Magnetic attributes are harnessed for targeted drug delivery mechanisms and serve as mediators in MRI, while optical properties serve diagnostic functions, acting as substitutes for traditional organic dyes in imaging techniques [9].

Moreover, nanoparticles demonstrate improved specificity for targets and increased permeability through biological membranes, making them highly attractive as drug carriers with the potential for controlled drug release. Ongoing research endeavours are focused on harnessing nanoparticles, electronic, opto-electric, magnetic and optical properties for signal detection, transmission and amplification. Notably, shell structured nanoparticles are gaining traction in biomedical administrations owing to their added benefits and tailored functionalities. Nevertheless, the widespread adoption of nanoparticles is not without challenges, chiefly concerning their potential toxicity to biological systems. Their ability to penetrate cellular membranes and interfere with intracellular metabolic processes raise concerns regarding long-term adverse effects, including the onset of neurodegenerative disorders like Alzheimer's and Parkinson's disease [10]. Furthermore, the lack of effective nanoparticle clearance mechanisms in the body may lead to their accumulation, exacerbating potential health risks over time. Hence, while nanoparticles hold immense promise for scientific innovation, their application necessitates a cautious approach, mindful of their potential biological ramifications. In recent years, silver nanoparticles (Ag-NPs) have garnered significant attention from researchers due to their exceptional properties. These nanoparticles find wide-ranging applications in biomedicine, biology, coatings, antimicrobial activities and agriculture fields. In biomedicine, Ag-NPs are utilized for rapid diagnosis, imaging, tissue regeneration and drug delivery, contributing to the development of novel medical products. Their antimicrobial properties make them valuable as anti-infective agents and water purifiers. Additionally, Ag-NPs are employed in agriculture for their protective effects against microorganisms. This versatility highlights the diverse potential applications of Ag-NPs across different sectors. [11-16]

The versatility and unique properties of metallic nanoparticles, especially silver nanoparticles (Ag-NPs), have garnered significant attention in biomedical applications. Ag-NPs exhibit variable activities such as antimicrobial, antioxidant, antifungal, anti-inflammatory and anticancer properties [17, 18]. Research on Ag-NPs has made significant progress, particularly in their synthesis using green methods, which offer advantages such as safety, eco-friendliness, cost-effectiveness and rapid synthesis. Green synthesis methods utilize plants in many ways that results in well-defined nanoparticles with high yield, solubility, and stability.

In the biomedical field, Ag-NPs s as antimicrobial agents in wound dressings, topical creams to prevent infections and even as anticancer agents [19]. Their unique physicochemical properties, such as size, shape, optical activity and extraordinary surface area ratio, make them highly versatile for various purposes [20]. This article aims to provide an overview of greenly synthesized Ag-NPs, detailing their analysis and applications in life science. It delves into the anticancer and antiviral activities of Ag-NPs, elucidating their mechanisms of action on various cell types. Furthermore, the write-up discusses critical therapeutic and future hurdles in utilizing Ag-NPs for anticancer and antiviral activities.

Literature Review:

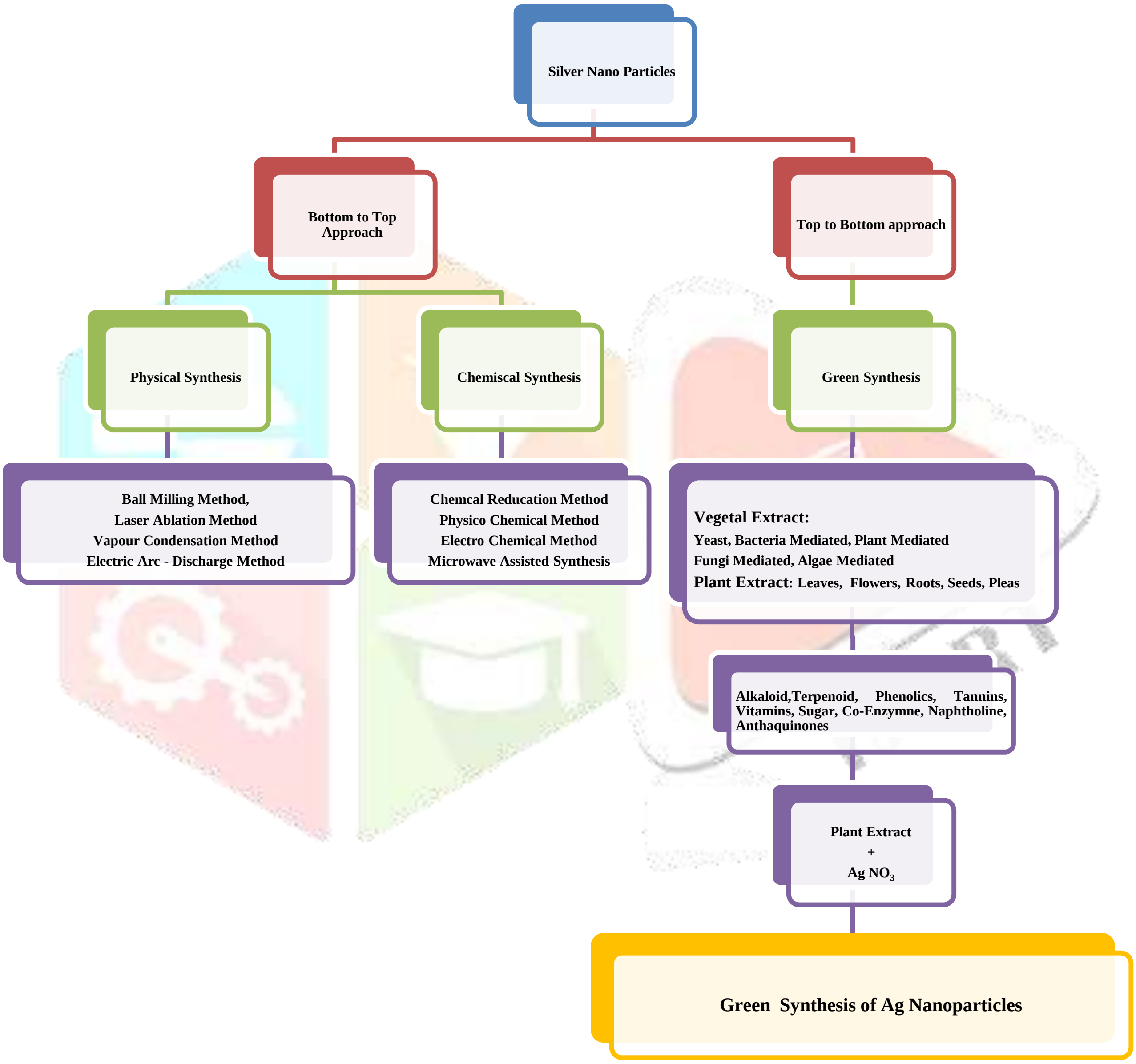
Silver nanoparticles have attracted considerable attention due to their distinctive characteristics and versatile applications. Silver nanoparticles (Ag-NPs) in particular have been extensively researched for their broad-spectrum activities, including antimicrobial, antibacterial [21, 22], antioxidant [23], antifungal [24], anti-inflammatory [25] and anticancer [26] properties. With sizes typically ranging from 10 to 100 nm, Ag-NPs exhibit unique physicochemical characteristics. Plant-mediated synthesis of Ag-NPs offers several advantages, including safety, eco-friendliness, cost-effectiveness and rapid synthesis [27, 28]. Consequently, the green synthesis method of Ag-NPs presents various benefits compared to conventional methods. Silver nanoparticles play a vital role in biomedical applications, particularly as antimicrobial agents in wound dressings, topical creams for wound infection prevention and anticancer agents. These nanoparticles play a vital role in biomedical applications, particularly as antimicrobial and anticancer substances. The unique properties of nano-sized metallic particles enable them to significantly modify their characteristics making them valuable for various purposes. Green synthesis methods produce Ag-NPs with high yield, solubility and constancy. Amongst the different approaches for Ag-NPs, biological procedures are preferred for their simplicity, rapidity, non-toxicity, reliability and environmentally friendly nature, enabling the production of distinct sizes and morphologies in ideal conditions for research purposes [29, 30].

In recent decades, several reviews have been dedicated to exploring the green synthesis of silver nanoparticles. These reviews predominantly highlight the use of various plant extracts such as cherry fruit, aloe leaf, Coffea arabica seeds, Macrodyloma uni-forum, Trianthema decandra and Rosa rugosa, along with biopolymers like chitosan and microbial sources, for Ag-NP synthesis [31]. Numerous characterization techniques, including UV-Vis spectroscopy, Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy-dispersive X-ray spectroscopy (EDX) and dynamic light scattering (DLS), have been used to elucidate the Ag-NPs, tailored for various applications. This review, unlike its predecessors, focuses on elucidating the synthetic methods, parameters, characterization techniques and biomedical applications, including biosensors, antibacterial and anticancer activities, associated with various green synthesis routes for Ag-NPs [32, 33]. The rapid evolution of nanoparticle and nanomaterial applications across diverse fields, such as healthcare, biomedicine, pharmaceuticals, cosmetics, food, environment, optics, electronics, aerospace, energy science, catalysis, chemical industries and nonlinear optical devices, among others, underscores the significance of their unique or enhanced properties attributed to size, distribution and morphology. These advancing technologies have expanded the horizons of application possibilities and laid the foundation for new discoveries. This includes the production of nanoscale materials for exploring their intriguing physicochemical and optoelectronic properties, driving innovation across multiple domains.

Eco-Friendly Synthesis of Silver Nanoparticles Using Plant Extracts:

Plant based silver nanoparticles production has garnered attention due to its rapid, eco-friendly, non-pathogenic and cost-effective nature, enabling one-step biosynthetic processes as given in figure 1.

Figure 1: Synthesis of Ag-NPs through Green synthesis method



The presence of diverse biological molecules in plant extracts, such as proteins, enzymes, amino acids, polysaccharides, alkaloids, phenolics, tannins, saponins, terpenoids and vitamins, facilitates the reduction and stabilization of silver ions. These compounds, which possess medicinal properties, contribute to environmentally friendly chemically complex structures [34-38]. The synthesis protocol entails several steps: first, herbal leaves from the desired plant species are collected from suitable sites and thoroughly rinsed multiple times with tap water to eliminate dust and soil particles. Subsequently, the leaves are washed to remove any remains. Once cleaned, the leaves are dried in the shade for 5-7 days and then pulverized using a domestic blender. To prepare the plant broth, approximately 10g of the dried powder is boiled with 100ml of distilled water [39].

The resultant infusion is meticulously filtered until the broth shows no signs of insoluble substances. When a 10^{-3}M $AgNO_3$ solution is combined with a small quantity of plant extracts, the reduction of pure Ag (I) ions to Ag (0) can be observed, with the progress monitored through regular UV-visible spectrum measurements of the solution [40]. Utilizing herbal leaf extracts, green and rapid syntheses of spherical silver nanoparticles measuring 50-100 nm in diameter have been achieved. The conversion of silver ions into silver nanoparticles using this extract typically occurs within 10-30 minutes. This method offers a rapid, straightforward and cost-effective alternative compared to conventional chemical and biological approaches. This review article aims to explore the potential applications of silver nanoparticles, including their antibacterial, antifungal, antioxidant, antiviral, anticancer and anti-diabetic properties [41].

Green Synthesis:

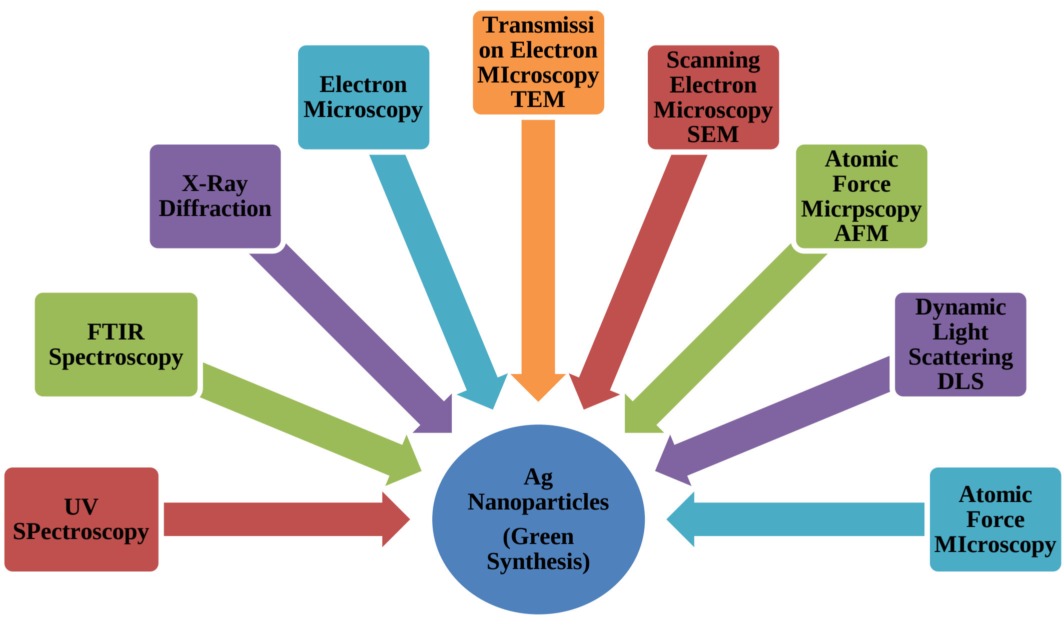
Green synthesis, a biological approach to producing nanoparticles, particularly silver nanoparticles (Ag-NPs), provides substantial benefits compared to traditional chemical and physical methods. This eco-friendly method requires no sophisticated equipment or toxic chemicals, reducing overall costs and environmental impact [42]. The resulting nanoparticles are typically more stable and exhibit desired shapes and sizes. [43,44]. Plant extracts contain a plethora of primary and secondary metabolic biomolecules, such as proteins, amino acids, vitamins, alkaloids, terpenoids, flavonoids and phenols, which reduce silver ions. When plant extracts are mixed with silver nitrate solution, the metabolites undergo oxidation and coat the developing nanoparticles. The process initiates nucleation followed by particle growth, resulting in various nanoparticle shapes [45, 46]. Factors like pH, temperature, extract concentration and reaction time influence nanoparticle synthesis.

Various plant extracts have been utilized for Ag-NP synthesis, demonstrating their efficacy as reducing and stabilizing agents [47]. For instance, Lonicera hypoglauca flower extract, Artocarpus integer leaf extract and Catharanthus roseus extract have been used, showing anticancer activity [48, 49]. Additionally, Clitoria ternatea and Solanum nigrum leaf extracts synthesized Ag-NPs with antibacterial properties, while Abelmoschus esculentus pulp extract produced Ag-NPs with anticancer and antimicrobial activity [50, 51]. These findings highlight the potential of green-synthesized Ag-NPs in drugs.

Characterization of Silver Based Nanoparticles

Various causes affect the properties of silver nanoparticles (Ag-NPs). Numerous methodologies available for analysis of these characteristics of nanoparticles are shown in Fig-2.

Figure 2- Characterization Methods of Green Synthesized Silve Nanoparticles



Various technologies can be used to study the characteristics and properties of silver nanoparticles (AgNPs):

i. **Shape, size, and crystallinity:** X-ray diffraction (XRD) delivers evidence about structure of the crystal and size of Ag-NPs, while scanning electron microscopy (SEM) and transmission electron microscopy (TEM) suggest conception of the shape, size and morphology at different scales.

ii. **Surface charge and coating:** Fourier Transform Infrared (FTIR) spectroscopy helps in analyzing the surface chemistry and functional groups present on the surface of Ag-NPs, which contribute to their surface charge and coating. Dynamic light scattering (DLS) can also provide information about the surface charge and stability of Ag-NPs in solution

i. **Biological activity:** Understanding the biological activity of Ag-NPs often involves assessing their interaction with biological systems. This can be studied using UV spectroscopy to monitor changes in absorbance related to biological interactions, SEM and TEM to visualize interactions at the cellular level and Atomic Force Microscopy (AFM) to study external interactions and mechanical properties.

These technologies collectively offer a comprehensive toolkit for researchers to investigate the various factors influencing the characteristics and properties of Ag-NPs, facilitating their submissions in diverse arenas such as nanomedicine, catalysis and environmental remediation.

UV- Spectroscopy: UV-spectroscopy serves as a fundamental and efficient method for characterizing nanoparticles, offering insights into their constancy and the circumstances under which they are synthesized [52]. This technique exploits the surface resonance (SPR) effect, where free electrons on the nanoparticle surface oscillate under electromagnetic radiation [40]. During the synthesis of silver nanoparticles (Ag-NPs), this process manifests as distinct absorption bands in the visible spectrum, typically within the range of 400–500 nm, resulting in a coloured reaction [54]. For instance, Ag-NPs loaded with curcumin exhibit absorption peaks, corresponding to different concentrations of pure curcumin used in the synthesis process. UV-spectroscopic analysis of green-synthesized nanoparticles from Salvia spinosa extract reveals the spectrum [55]. Moreover, UV-Visible spectroscopy is frequently employed to observe colour changes during the process and quantify reduction of silver ions [56-58].

Fourier Transform Infrared Spectroscopy FTIR: It is a highly dependable analytical technique capable of detecting and illustrating various aspects of molecular composition [60, 61]. In the context of characterizing silver nanoparticles (Ag-NPs), FTIR analysis serves to identify molecules and the reduced silver ions [62]. FTIR spectra often reveal the presence of various functional groups also during the synthesis of Ag-NPs [63]. For instance, Ag-NPs synthesized using from Catharanthus roseus leaf-extract exhibit major peaks at specific wavenumbers, indicating the presence of carboxylic acid, alkynes, ketones, alcohols, amides, phenyl rings, primary and secondary amines [60]. Similarly, FTIR analysis of nanoparticles synthesized with Tectona grandis seeds extract reveals characteristic bands at specific wavenumbers corresponding to stretching vibrations of the C=O bond, the amide bond in proteins and nitro compounds and the C-N amine bond [64]. Greenly synthesized Ag-NPs can be visualized effectively under electron microscopy during the interaction of when the beam of electrons with the nanostructured particles. This technique provides qualitative and quantitative information about Ag-NPs [62, 63].

Electron Microscopy: Electron microscopy stands out as a pivotal technique in the realm of nanotechnology for discerning nanoparticle morphology. When subjected to the electron beam, greenly synthesized Ag-NPs (silver nanoparticles) exhibit visualizations that unveil their nanostructured composition. This approach facilitates the qualitative and quantitative analysis of Ag-NPs, furnishing insights into crucial parameters such as size, shape, size distribution and dry diameter distribution. By leveraging electron microscopy, researchers can delve into the intricate details of nanoparticles, thereby advancing our understanding and utilization of these minuscule entities in various fields [62, 63].

Scanning Electron Microscopy:

It is instrumental in visualizing surface morphology of samples, operating on the principle of electron reflection from the sample's surface. This technique offers high-resolution images that provide a wealth of information including structural details, conductivity and other pertinent properties. Numerous instances of AgNPs synthesis have been considered using SEM [65]. For instance, SEM analysis of Acetyl-11-keto-β-boswellic acid-mediated AgNPs revealed spherical AgNPs ranging in size from 6 to 70 nm. AgNPs synthesized with Glycyrrhiza glabra root extract ranged in particle diameters from 20 to 30 nm, whereas those synthesized with Artemisia turcomanica leaf extract measured approximately 21.22 nm in diameter [66]. Additionally, field emission scanning electron microscopy (FESEM) of Tectona grandis seed extract loaded with silver nanoparticles revealed oval and spherical nanoparticles in sizes ranging from 10 to 30 nm. This analysis confirmed the face-centered cubic crystalline structure of silver. Such detailed characterization underscores the versatility and effectiveness of SEM in elucidating the morphological attributes of AgNPs synthesized through various methods [67].

XRD analysis: This method serves as pivotal technique for characterizing the crystallinity of Ag-NPs. In XRD, X-rays impinge upon the surface of a crystal and interact with its atoms, resulting in a diffraction pattern that unveils the atomic arrangement and crystalline structure. XRD allows researchers to determine the crystalline structure of nanoparticles. By analysing the diffraction pattern produced when X-rays interact with the atoms in the nanoparticles, XRD delivers evidence about the arrangement of atoms in the crystal lattice [68]. The position and intensity of diffraction peaks in the XRD pattern provides valuable insights into the size and shape of nanoparticles. By analysing peak positions and their intensities, researchers can determine the average particle size and distribution within the sample. XRD can identify different phases present in the sample. This is particularly useful when nanoparticles are synthesized using complex methods or when impurities or secondary phases are present [69]. By comparing the experimental XRD pattern with reference patterns from databases, researchers can identify the composition and purity of the nanoparticles. XRD can assess the degree of crystallinity of nanoparticles. Amorphous or poorly crystalline materials exhibit broad diffraction peaks, while highly crystalline materials display sharp and well-defined peaks. This information is crucial for understanding the structural properties of nanoparticles and their potential applications. XRD analysis can be used for quality control purposes during nanoparticle synthesis. By monitoring changes in the XRD pattern during different stages of synthesis, researchers can ensure that the desired crystalline structure and properties are achieved [70].

Overall, XRD analysis provides comprehensive information about the structural properties of nanoparticles, including their crystalline structure, size, shape, phase composition and crystallinity. This information is crucial for grasping the characteristics and behavior of nanoparticles, as well as for refining their synthesis and applications across fields like materials science, nanotechnology and biomedical engineering. In various research endeavours, XRD has been employed to ascertain the crystallinity of greenly synthesized Ag-NPs [62, 63]. For instance, Ag-NPs synthesized using the aqueous leaf extract of Urtica dioica Lin exhibited a crystalline structure with an average particle size of approximately 25 nm. The XRD analysis revealed strong reflections at 38.45°, 46.35°, 64.75°, and 78.05°, corresponding to the 111, 200, 220, and 311 crystalline planes respectively [68].

Similarly, XRD patterns of Ag-NPs prepared using Pedalium murex leaf extract displayed, with an average size of 14 nm [71]. Moreover, XRD analysis of silver nanoparticles synthesized using the leaf extract of Clitoria ternatea showcased intense peaks at specific angles, indicative of crystalline silver. Likewise, silver nanoparticles synthesized with the leaf extract of Solanum nigrum displayed distinct peaks in the XRD pattern, further corroborating the crystalline nature of the synthesized nanoparticles. These findings underscore the utility of XRD in elucidating the crystalline structure and characteristics of Ag-NPs synthesized through various green methods, thereby enhancing our understanding of their properties and potential applications [72].

Transmission Electron Microscopy (TEM): It offers direct visualization of nanoparticles through high-resolution images generated from transmitted electrons. This technique enables researchers to observe individual nanoparticles and their interactions with surrounding materials, providing crucial insights into their structural and chemical properties. TEM allows for detailed examination of nanoparticle morphology, including size, shape and geometry, which is essential for understanding their properties and applications. Additionally, TEM can be used to investigate the crystalline structure of nanoparticles, measure size distribution and analyse chemical composition using techniques like energy-dispersive X-ray spectroscopy (EDS) or electron energy loss spectroscopy (EELS). Overall, TEM is a versatile and powerful tool for studying nanoparticles, contributing to advancements in various fields such as nanotechnology, materials science, catalysis, biomedicine and environmental science.

In nanoparticle research, TEM has been extensively utilized for the characterization of silver nanoparticles produces by green chemistry synthesis. Various studies have employed TEM to visualize Ag-NPs synthesized using leaf extracts of Viburnum lantana, Couroupita guianensis, Malachra capitata, and Lysiloma acapulcensis [62]. For instance, Ag-NPs prepared from these leaf extracts exhibited size ranges of 20–70 nm, 25–40 nm, 30–35 nm, and demonstrated predominantly spherical shapes, respectively [73-75]. TEM analysis of Ag-NPs loaded with Lysiloma acapulcensis extract revealed a crystalline structure with visible lattice fringes. TEM's capability to directly visualize nanoparticles and their interactions with the electron beam makes it a preferred technique for studying AgNP formation. Its high resolution allows for the detection and analysis of core structure, diameter, size, shape and other essential characteristics of nanoparticles. Overall, TEM stands as a crucial tool in nanoparticle research, offering invaluable insights into their morphology and properties [63].

Atomic force microscopy: This technique is a unique method for analysing nanoparticles, including nano particles. By utilizing a phosphorus-doped silicon probe, AFM enables the examination of size, surface morphology, mechanical properties and other physical characteristics of nanoparticles. In the case of silver nanoparticles (AgNPs), AFM analysis involves preparing a sample by dissolving AgNPs in a solvent, depositing the solution onto a silicon substrate and allowing it to dry. The dried sample is then analyzed using AFM to obtain information about nanoparticle size and distribution. Studies on tamoxifen-loaded Ag-NPs using AFM have revealed an average size range of 17.5 ± 2.5 nm [62]. Overall, AFM serves as a valuable tool for nanoparticle characterization, offering high-resolution imaging and precise measurements that helps in better understanding of their properties and possible applications. Atomic force microscopy (AFM) is a valuable technique for analysing the size, surface morphology, mechano-structural and physical properties of materials, including nanoparticles [63]. In the context of characterizing silver nanoparticles (Ag-NPs), AFM provides insights into their size distribution and surface characteristics.

For characterization using AFM, a sample containing Ag-NPs is typically prepared by dissolving them in a solvent such as water or ethanol. A droplet of this solution is put onto a silicon film and left to dry, creating a thin coating containing the nanoparticles. Subsequently, AFM analysis is conducted by scanning the silicon substrate surface with a phosphorus-doped silicon probe. Studies utilizing AFM for analysing tamoxifen-loaded Ag-NPs have demonstrated an average size range of 17.5 ± 2.5 nm. This information not only provides details about the size of the nanoparticles but also offers insights into their distribution and morphology [77]. Overall, AFM serves as a valuable tool for the characterization of nanoparticles, offering high-resolution imaging and precise measurements of their physical properties.

Biological Applications and Biopotential of Silver Nanoparticles:
Antibacterial and antifungal activity:

Recently, there has been growing interest in the utilization of silver nanoparticles for their antibacterial and antifungal properties [78]. These particles have demonstrated increased antibacterial efficacy against Gram-negative bacteria, with sheet-like RuO_2 nanomaterials exhibiting a more pronounced inhibitive effect compared to spherical types. The unique bactericidal mechanisms of silver nanoparticles, along with their ability to penetrate bacteria, make them effective in combating antibiotic-resistant infections. Furthermore, silver nanoparticles have also been found to inhibit the formation of biofilms, which are a major challenge in eliminating bacterial infections [79]. Silver nanoparticles have been extensively studied and have demonstrated outstanding antimicrobial properties, particularly against biofilms. These properties make them a potential substitute treatment for reducing the severity of diseases caused by Pseudomonas aeruginosa infections. Overall, the use of silver nanoparticles shows great promise in the field of medication and hygiene. Furthermore, the use of nanomaterials, particularly metal nanoparticles and their nanocomposites, has emerged as a promising solution in eliminating bacterial biofilms

The escalating challenge posed by antibiotic-resistant bacteria from genera such as Escherichia, Streptococcus, Salmonella and Pseudomonas has become a pressing medical concern. In this pursuit of novel biotherapeutics, silver nanoparticles (Ag- NPs) have emerged as a promising weapon against pathogens. Extensive research has confirmed the efficacy of Ag-NPs in inhibiting growth and inducing the demise of various pathogenic microorganisms responsible for a spectrum of human diseases worldwide. The continuous antibacterial effect of Ag-NPs is attributed to their ability to bind to diverse biomolecules within microorganisms. Plant extracts have emerged as an invaluable resource for AgNP production, often possessing inherent therapeutic properties and serving as effective capping agents. Table 1 highlights a fraction of the established antibacterial effects of nanoparticlessynthesized from different plant extracts.

Table 1: Antimicrobial Properties of Silver Nanoparticles Derived from Various Plant

Plant Extract	Microbes	References
Euphorbia hirta leaf extract	C. albicans, C. kefyr	**79**
Adathoda vasica leaf extract	V. parahaemolyticus	**80**
Citrus limon leaf extract	F. oxysporum, Alt. brassicicola	**81**
Bergenia ciliate leaf extract	A. fumigatus, F. solani, A. niger, A. flavus, S. aureus, E. aerogenes, B. bronchiseptia	**82**
Svensonia hyderobadensis leaf extract	Fusarium, Rhizopus, Proteus, A. flavus, A. niger	**83**
Rhinacanthus nasutus leaf extract	St. aureus, B. subtilis, Ps. aeruginosa, E. coli, K. pneumonia, A. niger, A. flavus	**84**
pu-erh tea leaves	E. coli, K. pneumoniae, S. typhimurium, S. enteritidis	**85**
Neurada procumbens leaf extract	K. pneumoniae, Acinetobacter baumannii	**86**
Melissa officinalis leaf extract	S. aureus, Escherichia coli	**87**
Usnea longissima extracts	St. aureus, Str. Pyrogenes, Str. Viridans, Corynebacterium xerosis	**88**
Boerhaavia diffusa	Aeromonas hydrophila, Pseudomonas fluorescens and Flavobacterium branchiophilum	**89**
Aloe vera	E. coli	**90**
Cucumis sativus plant extract	M. tuberculosis	**91**
Vigna radiata	S. aureus, Escherichia coli	**92**
Solanus torvum	P. aeruginosa, S. aureus, A. flavus and Aspergillus niger	**93**
Ipomea patatas	Vibro cholera, protus mirabilis	**94**
Green tea	Klebsiella pneumonia, Pseudomonas aeruginosa	**95**
Green tea	*Bacillius subtilis, Escherchia coli, Staphylococcus aures and streptococcus pyogenes*	**96**
Abutilon indicum	S. typhi, E. coli, S. aureus and B. substilus	**97**
Cymbopogan citratus	P. aeruginosa, P. mirabilis, E. coli, Shigella flexaneri, S. somenei and Klebsiella pneumonia	**98**
Argimone mexicana	Escherichia coli; Pseudomonas aeruginosa; Aspergillus flavus	**99**

Bioactivity: Anti cancerous Potential

Plant-based silver nanoparticles have emerged as promising agents for effectively combating cancer by targeting the hallmark characteristic of cancer cells: their evasion of apoptosis or programmed cell death, which allows them to continue proliferating. Two main signalling pathways are convoluted in activating apoptosis [100]. However, cancerous cells often lack apoptosis, making it a focal point for cancer therapy development. Silver nanoparticles can exert anticancer effects through several mechanisms. Silver nanoparticles can induce programmed cell death in cancer cells. By disrupting mitochondrial function and increasing the levels of reactive oxygen species, they can trigger apoptotic pathways [101]. Silver nanoparticles can further catalyse the production of ROS within cancer cells, leading to oxidative stress, which can damage cellular components such as DNA and proteins, ultimately leading to cell death [102]. The increased ROS can cause significant damage to the DNA within cancer cells, preventing their replication and causing cell death [103]. Silver nanoparticles may interact with the lipid bilayer of diseased cell or death. They can affect the signalling pathways that regulate cell division, hindering the proliferation of cancerous cells [104].

However, the exact anticancer mechanisms of silver nanoparticles can vary depending on their size, shape, coating and the cellular environment. Further studies are underway to comprehend these mechanisms better and to harness silver nanoparticles potential in cancer therapy. It's important to note that while silver nanoparticles hold promise for cancer treatment, their safety and efficacy need thorough evaluation before they can be widely adopted in clinical settings. Silver nanoparticles synthesized using a bioactive part of Pinus roxburghii have demonstrated cytotoxic activity against cancer cells. These nanoparticles trigger apoptosis via the intrinsic pathway by inducing mitochondrial depolarization and damage of the DNA. They also rise the reactive oxygen species levels ultimately leading to cancer cell death. Similarly, silver nanoparticles synthesized with Phyllanthus emblica leaf extract display anticancer activity against hepatocellular carcinoma (HCC) [105-107].

Liposomes containing silver nanoparticles (Lipo-AgNP) induce cytotoxicity by generating ROS and causing DNA damage, ultimately leading to cell death in macrophages. Biologically synthesized silver nanoparticles exhibit antimicrobial and anticancer effects against breast cancer cell lines and Ehrlich ascites carcinoma in mice. These nanoparticles induce apoptosis through various mechanisms, including endoplasmic reticulum stress and modulation of apoptotic proteins [108]. Silver nanoparticles of different sizes have also demonstrated anticancer effects at the G2/M phase and regulating apoptotic proteins such as P-53, Bax, and Bcl-2. Additionally, silver nanoparticles synthesized with plant extracts like Cynara scolymus, Moringa oleifera, Tropaeolum majus, Gloriosa superba and Teucrium polium have shown cytotoxicity against various cancer cell lines. These nanoparticles modulate mitochondrial apoptosis, generate ROS and regulate apoptotic proteins, ultimately leading to cancer cell death. Overall, plant-based silver nanoparticles hold significant potential as effective anticancer agents, offering various mechanisms to induce apoptosis and combat cancer cell proliferation [109-111].

Table 2 highlights a fraction of the established anticancerous effects of silver nanoparticles synthesized from different plant extracts.

Type of Cancer	Name of the Plant/Plant part	References
Human Breast Cancer	Artocamphus integer (leaf)	[112]
	Cynara scolymus (leaf)	[113]
	Annona squa- (Leaf)	[114]
	Camellia Sinen-sis Green tea (leaf)	[115]
	Couroupita(leaf)	[116]
	Glycyrrhiza (root)	[117]
	Juglans regia walnut fruit	[118]
	Lonicera (flower)	[119]
Human T-cell lymphoma	Abelmoschus esculentus (pulp)	[120]
Prostate cancer cells	Alternanthera sessili (leaf)	[121]
Gastric cancer cells	Artemisia tur- comanica 9leaf)	[122]
Hepatic cancer	Asafoetida (gum)	[123]
	Myrtus com- munis	[124]
Lung Carcinoma	Bauhinia (leaf)	[125]
Human Skin Cancer	Boswellia serrate (bark)	[126]
	Gelsemium semperviren (whole plant)	[127]
	Hydrastis canadensis (whole plant)	[127]
	Phytolacca decandra (whole plant)	[127]
	Thuja occiden-talis(whole plant)	[127]

Biopotential: Antiviral Activity:

Throughout human history, viruses have emerged as formidable pathogens, posing significant health threats. Their pathogenicity typically involves attachment and entry into host cells, wherein viral proteins interact with cell membrane ligands and proteins. Disrupting this binding process represents a key strategy for preventing cell infection. Silver nanoparticles have been observed to initiate the apoptotic pathway, producing reactive oxygen species that demonstrate in vitro antitumor effects [128]. By disrupting normal cellular functions and influencing membrane integrity, silver nanoparticles activate various apoptotic signalling genes in cells in mammal, ultimately leading to cell death [129]. Similarly to their antioxidant and anticancer properties, silver nanoparticles synthesized using common bio factory plants have shown promising antiviral activity. Additionally, organisms such as fungi and bacteria, including A. fumigatus, have been utilized for nanoparticle synthesis [130,131]. With potent anticancer properties and minimal toxicity, silver nanoparticles hold significant promise as anticancer agents. Further exploration of their antiviral potential may unveil new avenues for combating various virus-induced diseases.

Plant-based silver nanoparticles have garnered responsiveness for their potential as antiviral agents against various life-threatening viruses. Studies suggest that Ag-NPs may exert their antiviral effects through different mechanisms, such as intracellular inhibition of viral replication or extracellular interaction with viral proteins, such as gp120, to block viral entry. This mode of action may vary depending on the specific virus being targeted.

Ag NPs have demonstrated effectiveness against a range of viruses, including feline coronavirus (F Co V)[132], influenza virus [133], HIV [134], adenovirus [135], herpes simplex virus [136], dengue virus [137], chikungunya virus [138], nor virus [139], bovine herpes virus and human Para influenza virus type 3 [141]. This diverse antiviral activity highlights the potential of Ag NPs as a novel pharmacological agent for combating viral infections. Further research into the mechanisms of action and safety profile of plant-based Ag NPs could pave the way for their development as effective antiviral treatments [142].

Bioactivity: Antioxidant Potential

Numerous studies have investigated the free radical scavenging abilities of silver nanoparticles synthesized using plant extracts over varying durations. These nanoparticles exhibit heightened antioxidant activity, likely attributed to the efficient absorption of antioxidants from the plant extracts onto the nanoparticle surface. The antioxidant properties of silver phyto-nanosystems render them valuable in disease treatment. Consequently, silver phyto-nanoparticles derived from plant extracts have demonstrated significant antioxidant activity [143].

Salari et al. demonstrated that silver nanoparticles synthesized using an aqueous extract of Prosopis farcta fruit displayed exceptional free radical scavenging abilities [144]. Similar effects were observed in vitro with aqueous extracts of apple [38], Indigofera hirsuta [145] and leaf extracts of Elephantopus scaber [146]. Hence, the robust antioxidant activity of these phyto-nanoparticles may be attributed to the specific capping of Ag-NPs, particularly from medicinal plants rich in diverse antioxidants such as polyphenols and flavonoids.

Biopotential: Antidiabetic Activity:

Nanotechnology is increasingly applied in disease treatment, notably in diabetes mellitus, through manipulation of phytochemical sizes to enhance bioavailability and efficacy [148]. Research commonly utilizes organic plant extracts, particularly in the green synthesis of silver nanoparticles (Ag NPs) from leaf extracts. Characterization of Ag NPs is crucial prior to biological testing, with FTIR spectroscopy proving instrumental in determining molecular composition and structure based on spectral analysis of infrared absorption frequencies [149]. In the management of diabetes, targeting alpha-amylase and glucosidase, key enzymes in carbohydrate metabolism, is crucial. Inhibiting these enzymes prevents the breakdown of carbohydrates into glucose, thereby controlling blood sugar levels. Several studies have identified silver nanoparticles (Ag NPs) as effective alpha-amylase inhibitors both in laboratory experiments and animal studies, suggesting their potential in modulating blood glucose levels when consumed with starchy foods [150, 151]

Conclusion:

The green biosynthesis of silver nanoparticles mediated by plant extracts offers several advantages over alternative methods, primarily due to its environmentally friendly and cost-effective nature. This approach is highly conducive to producing nanoparticles devoid of toxic contaminants, essential for various bio-applications. The use of plant-mediated biosynthesis yields silver nanoparticles with notable nano-technological features, facilitating unparalleled applications. Compared to other biological methods, nanoparticle synthesis using plant materials is particularly advantageous due to their ease of handling, safety, wide distribution and ready availability. Recent reviews, drawing from various literature sources, underscore the significance of plant extract-mediated biosynthesis of silver nanoparticles. These nanoparticles are characterized as effective agents against bacterial and fungal infections, possess antioxidant properties, exhibit antiviral activity and demonstrate potential in cancer therapy.

Abbreviation:

Ag- Silver
DLS - Dynamic Light Scattering
EDX- Energy-Dispersive X-Ray Spectroscopy,
FTIR -Fourier-Transform Infrared Spectroscopy

MRI-Magnetic Resonance Imaging
NP- Nano Particle
SEM -Scanning Electron Microscopy
TEM - Transmission Electron Microscopy,
UV-Ultra- Violet Spectroscopy
XRD- X-Ray Diffraction

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