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Silver nanoparticles (AgNPs) from plant extracts

Samiyah Saeed Al-Zahrani

Faculty of Science || King Abdulaziz University || Jeddah || KSA

Abstract: Synthesis of silver nanoparticles have achieved a distinct focus with an emphasis on their biosynthesis using biological sources such as plants and microorganisms. since plant extracts provide best opportunity for improving green nanotechnology by creating a large array of nanoparticles with antimicrobial efficiency against a wide range of microorganisms such as pathogenic bacteria and plant pathogenic fungi, numerous studies have discussed the deep inroad of antibacterial effect of AgNPs. While there is a lack of studies that advent AgNPs efficiency against toxigenic fungi and control mycotoxins that associated with fungal contamination of food products. This review aimed to summarize the biological synthesis of AgNPs from different natural sources focusing on using this approach as antifungal agent against the most important toxigenic fungi to resolve the mycotoxins evolving issues which influence human and animals' lives.

Keywords: Silver Nanoparticles, Antifungal, Mycotoxins, Aflatoxin, plant extracts.

جسيمات الفضة متناهية الصغر من مستخلصات النبات

سامية سعيد الزهراني

كلية العلوم || جامعة الملك عبد العزيز || جدة || المملكة العربية السعودية

الملخص: تعتبر السموم الفطرية سبباً رئيسياً لمرض الإنسان وحيوانات المزرعة الخاصة به في جميع أنحاء العالم، وتعتبر السيطرة على منتجي السموم مسألة ذات أهمية. الفطريات المنتجة للسموم تلوث السلع الغذائية وتنتج السموم الفطرية، مثل أنواع الاسبرجللس المنتجة الأكثر أهمية. تستكشف هذه المراجعة أهم السموم الفطرية التي تؤثر على حياة الإنسان والحيوان وأهم المنتجات للسموم الفطرية فطريات الاسبرجللس. أيضا تستكشف هذه المراجعة فعالية استخدام النبات كمبيدات فطريات ضد هذه الفطريات المنتجة للسموم لتقليل التعرض الخطير للسموم الفطرية، وكمصدر بيولوجي لتحضير الفضة متناهية الصغر كذلك. حيث إن المركبات النشطة للنباتات توفر أفضل فرصة لتحسين تكنولوجيا النانو الخضراء بكفاءة مضادة للميكروبات ضد مجموعة واسعة من الكائنات الحية الدقيقة مثل البكتيريا المسببة للأمراض والفطريات المسببة للأمراض النباتية. ولهذا الغرض، تقدم هذه المراجعة قائمة بالدراسات السابقة التي ناقشت تحضير جسيمات الفضة حيويا باستخدام النباتات والكائنات الحية الدقيقة منذ أن أثبتت جسيمات الفضة متناهية الصغر أنها بديل مثالي مضاد للميكروبات لحل مشكلة المقاومة الفطرية والتعرض للأخطار الصحية لمبيدات الفطريات الكيميائية.

الكلمات المفتاحية: السموم الفطرية، جسيمات الفضة النانوية، مضاد للفطريات، الأفلاتوكسين، مستخلصات نباتية.

1. Introduction

Toxigenic fungi invade food products and produce health hazard mycotoxins as secondary metabolites in infected plants or in stored products, such as Penicillium, Fusarium Alternaria and Aspergillus spices which considered as the utmost significant producers of mycotoxins. The toxigenicity of these fungi threatening the lives of humans and animals worldwide. [1][2][3][4]. Since these fungi reported as critical responsible for the illness of human and his farm animals in world trade, the control of toxin producers is a matter of importance. Anti-fungal agent's approaches have been exercised years ago to remove contaminant fungi with excluding damage to the host [5]. Thus, the concern in resistance of fungi and health-threatening exposure to chemical fungicides revolutionizing an economic attention to develop enhanced alternative antifungal agents. In this aspect, latest studies set out to eliminate this issue by creating a novel control of contaminant fungi with the aid of metal nanoparticles due their antimicrobial efficiency [6,7,8]. Today, nanotechnology has framed the premise of various applications and revealed the great efficiency of metal nanoparticles as antimicrobial agents likewise their applications in medicine and pharmaceuticals field [9][10]. Latest studies revealed that amid the metal nanoparticles silver nanoparticles (AgNPs) ideally hold huge assurance as antifungal agents towards fungal species as Aspergillus fumigatus [11,12] even towards fungal species A. flavus and, A. niger [12]. Exhaustive approaches have been generated to synthesis silver nanoparticles (AgNPs) from biological sources such as plants extracts and microorganisms. Afterwards, research scientists have raised concentration on plant capability to synthesis AgNPs. Green synthesis of nanoparticles, a term given to synthesis of (NPs) by biologically active composites of plant sources. By reason of plant's rich wellspring of vast bioactive compounds such as, flavonoids, tannins, terpenoids, and alkaloids which may enhance the synthesis of AgNPs with the cost-less and eco-friendly method [13]. Nearly about 50 plant origin extracts confirmed the capability of synthesis AgNPs biologically. Besides, the AgNPs synthesize from plant extracts parts (leave, roots, stems, and seeds) were used as a part of conventional antimicrobials which can be beneficial assets for new antifungal agents [14]. Thus, this review was aimed one hand to summarize the capability of plant extracts in biosynthesis AgNPs. On the other hand, review the antifungal efficiency of the biosynthesized AgNPs from plant extracts specially against toxigenic fungi.

2. Mycotoxins

Toxigenic fungi known as a group of filamentous fungi occurring in food that are responsible for food deterioration and mycotoxins production. The World Health Organization (WHO) has identified mycotoxins as food-borne diseases of contaminant food and feed with fungi [15]. These mycotoxins are secondary metabolites can cause a variety of illness to humans and animals following consumption of contaminated food. Mycotoxins mainly produced by filamentous fungi mycelia of some fungal strains and server no significant function in the fungal physiological process [16,17]. Consumption of these mycotoxins can cause powerful toxic effects known as mycotoxicosis. St. Anthony's Fire was the first mycotoxicosis that has been documented in the Middle Ages in France which called ergotism by the l850s. Ergotism was indicated after consumption of rye contaminated by Claviceps purpurea sclerotia [18]. Later, in 1948, trichothecene mycotoxin have been isolated for the first time by Freeman and Morrison from Trichothecium roseum which was suspected to be the etiological agent caused alimentary toxic aleukia in Russia during the world war II [19]. During the late 1950s, a mycotoxin called aflatoxin have been isolated from the mold Aspergillus flavus which increased the interest in mycotoxins and gave rise to people's health guard by establishing limits of mycotoxins in food and feed by many countries [18]. Nowadays, almost four hundred mycotoxins have been isolated and chemically diagnosed. Nevertheless, research has been heavily focused on those causing critical harm to humans, animals, and crops [20]. Aflatoxins are the significant mycotoxins produced by Aspergillus species including four types known as aflatoxin B1, B2, G1, G2 which named for the color of their fluorescence under ultraviolet light, and their relative position on TLC plates [21]. Aflatoxins are produced by some strains of Aspergillus flavus and A. parasiticus. Theses molds found in field postharvest when moisture is present, allowing for the mold growth [22, 23]. Additionally, extensive researches have examined aflatoxins role in contamination of various commodities in stores such as corn, peanuts, cottonseed and almond [24 , 25]. The exposure to mycotoxins may occur at all levels of the food chain by consumption of contaminated plant materials products or from consumption of animals carrying mycotoxins in their milk or meat like aflatoxin M which found in milk, meat, or other products of animal origin [26]. It has been estimated that approximately 4.5 billion of the whole world's population is exposed to aflatoxins [27]. While, ochratoxins poses a health hazard to human and animal's health by causing nephrotoxic effects on all mammalian species [28]. Also, ochratoxins been known for its teratogenic, immunosuppressive and carcinogenic properties [29,30]. Furthermore, it may produce by some Penicillium species like Penicillium verrucosum which is the principal producer of ochratoxins and some Aspergilli species such as A. ochraceus and A. carbonarius [31].

2.1 Important toxigenic Aspergillus species

The genus Aspergillus is one of the most important filamentous fungal genera which form large mycotoxin producers. A. flavus which have a powdery colony with yellow-green spores containing degradative enzymes in the mycelium which make it capable of breaking down complex nutrients in plant materials [32]. Besides its capability to produces aflatoxins B1, B2, M1, and gliotoxin. As well A. parasiticus that known to produce aflatoxins, it is closely related to A. flavus. Nevertheless, A. parasiticus produces aflatoxins B1, B2, G1, and G2, unlike A. flavus which produces only aflatoxin B1. While A. niger produces gliotoxin, which founded in humans and mice serum that diagnosed with aspergillosis. In addition, A. niger may produce ochratoxins A, fumonisin B2, B4 and some other toxins [33].

Furthermore, A. ochraceus is mostly responsible for the production of ochratoxin A and other toxins it might produce as penicillic acid, xanthomegnin, and viomellein. Due to the significant threat of mycotoxins as aflatoxins (B1, B2, G1, and G2) produced by A. flavus and A. parasiticus and ochratoxins produced by A. ochraceus and A. niger to humans and domestic animals worldwide. This review aims to find an effective way to inhibit the growth of toxigenic fungi using AgNPs synthesized by plant extracts since prevention of their growth could eliminate their toxins. As AgNPs may be considered as useful candidates to eliminate aflatoxin contamination in food and feedstuffs [34].

There are various approaches used to control fungal growth thus eliminate mycotoxin biosynthesis in crops by using chemical processing, food preservatives, physical and biological treatments [34]. These methods need subtle instrumentation and valuable chemicals. Chemical management of fungi and mycotoxins make diverse sorts of environmental pollution peril and disturb the stability of the environment [35]. Using of plant substances inform of plant extract or its essential oils is accepted to be less harmful and provides a chance to avoid artificial chemical preservatives and chemical fungicide's hazardous risks [36].

3. Plant extracts as natural antifungal agents

A wide range of antifungal agents are used in combating biodeterioration of food and food products. Carlile and Watkinson, 1996 clarified that every antifungal agent has its chemical nature, properties and its mode of action [37]. Antifungal compounds may be lethal to microorganisms or they may simply inhibit the production of metabolites such as mycotoxins. But certain number of studies showed that the use of sub-lethal concentration could favour the production of the toxins [38]. Plants, herbs, and spices as well as their essential oils, have a wellspring of numerous constituents that are known to inhibit various metabolic activities of bacteria, and fungi [36]. As a rule, plants with antimicrobial activity contains a wide range of polyphenolic compounds, terpenes, aldehydes, acids and flavonoids [13]. Plants extracts assume a crucial part in the improvement and progression of the antimicrobial agent which have framed the premise of numerous applications against a wide range of microbes, especially against fungi [13]. Further, plant extracts are secure and effective considering their antifungal properties which have been reported of several plant species by a large number of earlier workers over the years. The effectiveness of several plant active compounds on toxigenic molds indicates its possible exercise as fungicides to minimize mycotoxins hazardous exposure as well. Many reviews have demonstrated the inhibitory effect of plant extracts against fungi. Among several plants which have been studied for their antimicrobial properties, clove has received the most comprehensive studies [39]. As indicated, whole clove inhibited the growth of Aspergillus flavus and Penicillium citrinum and their mycotoxins in vivo and in vitro study [40, 41]. While many researchers reported the inhibitory effect of the clove oil with main component eugenol against Aspergillus sp. growth and aflatoxin B1 production [42, 43]. As well as the essential oils of several plants which showed noticeable antifungal properties such as the essential oils of Cinnamomum jensenianum, Ocimum sanctum, and Zataria multiflora have been efficacious on Aspergillus flavus growth and the amount of aflatoxin B1 produced [44] [45] [46]. The efficiency of neem extracts inhibiting the production of aflatoxins (B and G) in the mycelia has been reported [47]. While methanolic extracts of Agave asperrima and Agave striata reduced aflatoxin synthesis in A. flavus and A. parasiticus [48]. Several authors have confirmed that 100 plant species out of 280 have been examined for antifungal effect against toxic species of Aspergilli, have been effective in inhibiting the growth of fungi or inhibition of toxin production [49]. Many researches has been done in this area during recent years testing plant extracts and their essential oils [50,51,52,53,54]. Hence some plant components are showing an unusual antimicrobial activity protecting food and feed from toxigenic molds [55]. The most relevant studies reviewed were subsequently conducted by analyzing the active substances in plants essential oils that inhibited the growth of toxigenic fungi and their toxins [56]. As well plants component and plant products such as piperine (alkaloid extracted from piper species), lutein, xanthrophyll, and carotenoids which found naturally in some fruit and vegetables that markedly suppressed the toxicity and mutagenicity of aflatoxin B1[57,58,59]. The basic problem must be taken into account is the contact with plant extract or essential oils may enhance the fungal production of toxins. Thus, it is important to study each individual case since some plants such as the herbal plant Chromolaena odorata which considered to be potent against insects have induced toxigenic Aspergillus flavus and toxin production by making an excellent substrate for growth of storage fungi [60, 61]. Also, Khaya senegalensis bark used as insecticide have significantly increased the aflatoxin production in maize [62].

Nevertheless, caution must be applied, because some plant materials are a natural medium for toxigenic fungi and may make the situation worse. When inhibiting partial growth, we cannot be sure of toxin inhibition because in this case, the antifungal activity may stimulate the secretion of toxins and secondary metabolites in response to stress [63].

4. Nanotechnology

Nanotechnology is defined as the technology that uses nanomaterials in their design and applications (1-100) nm in size and having novel chemical and physical properties [64]. It is also the most promising field generating a new application in medicine [65]. Among all Nanometals, silver nanoparticles have been used since the 1880s [66]. Because silver has broad-spectrum antimicrobial activity against wide range of microorganisms which may induce much less resistance than alternative antibiotics [67]. Nanotechnology is fast-growing with nanoparticles produced and utilized in a wide range of pharmaceutical and commercial products worldwide. This environmentally friendly synthesis method of silver nanoparticles to using plant extracts is conventional to chemical synthesis and can potentially be used in various areas such as food, cosmetics, and medical applications [68]. Physically and chemically techniques for the production of metallic nanoparticles have been presented by the scientists in numerous research (Figure1). But, these synthetic methods involving different chemicals are expensive and may lead to the presence of toxic chemical tangled on the surface of nanoparticles, which may have adversarial effects in various biological and biomedical applications [69].

The growth of green biosynthesis methods of nanoparticles became an essential branch of nanotechnology in the 21st century [70]. The first report of the plant used in the synthesis of nanoparticles is credited to Medicago sativa which is capable to synthesis silver and gold nanoparticles [71]. Since then, enormous attention has been given to plant as a source of nanoparticles synthesis. Among all noble metal (NPs), silver nanoparticles had grown unlimited attention due to their exceptional properties such as chemical stability, excellent conductivity, catalytic and most important antimicrobial activity [72] and possess anti-fungal activity [73].

4.1 Silver nanoparticles (AgNPs)

In particular, silver nanoparticles (AgNPs) show good antimicrobial properties due to their large ratio of surface area to volume; these properties are used as bactericide on burn wounds, fillers in dental cavities to prevent infection, thin coats on medical devices to prevent microbial biofilm formation, in air and water purification systems, in wastewater treatment plants, and in food processing for controlling microbial contamination [74, 75]. Also, silver is known as being nontoxic and harmless to the human body at lower concentrations, contrasting other metal nanoparticles [76]. Lea,1889 had synthesized AgNPs for the first time. Then, several techniques for synthesis silver nanoparticles with various coating agents and diameters had been advanced and used commercially and therapeutically [75]. Recently, Nano-biotechnology has large interests to advance a new approach to test new drug formulations based on biosynthesized silver nanoparticles with different biological potential and physicochemical properties [77].

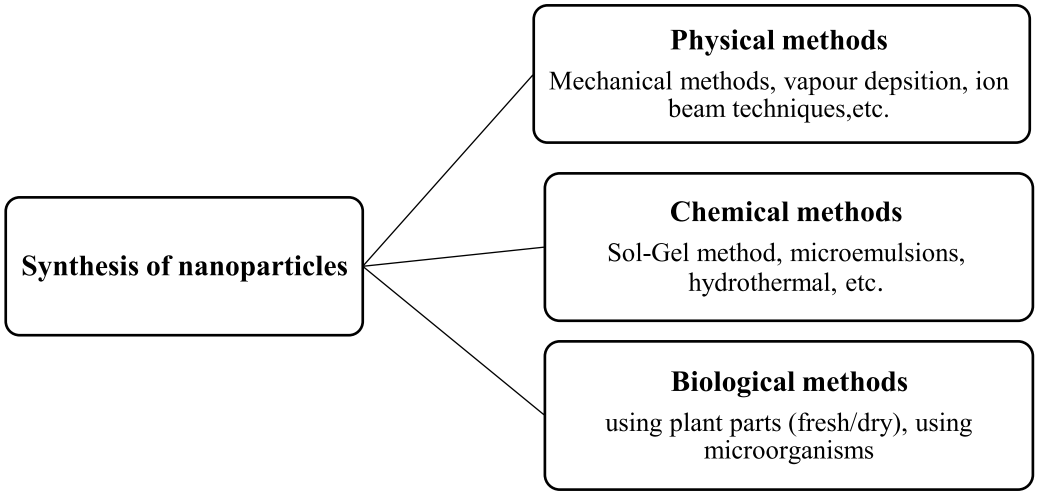

Figure (1) Different methods of nanoparticles synthesis

4.1.2 Antimicrobial properties of Silver nanoparticles

Silver nanoparticles have physical properties that are distinctive from silver ions and bulk material; their biological activity is greatly higher due to the high surface area to volume ratio that makes them promising antimicrobial against all types of pathogenic microorganisms [78, 79].The antibacterial effect silver nanoparticles have been represented against bacteria such as Escherichia coli, Vibrio cholera, Pseudomonas aeruginosa, and Salmonella typhi [80]. Also, in a study examined the antibacterial potential of silver nanoparticles on the pathogenic bacteria strains P. aeruginosa, resistant E. coli, and Streptococcus pyogenes [81]. Biosynthetic AgNPs showed high antibacterial activity against biofilm-forming S. epidermidis strain [82] and against E. coli [83]. These silver nanoparticles could exhibit inhibition to bacterial growth immediately when they contact them, by killing bacteria [84]. While AgNPs antimicrobial efficiency against bacteria has been studied more than against fungi. Consequently, bioactivity mechanism of AgNPs against fungal pathogens has not been indicated [85]. In addition to antibacterial activity, some authors reported the significant antifungal activity of AgNPs against Candida species and dermatophytes species Trichophyton mentagrophytes [86, 87] and against different fungal species like Dothiorella sarmentorum [88]. Whereas antifungal activities of AgNPs against different kinds of fungus have not been reported as much as antimicrobial activities of them by researchers [89]. It was reported that AgNPs could inhibit fungi in low concentrations and those levels had no toxic effect on human cells [90]. In a recent study, AgNPs showed inhibiting AFB1 production by A. parasiticus in addition to the ability for active fungal growth inhibition [91]. In another study, it showed antifungal activity against spoilage fungal isolates A. flavus and A. ochraceus [92].

4.5 Biosynthesis of silver nanoparticles using microorganisms

Nanoparticles prepared by different chemical and physical methods and biological methods. The physical and chemical methods are cost intensive and the use of hazardous chemicals during the processes limits their use in clinical applications. While the biological synthesis technique is an environmentally friendly procedure to usual chemical synthesis and can possibly be used in many areas such as food, cosmetics, and medical applications. Microorganisms (such as bacteria, fungi, yeast) have been used as potential nanofactories and as alternatives to the conventional routes to prepare metal nanoparticles [93, 94]. There are numerous studies which concerns on the ability of various fungi to biosynthesis AgNPs (Table1).

Table (1) Biosynthesis of silver nanoparticles using biological materials

Biological source	AgNPs size	Reference
Plant sources		
Ocimum sanctum	4 –30 nm	[95]
Mentha piperita	90 nm	[96]
Ficus benghalensis	16 nm	[97]
Nelumbo nucifera	45 nm	[98]
Arbutus unedo	20 nm	[99]
Catharanthus roseus	35-55 nm	[100]
Artemisia nilagirica	70–90 nm	[101]
Solanum tricobatum	53 nm	[102]
Syzygium cumini	41 nm	
Centella asiatica	52 nm	
Citrus sinensis	42 nm	
Garcinia mangostana	35 nm	[103]
Chenopodium murale	30-50 nm	[104]
Hibiscus cannabinus	9 nm	[105]
Sesbania grandiflora	10-25nm	[106]
Azadirachta indica	34 nm	[107]
Olive leaf extracts	20–25 nm	[108]
Morinda pubescens	20-40 nm	[109]
Rhizophora mucronata	60-95 nm	[110]
Gelidiella acerosa	22 nm	[111]
Bacteria		
Bacillus subtilis	5-60 nm	[112]
Serratia nematodiphila	10-31 nm	[113]
Escherichia coli		
Bacillus megaterium		

Biological source	AgNPs size	Reference
Acinetobacter sp.		
Stenotrophomonas maltophilia	15-50 nm	[114]
Brevibacterium casei.	10-50 nm	[115]
Lactobacillus sp. mixture	30–100 nm	[116]
Klebsiella pneumoniae	5-32 nm	[117]
Fungi		
Candida albicans	61-66 nm	[118]
Aspergillus flavus	8.92 ± 1.6nm	[119]
Aspergillus fumigatus	5–25 nm	[120]
Alternaria sp	4–30 nm	[121]
Penicillium decumbens	30-60 nm	[122]
Penicillium brevicompactum	23–105 nm	[123]
Penicillium italicum	33 nm	[124]
Curvularia pallescens	3-13 nm	[125]
Guignardia mangiferae	5–30nm	[126]
Penicillium atramentosum	5-25 nm	[127]
Penicillium citrinum	5-25 nm	[128]
Aspergillus tamarii	40 nm	[129]
Fusarium oxysporum	90 nm	[130]
Fusarium oxysporum	5-13 nm	[131]
Algae		
Pithophora oedogonia	25- 44 nm	[132]
Caulerpa racemose	5-25 nm	[133]
Chlamydomonas reinhardtii	5-15 nm	[134]
Chaetomorpha linum	3-44 nm	[135]
Cystophora moniliformis	50-100 nm	[136]
Enteromorpha compressa	40-50 nm	[137]
Gracilaria corticata	18-46 nm	[138]
Spirogyra varians	2-20 nm	[139]
Padina tetrastromatica	10-100 nm	[140]
Porphyra vietnamensis	3-13 nm	[141]

4.6 Biosynthesis of silver nanoparticles using plant extracts

Plant-mediated synthesis or green synthesis of AgNPs is an economical way, non-hazardous and there is no need for chemical reducing and capping agents. Because of that numerous studies by researchers established to evaluate of their microbial activity. Moreover, they have huge applications in molecular biology and medicine (Figure 2).

A new process for producing AgNPs demonstrated by the reduction of $AgNO_3$ in aqueous solutions with neem (Azadirachta indica) leaf broth [142]. Later, different green process for the preparation of AgNPs has been developed by using Eucalyptus citriodora and Ficus bengalensis fresh leaf extract along with $AgNO_3$ in aqueous solution and without reducing or stabilizing agents at room temperature for 25 minutes. Reduction and stabilization of Ag+ ions were enhanced by functional groups present in the polysaccharide constituents in leaf extract [143].

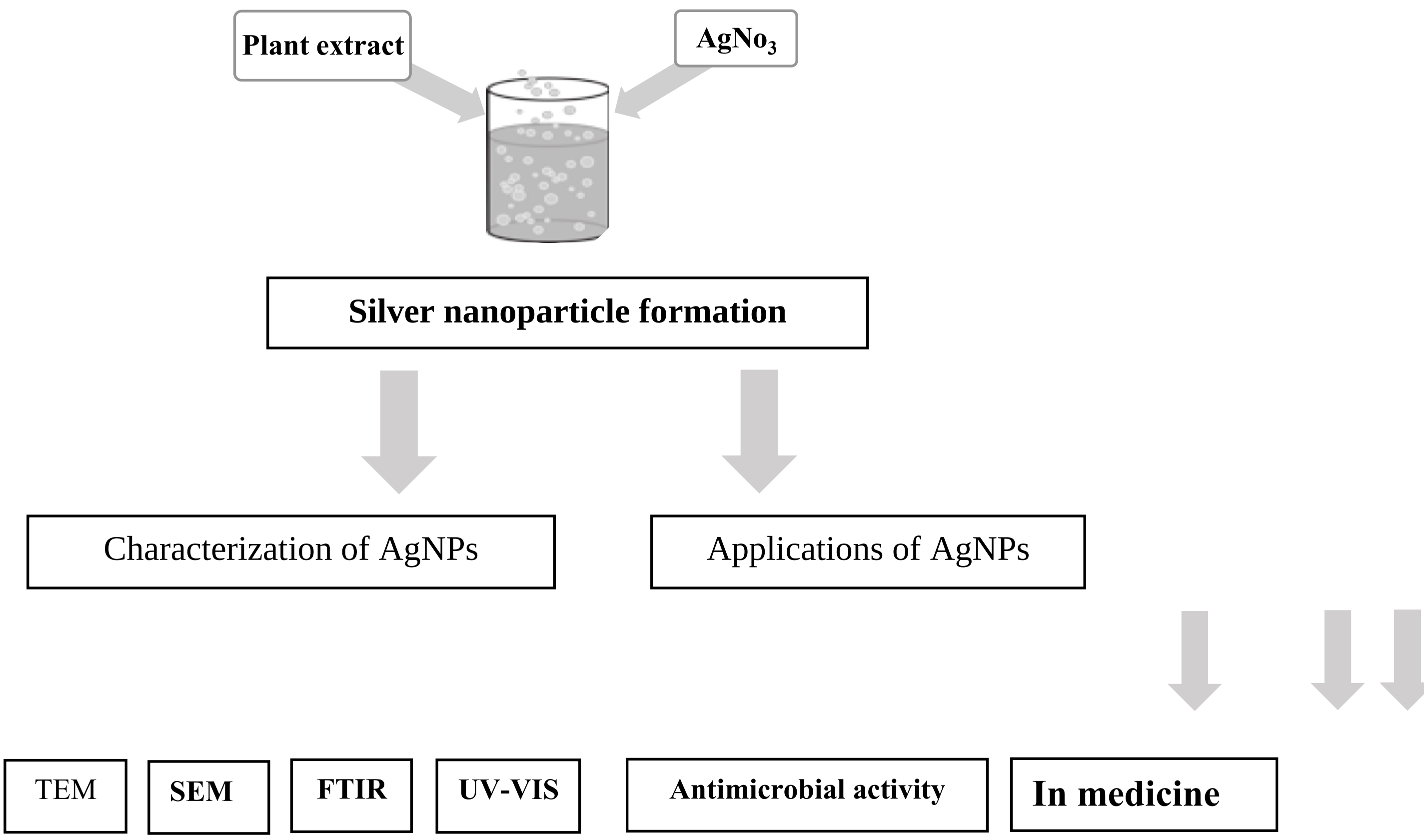

Figure (2) Methodology of Synthesis of silver nanoparticles using plant extract, characterization and application.

Recently, Silver nanoparticles have been biosynthesized by using leaf extracts of the plant such as Aloe vera leaf extract [144], Ricinus Communis leaves extract [145] leaf extracts of Piper nigrum [146] and Ocimum sanctum leaf extract [147]. Also, AgNPs have been biosynthesized by using root extracts of the plant such as Zingiber officinale root extract [148], And by using bark extracts such as Afzelia quanzensis bark extract [149]. AgNPs were prepared by biological reduction of $AgNO_3$ as a precursor using Mentha piperita (Lamiaceae) leaf extract in ambient conditions, most probably because of the presence of phytochemicals in the extract, thereby reducing Ag+ into Ag0 [150]. In addition to using fruits extracts such as Momordica charantia fruit extract [151] and Prunus armeniaca fruit extract [152]. Although, seeds such as extracts of Sinapis arvensis seeds [153], Cydonia oblong seed [154] and seed extracts of Nyctanthes arbor-tristis [155]. A simple green and cost-effective approach for the synthesis of Ag-NPs with an average size of 12 nm using garlic clove extract as a reducing/stabilizing agent in aqueous solution was reported [156]. This was attributed to the presence of antioxidants within garlic extract and their decisive role in reducing Ag+ to Ag0. While the synthesis of AgNPs using banana peel extract as a reductant and $AgNO_3$ as a precursor in an aqueous medium under various conditions was demonstrated [157]. Reduction of the nominated metal ions to nanoparticles as well as stabilization of these nanoparticles might be facilitated by the presence of reducing sugars, terpenoids, and flavanone constituents in the broth. Silver nanoparticles synthesized using plant extract like Solanus torvum [158], Argemone Mexicana [159] and Aloe vera showed antifungal activity against Aspergillus species [160].

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