

Review Article

Selenium nanoparticles: A review of their plant-mediated synthesized and evaluation their biomedical applications

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Abstract

Nanotechnology holds great potential for a variety of biological applications. The chemical methods often require harsh conditions, expensive equipment, and produce toxic byproducts. Green synthesis using plant extracts provides a more eco-friendly, low-cost, and sustainable alternative that can achieve high yields. Various plant materials, including leaves, roots, tubers, fruits, peels, seeds, and herbs, have been successfully used for the green synthesis of Selenium nanoparticles (Se-NPs). The phytochemicals present in these extracts, such as flavonoids, alkaloids, and polyphenols, facilitate the reduction of selenium ions and stabilize the nanoparticles. The characteristics of the Se-NPs, such as size, shape, and stability, can be tuned by controlling the synthesis parameters and the choice of plant extract. The biogenic Se-NPs exhibit a range of beneficial properties that make them attractive for diverse biomedical applications. These include antioxidant, antimicrobial, anti-inflammatory, and anticancer activities. The Se-NPs can also be used as drug carriers and for wound healing. Compared to chemically synthesized Se-NPs, the green-synthesized counterparts are more biocompatible and less toxic, making them safer for biomedical use. Overall, the green synthesis of Se-NPs using plant extracts combines the unique properties of selenium with the advantages of natural phytochemicals, offering a promising approach for developing safe and effective biomedical applications.

Keywords: Green synthesis; Selenium nanoparticles; Plant extracts; Bio-medical applications

Introduction

Nanotechnology is the capacity to observed, measure, control, assemble, and manufacture materials at the nanoscale to translate the nanoscience theory into practical applications [1].

Nanotechnology was defined as "a science, engineering, and technology conducted at the nanoscale. An important trace element, selenium has a number of biological properties, such as anti-inflammatory, chemo preventive, and antioxidant properties [2]. Selenium is found in nature in two forms: organic (seleno methionine and seleno cysteine) and inorganic (selenite and selenate). The elemental (Se^0) is naturally insoluble and can form selenium nanoparticles (Se-NPs). Due to their increased bioavailability, reduced toxicity, and enhanced biocompatibility over inorganic selenium compounds. Nanotechnology has enabled the development of selenium nanoparticles (Se-NPs) with unique properties and applications in biomedical sciences [3]. Green synthesis methods using bacteria, fungi, algae and plants produce Se-NPs in an eco-friendly manner. The capping agents from these biosources can enhance the biocompatibility and biological effects of Se-NPs [4,5]. Se-NPs synthesized through these methods show promise in various fields, particularly in biomedicine, due to their antioxidant, antimicrobial, and anticancer properties. The choice of synthesis method significantly influences the properties and applications of Se-NPs, with green synthesis gaining popularity for its environmental benefits and lower toxicity [6,7].

1. Synthesis of Selenium nanoparticles

Selenium nanoparticles (Se-NPs) can be synthesized using various chemical methods such as, Sol-Gel Process, Reduction of Selenium Salts, Microwave and Sonochemical Synthesis. In addition to physical methods such as, Pulsed Laser Ablation, and Vapor Phase Deposition, which vary in complexity, cost, and environmental impact, because they often require harsh conditions, expensive equipment, and produce toxic by-products [8]. As shown in **Figure.1**.

Compared to physical and chemical synthesis approaches, the green synthesis of Se-NPs utilizing plant extracts is a safer and more environmentally friendly process [9]. Plant extracts have the ability to function as stabilizing and reducing agents, which makes it easier to synthesize stable Se-NPs in a single step [10]. The phytochemicals included in plant extracts, including polyphenols, alkaloids, and flavonoids, are essential for stabilizing the resultant Se-NPs and reducing selenium precursors [11].

Based on the search results, the study that presented by, Jay,V., et.al [12] to synthesis, characterization and antioxidant potential of selenium nanoparticles which was synthesized by *Allium sativum* and *Aloe vera* extracts, which observed as hollow and spherical particles in size ranging from 7-48nm and 9-58nm respectively. Several plant extracts was used in the study by Cittrarasu, V., et.al. That have been effectively used for the green synthesis of selenium nanoparticles (Se-NPs) such as, Extract of *Ceropegia bulbosa* tubers that showed Se-NPs that were

quickly produced using *C. bulbosa* tuber extract had strong antibacterial activity, considerable cytotoxicity against breast cancer cells, and larvicidal activities against dengue vectors [13].

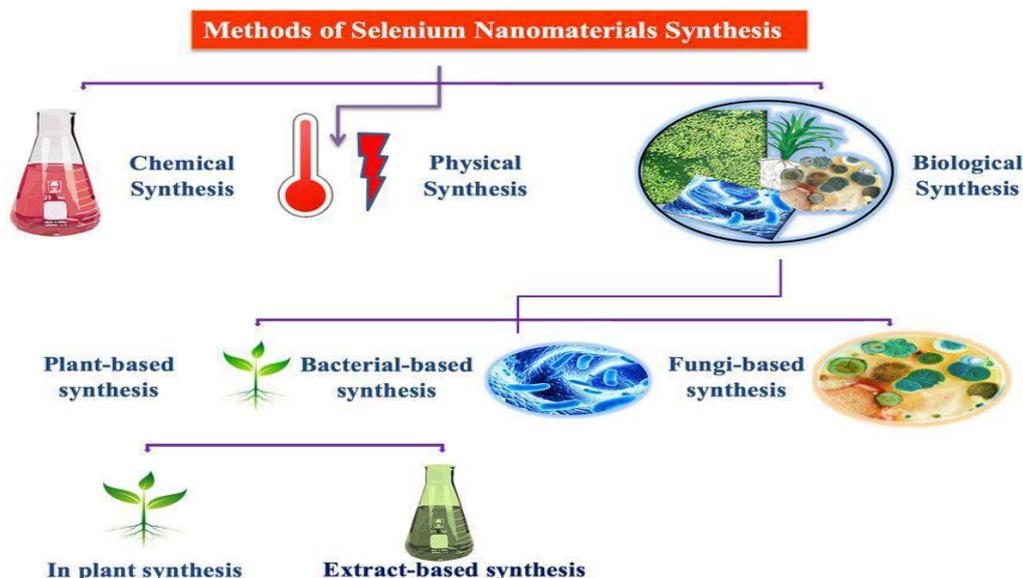


Figure.1: Different routes for the synthesis of Se-NPs

Se-NPs synthesized using *Murraya koenigii* (*curry leaf*) berry extract, Yazhiniprabla, M., and Vaseeharan, B. [14], showed effective antioxidant capacity and antibacterial activity against *S. mutans*, *E. faecalis*, *S. sonnei*, and, *P. aeruginosa*. Depending on study by Vennila, K., *et.al*. [15], selenium nanoparticles and other (NPs) were synthesized using *Spermacoce hispida* aqueous leaf extract (Sh-ALE), demonstrated strong antibacterial, anti-inflammatory, and anticancer effects against human cervical cancer cells.

The green of Se-NPs by simple mixing of *Withania somnifera* (*W. somnifera*) leaves extract and selenious acid (H_2SeO_3) solution, were found to possess significant antioxidant activity ($IC_{50} = 14.81 \mu g/mg$) and considerable antibacterial activity on *B. subtilis*, *K. pneumonia*, and *S. aureus*, antiproliferative, effects of Se-NPs possess great growth control against A549 cells (IC_{50} at $25 \mu g/ml$) by Sivaraj, R., *et.al*, [16]. Othman, M. S., *et. al*, [17]. Studied the effects of Se-NPs on MCF-7 cells that inhibit proliferation using Carvacrol on human breast cancer MCF-7cells demonstrated the potential of Se NPs-CV therapy to efficiently and viability in a dose-dependent manner. The potential anti-inflammatory and anticancer properties of Se-NPs, which are synthesized using clove extract (*Syzygium aromaticum*) indicated potential anti-ageogenic effects, antioxidant activity (IC_{50} value: $0.437 \mu g/mL$), and antibacterial effectiveness against the bacterial pathogen *S. species*. Biocompatibility was also confirmed in toxicity tests conducted on *Artemia nauplii*, by Nagarajan, K., *et.al*, [18]. The presented study by Ferdasdegh, B., *et.al* [19], focuses on the biogenic synthesis of selenium nanoparticles (Se-NPs) using *Pelargonium zonale* leaf extract to

evaluate the antibacterial and antifungal activities of the synthesized Se-NPs against *E. coli*, *S. aureus* (G⁺) bacteria and *C. coccodes* and *P. digitatum*, which observed that the created NPs had higher inhibition rate toward the Gram-positive bacteria and pathogenic fungus. The walnut (*Juglans regia* L.) leaf extract has been used for the green synthesis of the Se-NPs and the obtained results indicated that spherical and monodispersed Se-NPs with a mean particle size of 150 nm were formed and gave high activity as antibacterial against *E. coli* and *S. aureus* [20]. Tarragon extract was used to perform green nano-biosynthesis of selenium nanoparticles by Yilmaz, M. T., *et.al*, [21]. And the Se-NPs synthesized giving rise of formation in the shape of quasi-spheres without clustering with the sizes range (20-50) nm with high thermal stability. And these (NPs) could remarkably high activity as antibacterial toward many types of pathogenic bacteria. Green synthesis of Se-NPs using various source of biomedical plants as extracts such as, *Spirulina platensis*, *Calendula officinalis* L., and *Encostema axillare*, that gave high capable to producing Se-NPs with spherical morphologies and ranging size between (10-180) nm relatively. Furthermore, high activity in various biological and industrial applications [22-24].

Based on the search results in recent years, it has given promising results for the use of plant extracts as reducing and synthesizing agents of Se-NPs including, *solanum nigrum* fruit, *Artemisia chamaemelifolia*, *Azadirachta indica* leave, *Amphipterygium glaucum* leaves, *Pistachio vera* L (*Siirt pistachio*), *Melia azedarach* leaves, *Crataegus monogyna*, Tea, Herb, *Moringa oleifera*, *Orthosiphon stamineus* Leaf, Green Coffee, *marine microalgae*, and *Nannochloropsis oceanica* that yield the most stable selenium nanoparticles (Se-NPs) are those containing high levels of poly-phenolic compounds, such as flavonoids and phenolics. These compounds are effective at synthesizing Se-NPs with high stability and biological activity in medical field [25-37].

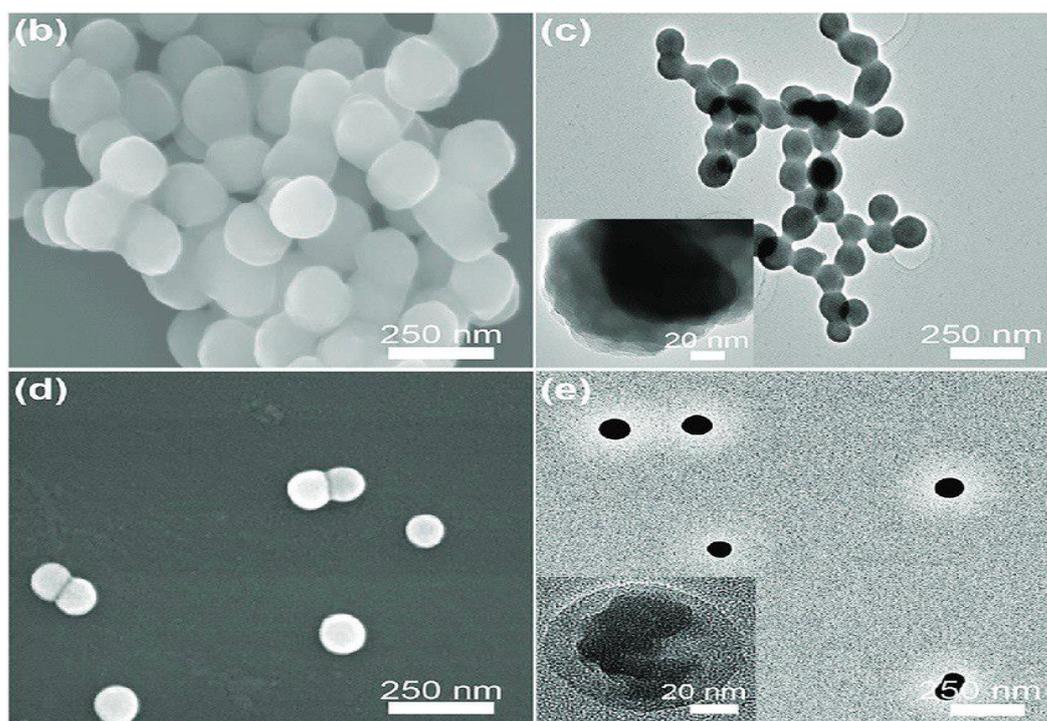
2. Characterization of Se-NPs

Characterization of Se-NPs is essential to understand their properties and potential applications. Common techniques include:

- UV-Vis Spectroscopy: Used to confirm the formation of Se-NPs and assess their optical properties.
- High-Resolution Transmission Electron Microscopy (HR-TEM): Provides information on the size, shape, and morphology of Se-NPs.
- Dynamic Light Scattering (DLS): Measures the size distribution and stability of Se-NPs in colloidal solutions.

- Fourier Transform Infrared Spectroscopy (FT-IR): Analyzes the chemical bonding and functional groups present on the Se-NPs.
- Thermo-gravimetric Analysis (TGA): Evaluates the thermal stability and composition of Se-NPs.

These techniques and other techniques help in optimizing synthesis methods and enhancing the biological activity of Se-NPs for applications in medicine and nanotechnology [38-42].



b) SEM and (c) TEM images of Se-NPs. (d) SEM and (e) TEM images of Se-NPs The insets in (c) and (e) are HR-TEM image of Se-NPs

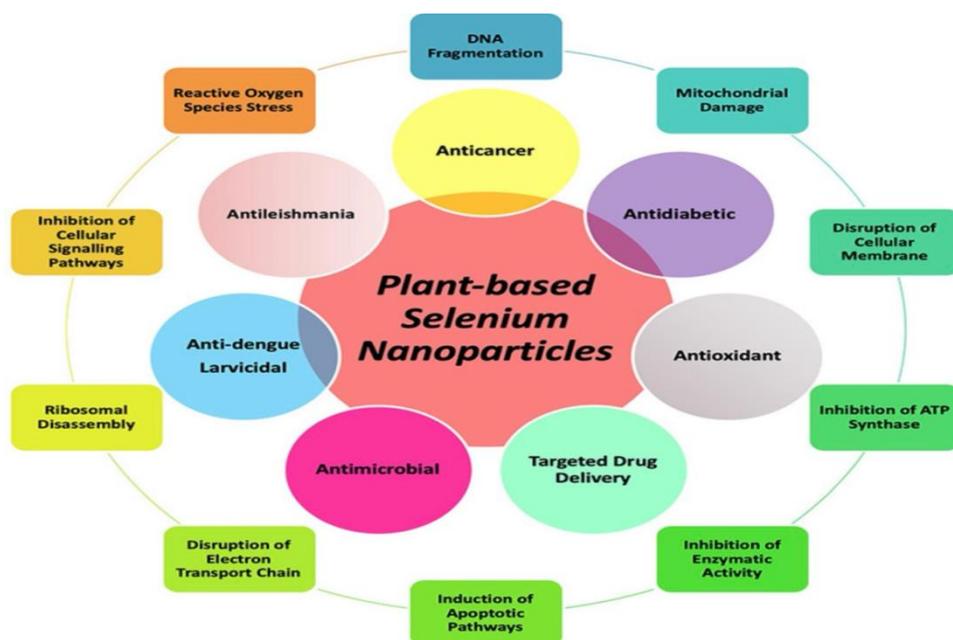
4. Biomedical applications of Se-NPs

The versatile biomedical applications of selenium nanoparticles highlight their great potential to revolutionize various fields of medicine and healthcare [43]. Se NPs have been extensively studied in various medical fields due to their superior performance over elemental Se. Se-NPs have improved bioavailability while being less harmful. Nanoparticles, especially Se-NPs, have immunomodulatory, antioxidant, and anti-inflammatory properties [44]. This is shown in Figure 2.

A detailed description of the biological properties of Se-NPs can be found here. We also outline recent advances in targeted strategies and new applications. [45].

Figure 2: Plant-based Se-NPs' potential for biomedicine is explained by the inner circle, while Se-NPs' mechanistic methods are explained by the outer circle [46].

3.1. Drug delivery applications



Se-NPs' distinct physicochemical characteristics make it possible to employ them as Nano-carriers for the precise and regulated delivery of medicinal drugs.

Se-NPs can increase a drug's bioavailability, stability, and solubility, hence boosting its therapeutic efficacy. In addition, Se-NPs can be delivered to specific tissues or cells more selectively by functionalizing them with a variety of targeting ligands [47,48].

3.2. Anti-cancer properties

Selenium nanoparticles (Se-NPs) have demonstrated promising anticancer effects through several mechanisms:

- Apoptosis induction: Se-NPs have the ability to cause cancer cells to undergo apoptosis, especially when doing so via the intrinsic apoptotic route. They cause the activation of caspases 3/7/9 and change the expression of proteins linked to apoptosis, such as death receptors and surviving [49].

- Proliferation inhibition: It has been demonstrated that Se-NPs, in a dose-dependent manner, inhibit the proliferation of many cancer cell lines, including those from the breast, prostate, lung, liver, and colon [50].
- Effects on antioxidants and cytoprotection: Se-NPs have the ability to scavenge reactive oxygen species and free radicals, shielding normal cells from oxidative damage while specifically causing oxidative stress in cancer cells [51].
- Effects on immunity: By stimulating the production of pro-inflammatory cytokines and natural killer cells, serine nucleic acids (Se-NPs) can boost the immune response and inhibit tumor growth in animal models [52].

Overall, the unique properties of Se-NPs, including their low toxicity, high bioavailability, and multifaceted anticancer mechanisms, make them a promising therapeutic approach for cancer treatment. As shown in **Figure 3**.

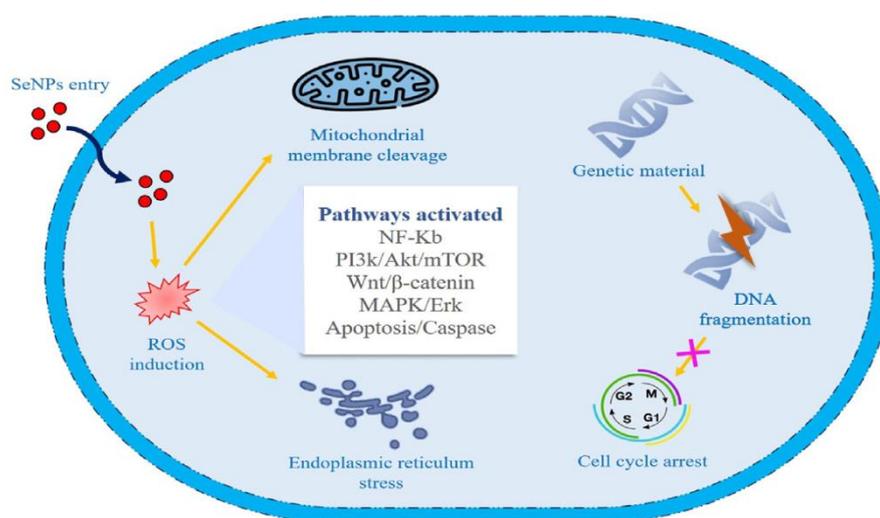


Figure 3: Illustration the bio-role of selenium nanoparticles in cancer [53].

3.3. Anti-oxidant properties

Selenium nanoparticles (Se-NPs) have shown potent antioxidant properties, making them promising active agents. They can scavenge. Their antioxidant activity has been shown to be size-dependent, with smaller Se NPs having exhibiting greater radical-scavenging ability. In addition to that, Se-NPs can protect normal cells from oxidative stress induced by various toxicants like heavy metals, chemotherapeutics, and UV radiation. This cytoprotective effect is particularly useful in reducing side effects of cancer treatments [54,55].

3.4. Anti-microbial properties

The antimicrobial properties of Se-NPs make them a promising alternative for treating infections, especially in cases where antibiotic resistance is a concern and demonstrating significant activity against a variety of microorganisms. They have been explored for applications in wound management, oral health, and nosocomial infections. The biogenic Se-NPs have been found to be more effective Synthetic Se-NPs as agents against oral bacterial and fungal pathogens. The mechanism of action of Se-NPs includes DNA damage, protein degradation, and cell destruction. These nanoparticles can damage cell membranes and disrupt cellular processes, leading to bacterial death. [56,57].

3.5. Anti-inflammatory activity

The anti-inflammatory properties of Se-NPs, particularly when combined with plant extracts, make them a versatile platform for developing therapeutics to manage a wide range of inflammatory conditions [58]. It has been demonstrate that Se-NPs synthesized using plant extracts such as *Thymus vulgaris* (*T. vulgaris*) extract, exhibited potent anti-inflammatory properties, with a percentage of inhibition reaching 92.6% at a concentration of 50 µl, which has shown higher anti-inflammatory activity compared to standard values [59]. By targeting multiple pathways involved in chronic inflammation, Se-NPs have shown promise in managing conditions like rheumatoid arthritis, inflammatory bowel diseases, and neurodegenerative disorders. Their ability to concurrently reduce oxidative stress and modulate inflammatory signaling makes them a versatile therapeutic option for patients with chronic inflammatory diseases [60].

3.6. Role of Se-NPs in diabetes

Hyperglycemia is the hallmark of diabetes mellitus (DM), a widespread disease that afflicted 415 million adults between the ages of 20 and 79 in 2015. By 2040, it is predicted that this number would increase to 642 million. Notably, the prevention and treatment of diabetes and its aftereffects depend heavily on the discovery of a medication with several bioactivities, such as antioxidant, antihyperglycemic, and antihyperlipidemic properties [61,62].

Based on the search results, selenium nanoparticles (Se-NPs) have shown promising anti-diabetic properties in various animal studies which have demonstrated that Se-NPs can help regulate blood glucose levels, improve insulin sensitivity, protect pancreatic beta cells, and reduce oxidative stress in diabetes models [63,64]. The proposed mechanisms of action include

Se-NPs' ability to scavenge reactive oxygen species, modulate inflammatory pathways, exhibit insulin-mimetic activity, and enhance insulin secretion [65]. In conclusion, while the animal data is encouraging, there is currently no evidence from human studies on the efficacy of Se-NPs as anti-diabetic agents [66]. Further clinical investigations are required to determine the feasibility and benefits of using Se-NPs for diabetes treatment in human patients. As shown in **Figure 4**.

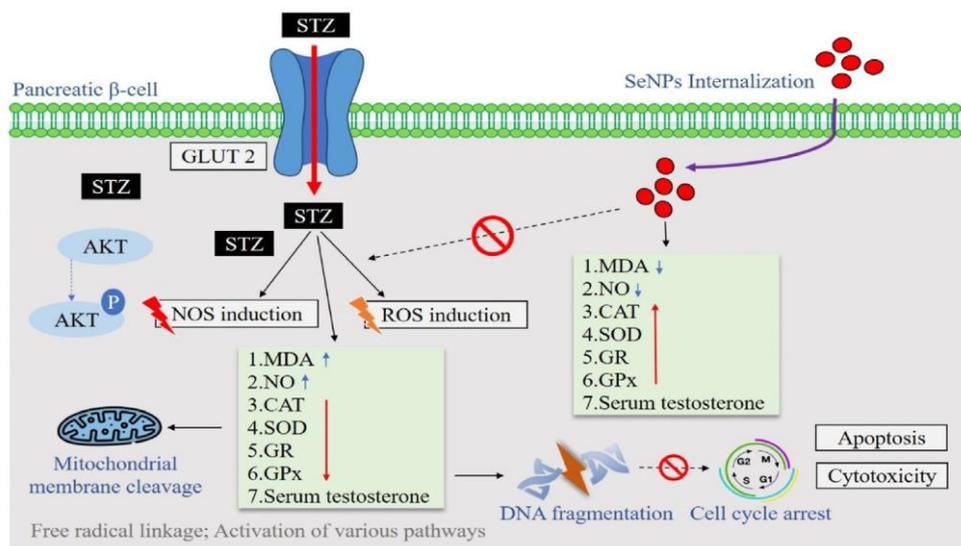


Figure 4: mechanism action of Se-NPs to improving Diabetes [65].

Table 1: Summary of the reactions carried out for synthesizing Se-NPs using different plant extracts and some biomedical applications.

No	Extract origin	Morphology and size of particles	Applications	Ref.
1	<i>Ceropegia bulbosa tubers</i>	O.D = 277.5nm with spherical shape	Chemopreventive against lung □ carcinoma	[67]
5	<i>Urtica dioica</i>	O.D = 280 nm, nano-spheres of 40–100 nm size	Antibacterial against Gram positive and Gram negative bacteria	[68]
6	<i>Murraya koenigii</i>	Nano-spheres of 40–100 nm size	anticancer studies on human colon, □ breast and hepatic cancers	[69]
7	<i>Withania somnifera</i>	Spherical with a diameter of 10–□ 50 nm, O.D = 263 nm	Antioxidant, antimicrobial, antibacterial, antifungal	[70]
8	<i>Olea ferruginea</i>	O.D = 299 - 599 nm, size = 400 nm	Anticancer (studies on mice with breast □ cancer), antioxidant	[71]
9	<i>Terminalia arjuna</i>	Size = 10-80 nm, O.D = 390 nm	Antioxidant	[72]
10	<i>Trigonella foenum-graecum</i> L.	Nano-spheres with a 5–12 nm diameter, O.D= 355nm	Breast cancer, antimicrobial	[73]
11	<i>Moringa oleifera</i> (drumstick) leaf	O.D = 270 nm Spherical with a particles size around 400 nm	Antibacterial activity against Gram (+) Gram (-) bacteria and fungi, anticancer □ activity against human breast cancer	[74]
12	<i>Crispum</i> (parsley)		-----	[75]
14	<i>Trigonella foenum-graecum</i>	O.D = 200–400 nm, , 50–150 nm oval particle	Anticancer activity against human □ breast cancer cells	[73]

4. Conclusion

In conclusion, Green synthesis of Se-NPs using plant extracts is a promising approach that offers several advantages. It is an eco-friendly, cost-effective, and sustainable process that leverages the reducing and stabilizing properties of natural phytochemicals present in plant materials. In addition, a variety of plant extracts have been successfully used for the green synthesis of Se-NPs, including leaves, roots, tubers, fruits, peels, seeds, and herbs. The phytochemicals in these extracts, such as flavonoids, alkaloids, polyphenols, and polysaccharides, facilitate the reduction of selenium ions and stabilize the nanoparticles. The characteristics of the Se-NPs, such as size, shape, and stability, can be tuned by controlling the synthesis parameters and the choice of plant extract and Compared to chemically and physically synthesized Se-NPs. The characterization techniques of Se-NPs such as, UV-visible, TEM, SEM, and DLS offer comprehensive insights into the physical and chemical properties of Se-NPs, essential for their application in various fields. The green-synthesized counterparts are more biocompatible and less toxic, making them attractive for various biomedical applications include, antioxidant, antimicrobial, anti-inflammatory, anticancer activities. And the Se-NPs can also be used as drug carriers and for wound healing. The resulting researches have great potential of Se-NPs for diverse biomedical applications, from treating infections to managing chronic diseases, while being environmentally friendly and sustainable.

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