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Green Synthesis of Selenium Nanoparticles: Characterization and Therapeutic Applications in Microbial and Cancer Treatments

S. Yasodha [a], A.S. Vickram [a,*], S. Rajeshkumar [b]

[a] Department of Biotechnology, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-602105, Tamil Nadu, India

[b] Nanobiomedicine Lab, Centre for Global Health Research, Saveetha Medical College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Chennai-602105, Tamil Nadu, India

* Corresponding Author Email: vickramas.sse@saveetha.com

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Abstract: Selenium is one of these micronutrients that are essential for animals, plants and microorganisms to remain functional. This review is about the green synthesis of selenium nanoparticles and its application in microbial and cancer therapies. Our hypothesis was that Se NPs produced using plant extracts might offer the biocompatibility and environmental friendliness advantages, and hence be a new prospect for medical applications. To test our hypothesis, we conducted a comprehensive analysis of recent literature, exploring various green synthesis conditions and processes for Se NPs. Various characterisation techniques such as spectroscopy, microscopy and physicochemistry were discussed in order to provide insight into the formation and function of green-synthesised Se NPs. Our findings show that Se NPs produced by green chemistry methods have good properties such as uniform size, shape and stability as detailed examples from recent studies reveal. Furthermore, we discussed the therapeutic and theranostic applications of Se NPs produced in this manner: their potential in antimicrobial and anticancer treatments. Through illustrations of cases where Se NPs inhibit microbial growth and cause apoptosis in cancer cells, the practical significance of our findings was underscored. In summary, our review affirms that using green-mediated synthesis Se NPs improves their biocompatibility and therapeutic efficacy, thus opening up new realms for their application in medical research.

Keywords: Selenium, Nanoparticles, Anticancer, Therapeutic, Antibacterial, Antioxidant

1. Introduction

Nanotechnology is one of the most promising technologies, which opens a large scope of novel applications in the area of science [1]. Nanotechnology utilises nanoscale materials, and they have unique advantages such as a large surface area to volume ratio with diversified properties such as magnetic, electric and biological properties [2, 3]. Hence, they have multifaceted applications ranging from agriculture to the biomedical field. Selenium (Se) is one such nanoparticle (NP), which is a vital element required for the proper functioning of the human and animal immune systems. Selenium helps protect us from various deadly and chronic diseases. In our human body, there are different selenoproteins; thus, Se behaves as a coenzyme of many active sites. In this way, Se protects us from severe injuries to tissues and cells and prevents oxidative stress [4].

Further, Se plays a major part in regulating iodine and other free radicals, thus providing disease resistance. Numerous liver diseases caused by the accumulation of various toxic substances, alcohol and heavy metals can be thwarted when Se is taken regularly. Se is an essential element in glutathione peroxidase required for safeguarding the S-H groups and degeneration of peroxidase [5]. Hence, Se acts as an antioxidant. Moreover, Se causes the death of different microorganisms due to its ability to augment the oxidation reaction of intracellular thiols. Hence, they have gained more interest in the biomedical field. Besides, See is also used for commercial and industrial purposes. This is because of its low melting point and good photocatalytic activity concerning oxidation and other hydration reactions. Selenium is present in some food products, yet there are issues of adsorption and bioavailability. Hence, Se supplements are consumed to avoid Se-related problems. When there is low Se in our body, it leads to cardiac, osseous, muscular and immune system disorders.

The statement is primarily about Se, how it is both beneficial and harmful. The importance of restricting Se intake cannot be overemphasized. Se intake above 400 µg may cause selenosis, showing the

urgent need for accurate levels. UK recommendation levels are 60 µg per day for women, 70 µg for men and while these reflect possible toxicity problems, the reasons behind them are infinite ramifications [6]. However, both traditional inorganically bound selenium minerals and organic forms themselves are challenging due to their toxic side effects. Nanotechnology offers a solution to the problems posed by selenium toxicity that also makes possible its therapeutic potential. Nano selenium (nano Se) has unique advantages in food supplements among the selenium deficient [7]. Harnessed through nanotechnology, Nano-Se can have not only greater bioavailability than traditional forms of selenium but also lower toxicity. This opens the door for safe and effective use of Se in therapeutic settings without any compromise on its beneficial effects. Moreover, Nano-Se exhibits potential for targeted delivery and controlled release, so that it may be precisely dosed according to individual needs. This is the central point that the paper makes about Nano-Se. By providing further elucidation and context, the manuscript furthers our understanding of how Nano-Se works to achieve its therapeutic efficacy and safety profile. In addition, the discussion of its use in food products makes Nano-Se more immediately relevant to society at large than some other drug of its kind [8]. Furthermore, the fact that it cures Se deficiency without side effects in the least far expresses just how important Nano-Se is to both clinical practice and nutrition. In conclusion, the incorporation of Nano-Se into therapeutic regimens represents a promising new approach for future research on Se-NPs. It offers fresh directions related specifically to Se poisoning while also avoiding potential risks associated with toxic elements [9].

Further, Nano Se is used for the targeted delivery of therapeutic drugs, and it possesses excellent antioxidant, antibacterial, anticancer, antidiabetic, antiparasitic, anti-inflammatory and antifungal properties. Only a few reports study the green synthesised Se NPs and their medical properties compared to those of Se NPs produced using physical and chemical methods. Hence, in this review, we focus on the recent research works that have studied the synthesis of Se NPs from different plant extracts. In addition, characterisation techniques of Se-based NPs are discussed. Finally, therapeutic and theranostic applications of green synthesised Se NPs are studied. Its significance lies in describing various natures and varieties of nanometer material and application areas specifically within nanotechnology [10]. It meticulously divides the good aptitudes which nanomaterial has inborn, its large surface-to-volume ratio and various forms of properties combining magnetic electric and living. This paper diligently analyzes key sociological literature concerning these major features for Nanotechnology in widespread fields and highlights its meaning as encouragement to pursue innovation in an unswerving direction [11]. The work describes a creative method for producing selenium nanoparticles (Se NPs) using environmentally friendly methods. This approach produces Se NPs with both reduced biotoxicity and a higher kill rate against infections. In this study, these nanoparticles were extensively characterized. This entailed employing advanced spectroscopic and microscopic techniques to look at their size, shape, stability and more. Furthermore, the therapeutic potential of Se NPs to be used in microbial inhibition and cancer treatment is discussed. Their excellent antibacterial and anticancer properties are emphasized here [12, 13]. A wealth of high-quality synthesis tools for Se NPs, as well as applications can also be found in this work. This is to advance sustainable biomedical research and clinical therapeutics.

2. Methods of Production of Nano Se

Generally, three types of methods are used to synthesise Se NPs. They are physical, chemical and biological methods. Techniques such as UV radiation, laser ablation, hydrothermal methods, microwave radiation, and laser cauterisation are used to produce Se NPs via physical methods. Chemical methods often involve reduction techniques that employ stabilisers, dispersants, and other reducing substances to convert Se salts into Se NPs [14]. Various methods, such as physical, chemical, and biological are used to synthesize selenium nanoparticles (Se NPs). For example, physical methods employ techniques like UV radiation and laser ablation [15]. Chemical reduction methods often involve stabilizers, such as polysaccharides, which are purportedly safer and more energy-conserving than other alternatives. However, with regard to energy consumption, can these claims stand up to a count. Use of hazardous materials in traditional methods Conversely emphasizes the need for novel, energy-efficient alternatives. Not only does it bring risks to human health or life, but also to the environment. As, more examples demonstrate, biological synthesis is a green route. Here organisms like bacteria, fungi, algae, and plants have been used as experimental subjects; as the results of several research studies, these non-toxic and biodegradable Se NPs are cost-effective [16]. For example, Zoogloea ramigera, a gram-negative nonpathogenic bacterium, has been used in previous studies on Se NP production.

Biological methods are known to be a kind of green route to make selenium nanoparticles (Se NPs) and emphasize in our paper, what specific presents remains a question. These questions need to be answered in order to explain their effects on overall synthesis of the desired products. More commonly, larger organisms such as bacteria, fungi and plants are seen in the process of SeNP production "Biological" typically indicates an ecologically friendly approach, which does not render the raw material inert instead

giving it useful life again.Bacteria of the species Zooglea ramiger previously used to manufacture Se NPs offer an indication that future directions in nanoscience may come from such alternative biochemical pathways [17]. In the field of nanotechnology, it is important that further research is conducted in order to develop new and novel methods for synthesizing smaller particles where years have gone by lacking a breakthrough (Figure 1) [18]. The synthesised NPs possess excellent stability for a period of up to 6 months. Bacteria contain certain proteins which help increase Se NPs' stability. Plants play a significant role in the biological methods for extracting Se NPs, as some plants naturally contain trace amounts of Se. Also, Se NPs are synthesised from plants comparatively quicker, and no toxic chemicals are involved. In addition, they require only mild conditions for the synthesis of NPs. Further, plants contain enzymes and phytochemicals such as flavonoids, alkaloids and terpenoids that serve as capping or reducing agents. Besides, plant NPs exhibit enhanced catalytic activity [19].

3. Green synthesis of Se NPs

Many types of NPs are synthesised using different parts of plants. As mentioned in the previous section, some plants naturally possess Se NPs. They imbibe the nanoparticles from the soil, mostly from sedimentary rocks. Plants that contain Se can be broadly categorised into two groups: (i) Plants that intake the entire Se that is present in the soil; (ii) Plants intake Se and store them in larger proportions when compared with the Se present in the soil. Selenium is present in plants in various chemical forms, which corresponds to its catalytic activity [20].

Several various parts of the plants, such as leaves, fruits, flowers, buds, nuts and seeds, were used to produce Selenium (Se). Initially, they were washed with deionised water, followed by drying, grounding, and boiling using water [21]. Some of the studies involve only soaking and constant stirring without applying heat. Some studies use microwave irradiation, such as the extraction of Se from cocoa beans. The solution was then filtered or centrifuged. The supernatant was used for further processes with respect to the biosynthesis process, plants contain phytochemicals, proteins, amino acids and sugars that have both therapeutic value and also act as reducing agents. NPs often accumulate, and hence, stabilisers are needed to inhibit the process of agglomeration. This will be carried out by using a coating with polymer or a surfactant that restricts the communication between NPs as they grow [22].

At certain times, phytochemicals present in plants are also used as stabilising agents. The main criterion for producing NPs from plants is forming small, stable particles. Parameters such as temperature, time, pH, and concentrations affect the production of NPs from plants. Hence, some studies use response surface methodology to optimise the process parameters to be used in the biogenesis of Se NPs. In most of the studies, different ratios of sodium selenite, selenite, or selenous acid were combined with plant extracts. Ascorbic acid was also added as it can initiate the reduction reaction [23]. The solution was stirred constantly at room temperature at different times from 12 - 72 h. Some studies require up to 7 days in dark conditions. Some studies involve heating at the required temperature and time - the solution's colour changes to red, indicating the formation of Se NPs. The Se NPs can be extracted using a high-speed centrifuge followed by thorough washing using water or any appropriate solvent.

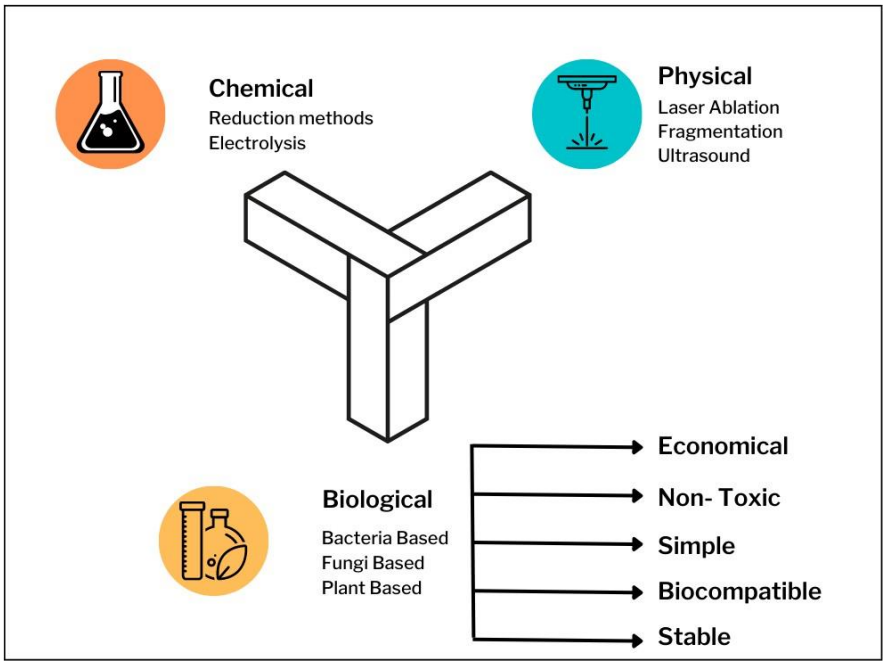

Figure 1. Methods of production of Nano Selenium

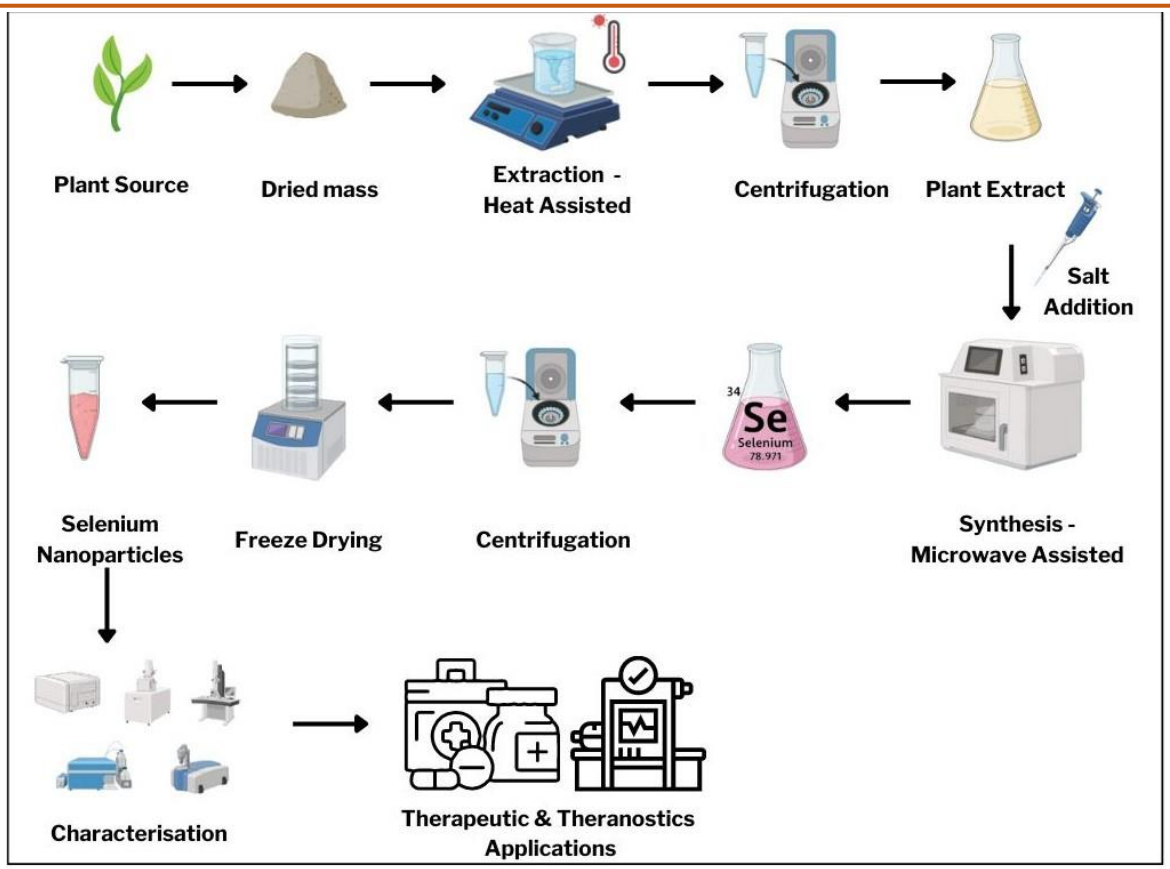

Figure 2. Methodology for the production of Nano Selenium from plant extracts.

A previous research work employed sodium selenite as the precursor for the reduction process [23]. This study used Catharanthus roseus flowers along with sodium selenite, which required an incubation time of about 7 days stated that the time needed to synthesise Se NPs from sodium selenite is more than for the Se NPs produced from orange peel extract. The optimum conditions were time (15 min), temperature (40 °C) and pH 4.

Cocoa bean shell acts as a reducing and capping agent for producing Se nanoparticles. Microwave irradiation was used to increase the reaction speed. It was observed from the study that the microwave process did not affect the Se NPs; the Se nanoparticles were found to be smaller in size, and the process needs only a limited number of precursors for the synthesis of Se NPs. One of the studies used RSM to optimise the process parameters employed in synthesising NPs from Pelargonium zonale leaves. The study assessed the effects of the concentration of plant extract as well as precursors on the particle size of Se. It was observed that when the concentration of plant extract and sodium selenite increased, the particle size of Se also tended to increase [24].

Aloe vera leaves were used in subcritical water conditions as the process can produce high pressure and temperature. The whole process took only 15 min to complete. RSM with CCD was used to determine the optimum conditions that affect the formation of colour intensity and size of NPs [25]. It was noted that when the concentration of plant extract increases while keeping a constant sodium selenite concentration, the concentration of Se NPs increases along with the increase in the intensity of the colour of NPs. Contrastingly, the colour intensity decreased when the precursor concentration increased, keeping the plant extract constant. This is because, in the case of experiments employing low concentrations of plant extract, the reducing agents present in plants react entirely with the Se ions [26]. However, an increase in the precursor concentration increased the amount of Se ions with a reduction in the formation of Se NPs. Hence, their concentration decreased as the reaction volume increased [27]. The common methodology used for producing Nano Se from plant extracts is illustrated in Figure 2.

4. Characterisation of Se NPs

The produced NPs using different plant extracts were characterised by several techniques in order to confirm the Se NP formation and also to assess the properties, structure and composition of the formed NPs. The Ultraviolet-visible absorption spectra (UV-Vis) were used to confirm Se NP [28]. This was performed using the formation of red colour in the NP. Moreover, the peak was observed between 200 and 400 nm, again confirming Se NP's presence. As the size of the particle augmented, a red shift befell in the absorption band of Se NPs. Sometimes, the peak formed between 450-600

nm when the se NPs were prepared using the reducing properties of certain bacteria. This is because of various enzymes in bacteria that alter the reduction process's catalysis [29]. Scanning electron microscopy (SEM) is another technique that evaluates size, shape, and distribution. It also reveals whether the NPs form accumulation or overgrow. Dynamic light scattering (DLS) aids in the determination of the size of formed NPs and their distribution. Energy dispersive spectroscopy (EDS) was utilised to assess the components present in the NPs and their purity level [30]. The highest purity of Se NPs (82%) was obtained from the leaf extract of Senna auriculata. This was followed by those produced from Clausena dentate (73%) and then Emblica officinalis (62%).

Fourier transform infrared spectroscopy (FTIR) was employed to confirm the formation of functional groups such as O–H, N–H, C=O and C–O in Se NPs. The peaks observed at 1375 cm−1, 1030 cm−1, 1462 cm−1 and 1250 cm−1 attributed to the formation of phenolic OH, bending of C-H bond, asymmetric bending in C-H bond and secondary O-H, respectively, which conveyed the synthesis of Se NPs via a green pathway [31]. X-ray diffraction (XRD) determines the overall morphological features of Se NPs and crystalline structure. Raman spectroscopy revealed the vibrational properties of crystals in the Se NPs [32].

Finally, the stability of the formed NPs is significant for their usage, which is assessed using zeta potential. Negative values were usually obtained for Se NPs. This is because of the presence of proteins, polysaccharides, and lipids with a considerable number of ionised carboxylic acid groups [33]. An absolute value is produced for the synthesised NP, and when this value is greater than 30 mV, the formed solution is stable without any overgrowth. It was observed from the previous studies that the least zeta potential was observed was – 36 mV for the Se NPs produced from lemon plants and ginger fruits. This was followed by the extracts from Java tea (-34.9 mV) [34]. When the synthesised NP exhibit a spherical size of 24.3 nm, it implied that it would be stable for a period of 3 months [35].

5. Therapeutic applications of Nano Se

Selenium (Se) has vast therapeutic properties, particularly in maintaining the genteel functioning of the body's immune system [36]. There is a continuous increase in the onset of diseases such as cancer, diabetes and other lethal diseases that challenge the medical system globally [37]. Numerous studies have previously observed that Se NPs have very low toxicity and can communicate effectually at tissue and cellular levels. Hence, they are used as therapeutic and theranostic substances [38]. In general, Se is a biologically active element and hence plays a crucial role in oxidoreductive cycles. Though Se has numerous advantages, its organic and inorganic forms are toxic, as seen in the previous section. Hence, Nano Se has been introduced into the limelight [39]. Besides overcoming the drawbacks, Nano Se possesses excellent antimicrobial, anticancer, antidiabetic, antiparasitic and antioxidant properties [40].

The important properties of Nano Se are listed in the upcoming sections, and they are also listed in the table (Table 1).

Table 1. Properties and biomedical applications of Nano Se obtained from different plant extracts

Sl. No	Plant extract	Properties of Nano Se	Biomedical applications	References
1	*Tinospora cordifolia* stem extracts	The characterisation study showed that the size of the produced NPs was between 100-200 nm. The NPs were stable with a zeta potential value of -23.9 mV.	Antioxidant and anticancer properties against human breast cancer	[41]
2	Coconut water	The synthesised NPs exhibited very low toxicity compared to their organic and inorganic forms, confirmed using Brine shrimp lethality assay and Zebrafish toxicology.	Excellent ant properties icancer	[42]
3	Extracts of *Fusarium semitectum*	Transmission electron microscopy analysis showed Se NPs from *Fusarium semitectum* with an average length of 61.18 ± 15.85	Antioxidant, anticancer, and antimicrobial properties	[43]

4	Carica papaya latex	A simple dispersion of uniform spherical-shaped NPs with an average diameter of 70 nm was observed. The zeta potential was - 17.8 mV.	Anticancer properties against human breast cancer	[44]
5	*Vitis vinifera* extracts	Spherical-shaped NPs with size 3–18 nm	-	[45]
6	*Allium sativum*	A dark pink solution was obtained. NPs size ranging from 7–45 nm, stability period of 2 months	Antioxidant	[46]
7	Drum stick leaves	Nanospheres and nanorods were obtained with a size of 18.9 nm	Anticancer properties against human colon, breast and liver cancers	[47]
8	*Diospyros montana* leaf extracts	Size of NPs ranging from 4-16 nm	Antibacterial, antifungal and anticancer properties	[48]
9	Mushroom extracts	The size of NPs ranges from 100 to 600 nm depending on the precursors' concentration.	Anticancer properties against human breast cancer	[49]
10	*Trigonella foenum-graecum* leaf extracts	Reddish oval-shaped Se NPs of size 50-10 nm	Anticancer effects against Breast cancer	[50]
11	*Averrhoa carambola* leaf extract	NPs size was 125 nm with a zeta potential of −23.20 mV.	antibacterial, ant anticancer ioxidant,	[51]

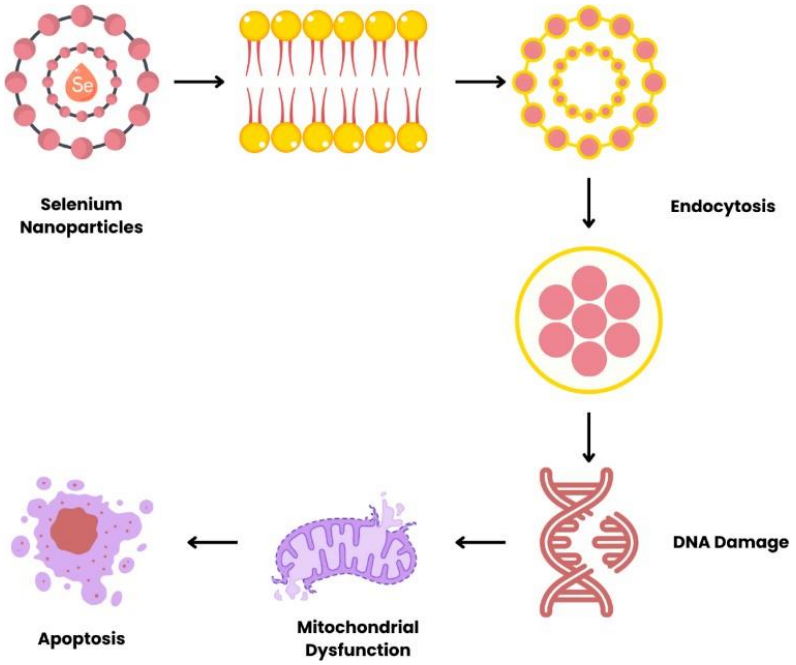

Figure 3. Mode of entry and mechanistic action of synthesised SeNPs against cancer cell line

Table 2. Mechanism of action of Se NPs against different types of cancer cells

Type of cancer cell	Mechanism	Effects	References
Cervical cancer	Se NPs were loaded with hyaluronic acid (HA) to form HA-Se NPs, which were combined with the drug doxorubicin (DOX). HA-Se@DOX exhibited greater activity to thwart HeLa cell proliferation and initiated HeLa cell apoptosis by activating the Bcl-2 signalling pathway.	DOX was released from HA-Se NPs faster in acidic environments than in the normal physiological environment, and 76.9% DOX was released in pH 5.4 during the initial 30 h.	[58]
Brain cancer	Chitosan was combined with Se NPs for the treatment of brain cancer cells. There was an increase in the cellular uptake of 0.2% Chitosan-Se NPs in U87 cells, which was produced by chitosan in Se NPs. Besides, the coumarin-6-associated chitosan-Se NPs could cross the blood-brain barrier, thus enhancing the therapeutic efficiency of Se NPs.	Chitosan-Se NPs exhibited a higher anticancer activity than Se NPs when used to treat brain cancer cells.	[59]
Breast cancer	Flow cytometric and PCR analyses showed that Se NPs synthesised from apigenin caused apoptosis in MCF-7 cells by directly targeting Bcl-2, Bax, and caspase-3.	Cytochrome C is discharged from mitochondria into the cytosol, along with cell death, causing DNA damage and killing MCF-7 cells.	[60]
Colorectal cancer	Se NPs were combined with RGDfC to form RGDfC-Se NPs, which were loaded with siDCBLD2 for colorectal cancer therapy. RGDfC-Se NPs increased the cellular uptake of siDCBLD2 in human HCT-116 colon cancer cells by directing polypeptide RGDfC on the colon cancer cells' surface. This is mainly done by using a clathrin-related endocytosis pathway.	RGDfC-Se@siDCBLD2 attached to the cancer sites exhibits a noticeable anticancer efficacy on HCT-116 tumour-bearing mice without side effects.	[61]
Liver cancer	Astragalus alcohol soluble polysaccharide was combined with Se NPs (AASP- Se NPs). Depletion of mitochondrial membrane potential and inducing accumulation of ROS. Increase of the Bax/Bcl-2 ratios and promote Cyt c liberation.	Inducing ROS and mitochondria-mediated apoptosis.	[62]

6. Anticancer properties

One needs a combination of treatments, such as chemotherapy and radiotherapy, to treat cancer. However, there are some promising results with respect to the above treatments, and harmful side effects are involved [52]. Previous studies claim that the intake of Se supplements and regular treatment for cancer aid in quick recovery and improve the status of patients' health. Selenium (Se) has good anticancer properties against various kinds of cancer, such as breast, lung, liver, kidney, colorectal and bone cancers, and they were confirmed by conducting both in vivo and in vitro investigations. The chemical form of Se compounds, including methyl selenocysteine, methylseleninic acid, and selenomethionine, possess excellent therapeutic effects on liver cancers. Laminarin polysaccharide was used to produce Se NPs, which were spherical in diameter of 60 nm and effective against human liver cancer (HepG2 cells). It was understood that the Se NPs help in cell death and thus prevent the late stage of autophagy [53]. Se NPs synthesised from plants tend to lessen the expression of anti-apoptotic factor B-cell lymphoma 2 and protect the influence of B-cell lymphoma 2 on Beclin-1 in human liver carcinoma cells. Another study used the plant extracts of Withania somnifera to produce Se NPs that cause apoptosis of adenocarcinoma human alveolar basal epithelial cancer cells [54]. Stability was initially affected in chromosomes, followed by inhibiting the process of mitosis, thus preventing the growth of human alveolar basal cancer cells. Carica papaya-based Se NPs alleviated breast cancer by disturbing the chromosomes and fragmentation process Figure 3.

Aqueous extracts of nettle leaves were utilised to prepare Se NPs, and they have excellent anticancer

properties and antimicrobial and antioxidant properties [55]. They are found to be effective against liver cancer (HepG2 cells) without affecting the viability of normal cells. Clove and cumin-based Se NPs were used against colon cancer, and it was found that they first cause condensation in chromatin followed by fragmentation of the nucleus [56]. This, in turn, causes the cell death of colon cancer cell lines. Another study discussed the synthesis of Se NPs from the fruit extract of Solanum nigrum, and their anticancer properties were determined along with antioxidant and antibacterial activity. Recently, pomegranate peel-based Se NPs were found to possess good anticancer properties, and they were tested against MCF7 and Mg63 cancer cell lines [57]. The mechanism of action of Se NPs against several types of cancer is presented in the table below (Table 2). In addition to the Se NPS being used alone, when combined with certain approved chemotherapeutic agents, it was witnessed that there was an enhancement in its therapeutic effect [63]. This is discussed in the below section.

7. Combination therapy of Se NPs with approved chemotherapeutic drugs

PEG, along with Se NPs, was used for the targeted delivery of the drug sesamol, which is used for the treatment of cancer [64]. Though sesamol has excellent antioxidant, anticancer, and anti-inflammatory properties, it has low oral bioavailability and stability. Hence, sesamol was attached to the surface of PEG-Se NPs by stirring the mixture at room temperature for 48 h. The resultant compound has a spherical shape and has anti-tumour properties against HepG2 cells [65].

Combining sesamol with PEG-Se NPs initiated ROS stress in cancer affected cells and, thus, apoptosis by activating caspases-3/9. Also, this helps decrease Bcl-2 expression and upregulation of Bax and PARP, leading to chromatin condensation, DNA fragmentation, and cell death (Liu et al., 2019). In another case, PEG-Se NPs are combined with crocin to treat lung cancer effectively. This is because the conjugation of crocin onto the surface of PEG- Se NPs initiated cell death in A549 cells [66]. This is by activating the apoptosis pathway in mitochondrial cells and reducing tumour volume without any noticeable side effects. Natural killer (NK) cells and pemetrexed (Pem) based chemotherapy techniques have a wide range of applications in efficient cancer treatment. However, their therapeutic application is greatly thwarted by the over-expression of NK cells on the surface of cancer cells. Besides, Pem has low cell internalisation efficiency. Therefore, Se NPs were combined with Pem-based and NK cell-based cancer treatment methods [67]. The combination can improve the delivery of Pem to cancer-affected areas and thus enhance Pem's chemo therapy effects by producing seleninic acid by the oxidation of β-seleno ester. In addition, the synthesised seleninic acid blocked the production of inhibitory receptors against NK cells. This, in turn, activates the immunogenicity of NK cells [68]. Both in vitro and in vivo studies have been conducted that exhibited the enhancement of chemotherapy and immunotherapy effects of Pem and NK cells when combined with Se NPs[69] .Sonodynamic therapy is an innovative treatment technique which has low-intensity ultrasound radiation by the utilisation of a sonosensitiser, which has greater merits when compared with routine methods that aid in the establishment of treatments in deep tumour cells, targeted delivery of chemotherapeutic drugs with negligible side effects and minimal invasiveness [70]. In this research work, Se Nps was combined with PEG and curcumin, and the cytotoxicity of pancreatic cancer cells was studied and compared to that of the drug gemcitabine (GEM). Se-PEG-Cur NPs and GEM were used against ASPC1 cell lines separately as well as combined with and without ultrasound radiation. The results of ultrasound radiation on the cytotoxic effects of Se-PEG-Cur NPs, GEM and their combination were examined by recording parameters such as cell viability, measurement of reactive oxygen species (ROS) level, and assessment of apoptosis promotion. It was found that the cells. The results revealed that sonodynamic therapy using Se-PEG-Curcumin NPs and GEM separately helped mainly in the production of ROS, thus causing apoptosis in ASPC1 cells [71]. However, a combination of the above compounds played a major role in inhibiting ASPC1 cells by enhancing the toxicity in pancreatic cancer cells initiated by the intensification of the ultrasound ratio. Besides Se NPs being good anticancer agents separately and in combination with chemotherapeutic drugs, they also possess good antimicrobial and antioxidant properties discussed below [72].

8. Antioxidant properties

Antioxidants are usually employed to diminish the production of free radicals. Se NPs are coated with different plant extracts and organic compounds that behave as antioxidants [73]. Both in vivo and in vitro experiments have been performed with Se NPs as they can suppress free radical formation, thus preventing oxidative damage. It was observed that sodium selenite prevented the growth of Candida utilis by enhancing the elimination and production of glutathione. Likewise, Se NPs, when decorated with chitosan, exhibited increased glutathione peroxidase and lipofuscin production in mice samples [74]. Besides the applications mentioned above, Se NPs produced via plant extracts have better antioxidant properties as they are more stable, aid in sustained release and are more biocompatible. It is noteworthy to observe that Se NPs produced via a green pathway showed enhanced antioxidant activity via ABTS and DPPH assays [75]. In a study, extracts of Mucuna pruriens and Aloe vera were utilised for producing Se-based NPs, and it was witnessed that the above-synthesised NPs exhibit good antioxidant properties in

safeguarding the cell from oxidative stress. Also, green synthesised Se NPs are applied in coronary heart infections and different types of cancer affected due to oxidative stress. Se NPs functionalised using gum Arabic showed tremendous antioxidant activity towards hydroxyl free radicals [76].

9. Antimicrobial properties

Multidrug-resistant microorganisms are one of the major threats listed by WHO. Hence, efforts are being taken to develop anti-multidrug-resistant drugs to treat several infections [77]. A wide range of NPs have been used to develop antimicrobial agents. Se NPs have been extensively used as they have good biological activity. Se NPs were coated with various polymers, such as polyvinyl chloride, polyurethane and silicon, which are employed in biomedical devices [78]. It was noted that the antibacterial performance was enhanced as the concentration of Se was also increased. It was also witnessed that Se NPs, along with the coating of polymers, can prevent the growth of Staphylococcus aureus, which was not observed in uncoated NPs [79]. Another study observed that Selenium-coated PVC has excellent antibacterial properties compared to silver-NP-coated PVC. Se NPs also help prevent biofilm formation on the surface of clinical devices. Extracts of Rosmarinus officinalis was used for the production of Se NPs, which were tested against various types of bacteria such as Mycobacterium tuberculosis, Staphylococcus aureus, Streptococcus mutans, Escherichia coli, Pseudomonas aeruginosa and Mycobacterium simiae. It was observed that, except for Mycobacterium simiae, the synthesised NPs were effective against all other types of bacteria [80].

10. Enhancing Synthesis and Expert Insights

Primary Literature in, we have carried out a systematic review of the primary literature on the green synthesis of Se NPs, and their properties and potential uses in microbial and cancer therapeutics [81]. This is to provide our readers with comprehensive information from a variety of research articles, reviews and patents. Analysis of expert views and opinions, to enrich the paper by drawing on the views and opinions of experts we have drawn on leading researchers and practitioners in the field of nanotechnology microbiology oncology [82]. Synthesis methods and characterization techniques are scrutinized, we have conducted a critical analysis of the green synthesis methods used to produce Se NPs and taken factors into consideration such as reaction conditions, precursor materials and environmental friendliness. Moreover, we have explained the characterization methods used to measure the physicochemical properties of Se NPs, providing readers with a comprehensive view of their structural, morphological and functional attributes [83]. Applications In medical treatment, besides summarizing the procedures and results of green synthesis of Se NPs, we have dived into their potential uses in microbial and cancer therapeutics. By means of experiments and clinical trials, we aim to find out the causes of Se NP's medicine-relevant effects on organisms; how effective they are; what their safety profile is in diseases such as infections and malignant pro-li-ferations of the body [84]. Discovery of gaps in knowledge and prospects for the future, by the critical analysis and synthesis of existing knowledge we have identified certain important points that are poorly understood currently a road to travel in the future. This includes such avenues as novel green synthesis pathways for Se NPs, understanding the mechanisms of efficacy and action in therapy, and improving their formulation to increase both efficacy and biocompatibility [85]. Review seeks to offer reader a complete synthesis of knowledge and expert opinion on the green-mediated synthesis of Se NPs and their applications in microbial and cancer therapeutics. From collating a variety of academic perspectives, analyzing experimental data and seeing the way forward for future research we aim to contribute toward the development of this expanding field and carry a new generation Se NP therapeutics into practical clinical use [86].

11. Conclusion

The sustainable and efficient green synthesis of Se NPs. has huge potential for future investigations into biomedical applications, such as antimicrobial treatments or cancer therapies. Environmentally friendly production methods can reduce the environmental footprint of Se NPs, and enhance their biocompatibility as well. Modern methods that we can characterize the properties of Se NPs thoroughly include principle (or high-end) experiments and experimental analysis, which have shown their size shape and stability then this completeness ensures that these properties are suitable for therapy Meanwhile, Se NPs holds great potential for therapeutic applications in microbial inhibition and cancer treatment supported by evidence from studies on the properties of anti-microbial action. Successful synthesis and application of Se NPs require attention to the choice of green synthesis method, thorough characterization of nanoparticles produced from different methods, optimization of reaction conditions, and an understanding that smaller is not always better. Also, crucially important for improving their efficacy in combating cancers and microbial infections is to fully understand the mechanisms underlying the therapeutic effects of Se NPsas such, their anti-oxidation & anti-inflammatory properties. In addition, the development of targeted delivery systems and combination therapies can further improve results for these Se NP-based treatments. In short, the green synthesis of Se NPs represents a sustainable and efficient way to tackle the common problems of microbial infections and cancer

that will be faced by future generations of biomedical researchers across the world. Advancing our understanding of the mechanisms of action and optimizing the therapeutic potential for Se NPs as new disease treatments against microbes and cancers: this will improve patient outcomes and further push forward healthcare.

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S. Yasodha: Conceptualization, formal analysis, Writing – Original Draft Preparation. A.S. Vickrama: Conceptualization, Investigation, Methodology, Supervision, Writing – Original Draft Preparation; S. Rajeshkumar: Methodology, Writing, review and editing. All the authors read and approved the final version of the manuscript.

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