The Bioscan
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
20(1): 263-269, 2025
www.thebioscan.com

Algal Synthesis of Selenium Nanoparticles: A Green Approach to Biomedical Solutions

Payal Chaurasia[1], Khushaboo Soni[2], Preeti Maurya[3], Sanjay Singh[4*]

Department of Botany, CMP Degree College, Prayagraj, 211002, Uttar Pradesh, India

DOI: https://doi.org/10.63001/tbs.2025.v20.i01.pp263-269

KEYWORDS
Selenium nanoparticles,
Algae,
Green synthesis,
Biomedical applications,
antioxidant activities

Received on:
17-11-2024
Accepted on:
15-12-2024
Published on:
31-01-2025

ABSTRACT

The green synthesis of selenium nanoparticles with algae is a sustainable and eco-friendly method. Algae have highly active compounds that serve as natural reducing agents by which inorganic selenium converts into selenium nanoparticles This process takes place via metabolic pathways, both intracellular and extracellular, that allow selenium ions to be reduced into stable nanoscale particles. UV-Vis spectroscopy, scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffraction (XRD), and dynamic light scattering (DLS) are used to characterize the size, shape, crystalline structure, and surface properties of algae-derived SeNPs. These SeNPs show impressive antioxidant, antibacterial, and anticancer properties, thus showing potential as candidates for many biological applications such as drug delivery, wound healing, and cancer therapy. In addition, their biocompatibility and biodegradability reduce the threat of toxicity, thus making them more amenable to therapeutic applications than chemically synthesized nanoparticles. The paper discusses the advantages of algae use for the synthesis of SeNPs, indicates procedures of characterization as well as possible biological usage of SeNPs and further expands on the troubles of the scaling up green synthesis procedure and the future need for further research toward the improvement of their application at the clinic level, resulting in an overall view of additional possibilities for medicine.

INTRODUCTION

Nanoparticles (NPs) are solid colloidal particles with at least one dimension ranging from 1 to 100 nm (Moghaddam et al. 2022). However, most materials used in drug delivery are between 100 and 200 nm. Inorganic nanoparticles, with their superior essential chemical, biological, and magnetic capacity, have been produced for numerous diagnostic (Yuan et al. 2018; Korany et al. 2020; Liu et al. 2021), therapeutic (Liu et al. 2021) health (Augustine and Hasan 2020), and agricultural purposes (Dimkpa et al. 2015; Kah et al. 2019). Several nanomaterials show considerable potential for merging diagnostic and therapeutic applications, such as monitoring the biological distribution and accumulating at the target site, recognizing and measuring drug release, and longitudinally assessing treatment effectiveness (Baetke et al. 2015; Liu et al. 2021). Being a component of antioxidant enzymes such as glutathione peroxidase and thioredoxin reductase, which are vital for the biochemical processes of biological defence systems, including antioxidant activity, selenium is a necessary microelement for life. Whereas an excessive amount of selenium is very harmful to live cells, insufficient quantities can cause cardiovascular disease or cancer. Because the range between therapeutic and harmful amounts of selenium is so small, using it in various therapies necessitates a very careful approach (Khurana et al. 2019a). Human toxicity arises from both excess and deficiency of selenium (Muecke et al. 2010; Rayman 2020). It has been linked to cancer, immunodeficiency and brain disorders, cardiovascular and inflammatory diseases, type 2 diabetes, fertility and reproductive issues, thyroid autoimmune diseases, and more (Roman et al. 2014; Bodnar et al. 2016; Rayman 2020). Since elemental selenium (Se) is the least harmful form, its nanoform has gained a lot of interest. It's interesting to note that functionalized SeNPs are less cytotoxic than their other forms, including inorganic selenium, selenate, selenite, and selenoproteins (Skalickova et al. 2017). According to Ikemoto et al. (2004), SeNPs have a detoxifying impact on heavy metal exposure, and are chemopreventive ((Zhang et al. 2001; Wang et al. 2007), anti-hydroxyl radicals (Gao et al. 2002). Nowadays, physical, chemical, and biological processes are used to synthesize SeNPs. The cheap manufacturing cost and little environmental toxicity of biological techniques of nanoparticle synthesis are making them increasingly appealing (Pyrzynska and Sentkowska 2022). SeNPs have been decorated and/or functionalized using a variety of techniques to increase formulation stability and attain the desired therapeutic impact.

Algae have emerged as a promising biological system for the synthesis of selenium nanoparticles. Many useful compounds present in algae act as reducing and capping agents that stabilize the nanoparticles. SeNPs surface modification has been accomplished by a variety of chemicals, including folic acid (FA), hyaluronic acid (HA), proteins, peptides, and amino acids (Ren et al. 2013; Feng et al. 2014; Fu et al. 2016; Zhang et al. 2018; Zou et al. 2019), among others (Khurana et al. 2019a). Because of their superior qualities, SeNPs have a wide range of biological uses. Because of their associations with different moieties like selenoproteins, selenocysteine, selenomethionine, etc., SeNPs are important in a variety of biological applications. Several research studies have demonstrated that SeNPs have potential in combating deadly illnesses such as cancer, diabetes, Alzheimer's, drug-induced toxicity, etc. SeNPs have shown an increasing potential as major therapeutic platforms, especially in anticancer therapy (Khurana et al. 2019b), including in combination with well-known chemotherapeutic agents like 5-Fluorouracil (5-Fu)(Liu et al. 2012), exhibiting synergistic anticancer activity and overcoming multidrug resistance (Khurana et al. 2019b).

In this paper, we have discussed biomedical potentials of biosynthesised selenium nanoparticles such as antimicrobial, anticancerous, antidiabetic, anti-inflammatory, antioxidant, antiparasitic, and wound healing activity

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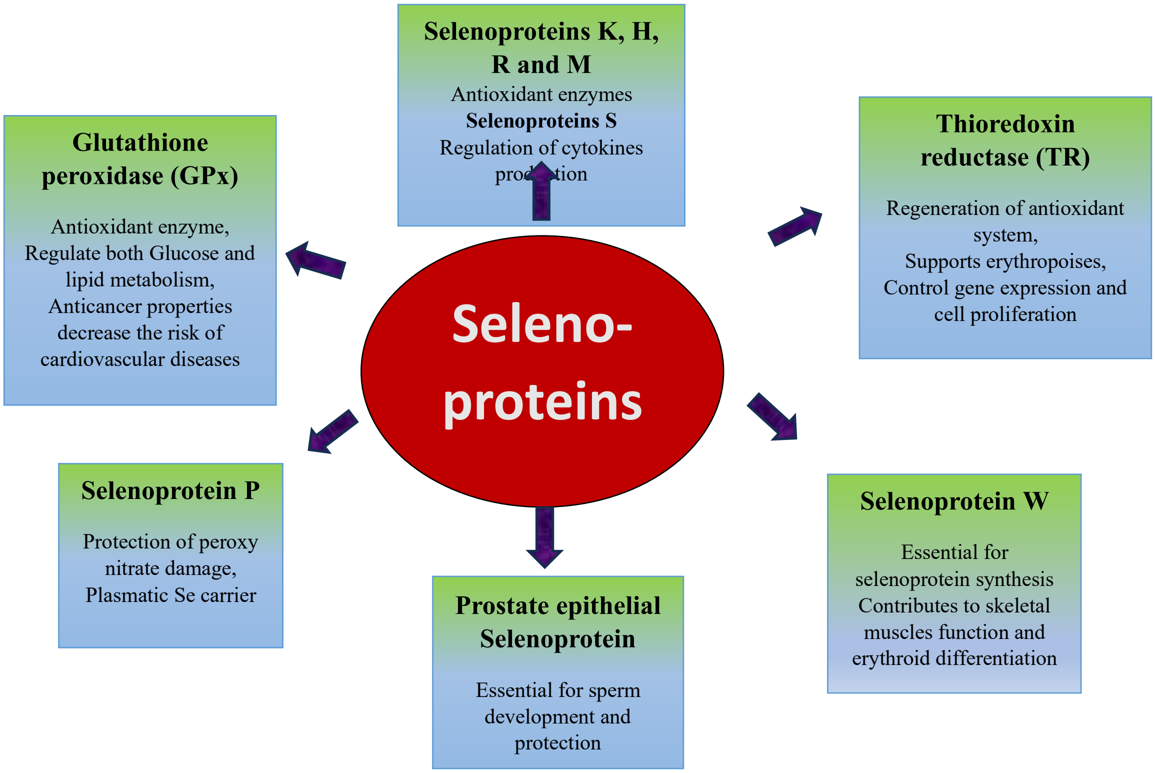

Fig 1. Functional role of selenoproteins in the human body

1. Algal-mediated synthesis of Selenium nanoparticles

Algae are called "bio-nano factories" since both the live/dead biomasses and their extracts were exploited for the phycosynthesis of metallic, non-metallic, and metalloid NPs (Khanna et al. 2019). In microalgae, phycosynthesis is mediated by a variety of chemicals found in crude extracts, including amines, amides, alkaloids, terpenoids, phenolics, proteins, and pigments, all of which aid in metal reduction and stabilization. Sodium selenite, sodium selenate, and selenious acid are used as the precursors for the synthesis of selenium nanoparticles. Algal-capped and stabilized NPs have received much interest for being low in toxicity, frequently obtained, cost-efficient, environmentally friendly, safer to use, and manufactured using green methods. Proteins or polysaccharides can serve as stabilizing or capping agents for the green synthesis of different NPs from algal species, while intracellular or extracellular compounds from algae are typically utilized for the biosynthesis of different NPs including selenium. Flavonoids, sugars, phenolic compounds, and ascorbic acid in algal extracts and fractions can be used as reducing agents.

Arthrospira indica (Afzal et al. 2019a) 2022), *Spirulina platensis* (ElSaied et al. 2021) (Afzal et al. 2019a), *Hapalosiphon* sp. (Chavan and Bhattacharjee 2016), *Synechocystis* sp. (Gouget et al. 2005), *Microcystis aeruginosa* (Zhou et al. 2021), *Anabaena* sp. (Banerjee et al. 2021), *Anabaena variabilis*, *Gloeocapsa gelatinosa*, *Oscillatoria* sp., and *Phormidium* sp. (Afzal et al. 2019a), *Hapalosiphon* sp. (Chavan and Bhattacharjee 2016) were found to biosynthesise selenium nanoparticles.

2. Characterization Methods of Selenium Nanoparticles (SeNPs)

Characterizing selenium nanoparticles (SeNPs) is crucial for several reasons, all of which further our understanding of their characteristics and their uses. These dimensions can be understood by methods like scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Furthermore, the stability and interactions of Se NPs with biological systems depend on the evaluation of surface characteristics, such as charge and hydrophobicity, using dynamic light scattering (DLS) and zeta potential studies. Their crystalline structure may be confirmed, and their potential reactivity can be inferred by identifying the chemical composition using techniques such as energy-dispersive X-ray spectroscopy (EDX) and X-ray diffraction (XRD). Analysis of optical characteristics using UV-Vis spectroscopy and photoluminescence is also crucial for photovoltaic and sensor technology applications.

3. Biomedical applications of Selenium Nanoparticles

Based on the improved properties of SeNPs over Se, they have been explored in various disease conditions. SeNPs offer improved bioavailability with the added advantage of decreased toxicity. SeNPs used for various therapeutic purposes including the conventional antibacterial, anticancer, anti-diabetic, wound healing, anti-inflammatory activity, antidiabetic, & antiparasitic activity.

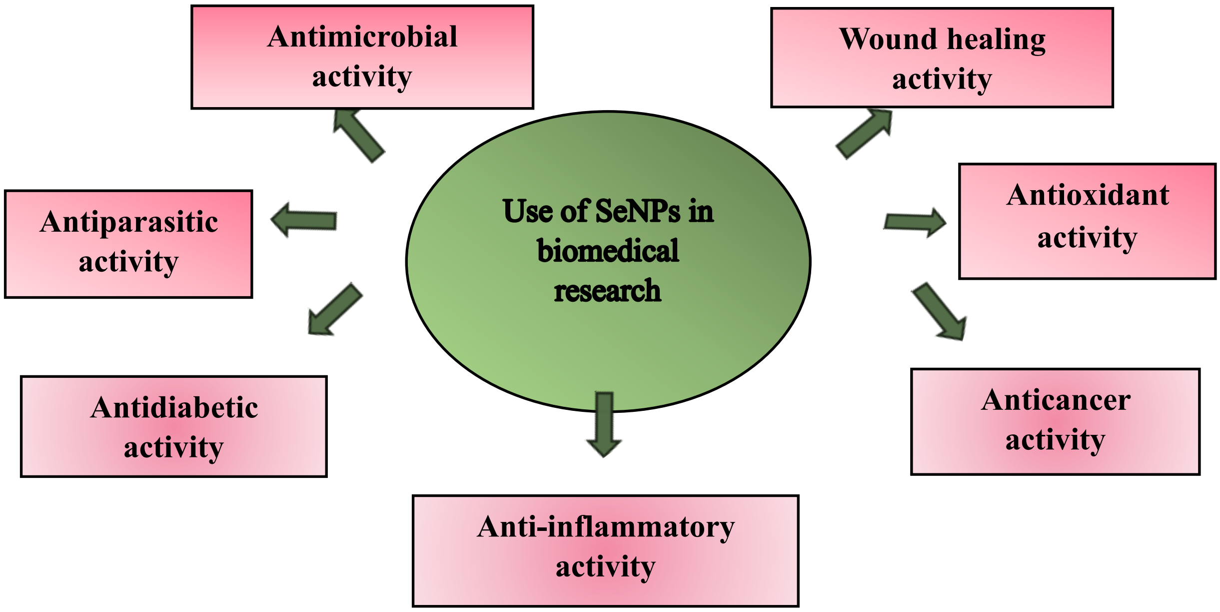

Fig 2. Biomedical applications of selenium nanoparticles

3.1. Antimicrobial Activity

SeNPs exhibit considerable adsorptive and biological activity, which enables them to be employed as an antibacterial agent because of their interactions with many functional groups of proteins, including C–O, C–N, NH, and COO– (Alvi et al. 2021). SeNPs derived from *Spirulina platensis* have demonstrated strong antibacterial action against Gram-negative bacteria and fungi (Abbas et al. 2021). The strongest antibacterial efficacy against *E. coli* MG1655 was demonstrated by SeNPs made from *Calothrix* sp., UU24112.

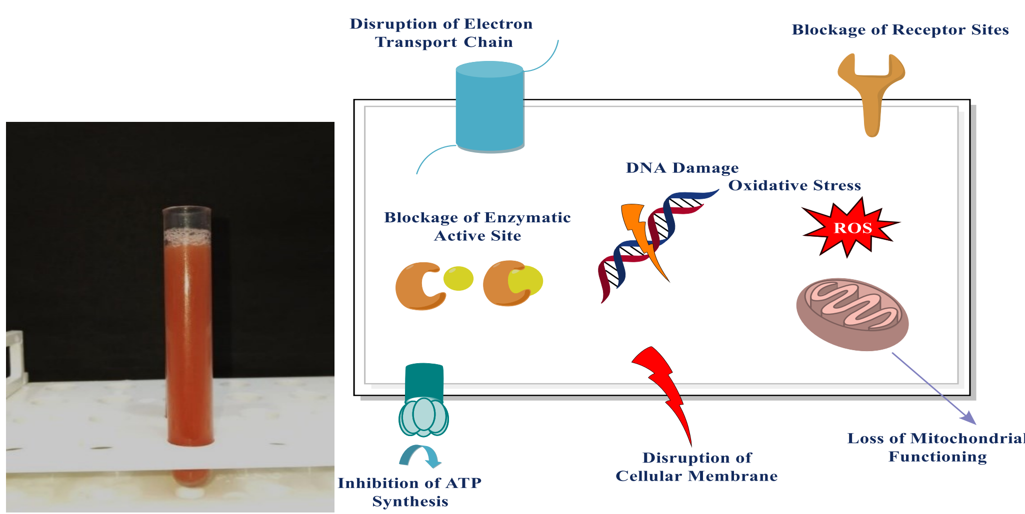

Fig 3. Damage to the bacterial cell by selenium nanoparticles

According to earlier research, selenium nanoparticles exhibited antifungal properties against *Candida albicans* and *A. fumigatus* (Shakibaie et al. 2013). Although *Polycladia*-mediated SeNPs had limited antiviral effectiveness against Adenovirus and HSV-2, with antiviral percentages of 8.64% and 17.39%, respectively, they exhibit high antiviral activity against the HAV-10 virus, with an antiviral percent of 40.25%. According to a study by Phong et al., the nanoparticles prevented the development of biofilms by inhibiting the growth of *Staphylococcus* bacteria by 60 times(Sampath et al. 2024).

Bacillus cereus, Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, Salmonella typhimurium, and *Salmonella enteritidis* are the six foodborne microorganisms against which selenium nanoparticles synthesised by Khiralla and Deeb are used for their antibacterial properties. Although several concentrations of SeNPs were used to test their antibacterial activity, all of the bacteria selected for the study were significantly affected by SeNPs at a concentration of 25 µg/mL (Khiralla and El-Deeb 2015). SeNPs affect bacteria in a variety of ways, causing lysis and ultimately cell death as shown in the figure. Additionally, when SeNPs penetrate the bacterial membrane, they disrupt it and induce bacterial lysis as seen in Figure 4. The size and form of the SeNPs determine their biocidal qualities; spherical nanoparticles between 50 and 100 nm in size are more effective than bigger ones because they can more readily enter bacterial cells and membranes and alter the biological activities of the bacteria (Mikhailova 2023).

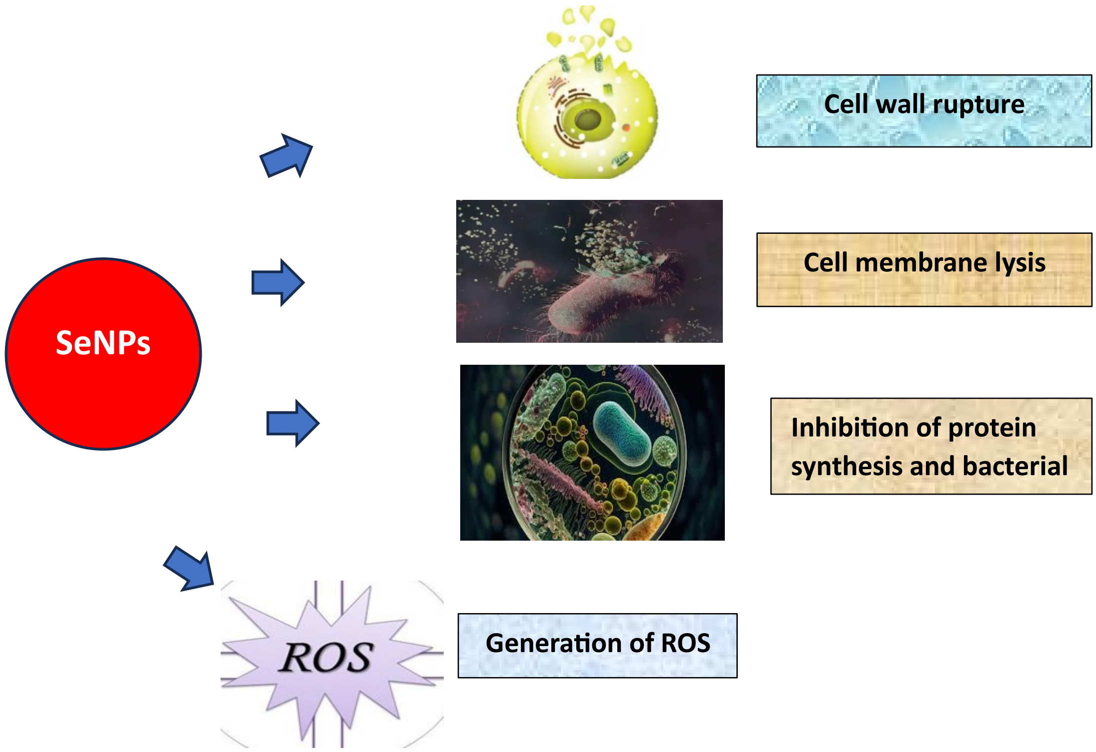

Fig 4. Different modes of action of selenium nanoparticles on bacteria

3.2. Wound healing activity of selenium nanoparticles

The wound-healing function of SeNPs acts on the trans-sulfuration pathway, where selenide and selenocysteine are converted to methionine, resulting in the replacement of selenomethionine, which is required for the wound-healing characteristic of SeNPs. An in vitro wound healing assay on human skin fibroblast cells (Hu02) demonstrated substantial wound closure at concentrations of 50 and 100 nM after 12 h, while no significant wound closure was observed at 200nM°. The results indicate that green synthesized SeNPs by whole cell of *Spirulina platensis* are promising nanoparticles for wound healing applications (Sadeghi et al. 2024).

3.3. Antidiabetic activity of selenium nanoparticles

Patients with diabetes frequently experience oxidative stress, necessitating the use of additional antioxidant species to lower the oxidative and inflammatory response(Zhou et al. 2016). Selenium is recognized to have strong antioxidant and anti-inflammatory properties against diabetic mellitus (Oztürk et al. 2015; Bahmani et al. 2016). Several researchers have looked at SeNPs' important therapeutic function in reducing major diabetes problems and insulin resistance (Zhao et al. 2017; Liu et al. 2018; Abdulmalek and Balbaa 2019).

SeNPs' antidiabetic activity can increase insulin production by protecting pancreatic cell integrity, suppressing oxidative stress, causing glucose depletion, and decreasing pancreatic inflammation (Ahmed et al. 2017). *Gracilaria lemaneiformis* used as a potential antidiabetic agent for food and medical applications.(Tang et al. 2021).

3.4. Anticancer activity of selenium nanoparticles

The anticancer properties of SeNPs derived from *Polycladia myrica* make them an excellent photothermal option for treating a variety of cancer cell types with minimal harm to healthy cells and great efficacy (Abo-Neima et al. 2023). Biogenic SeNPs exhibit anticancer activity depending on the dose (Ramamurthy et al. 2013; El-Zayat et al. 2021) and appear to be less toxic to non-malignant cells than their chemical analogs (Anu et al. 2017), whereas the surface modification does not affect anticancer activity or ceasing cell cycle induction (Krishnan et al. 2019). Se-induced cytotoxicity against malignant cells may be the result of ROS generation, as in the case of injecting biogenic SeNPs into the abdominal cavity of mice after inoculation with highly malignant H22 hepatocarcinoma cells (Ramamurthy et al. 2013). The molecular mechanism of *Sargassum wightii* SeNPs-induced A549 cell apoptosis was found to be through overproduced ROS-mediated activation of p53- and AKT-signaling pathways (Loganathan et al. 2022).

3.5. Anti-inflammatory activity of selenium nanoparticles

Green SeNPs decreased pro-inflammatory cytokine levels and inhibited the activity of the glial fibrillary acidic protein, demonstrating an inhibitory impact on epilepsy-associated inflammation and anti-inflammatory efficacy against PTZ-induced neuroinflammation. This protective effect increases SeNPs activity and plant extract flavonoids, phenols, and GSH components, which function as capping agents to inhibit free radical formation and minimize oxidative stress, inflammation, and apoptosis. Selenium nanoparticles' anti-inflammatory effects may be able to alleviate acute colitis symptoms. SeNPs coated with *Ulva lactuca* polysaccharides significantly lowered TNF-α and IL-6 levels in animals with DSS-induced colitis (Zhu et al. 2017).

3.6. Antioxidant activity of selenium nanoparticles

Antioxidants, whether hydrophilic or lipophilic, enzymatic or non-enzymatic, suppress oxidation by neutralizing the oxidative effect of free radicals and other chemicals. Many nanoparticles, including SeNPs, have been shown to have antioxidant properties. Their nanoparticle dispersibility may explain green SeNPs' capacity to neutralize these free radicals in the medium, which is due to their small particle size, as well as their high chemical activity and antioxidant activity. In vitro antioxidant capacity analysis is typically carried out using molecules such as 1,1-diphenyl-2-picryl-hydrazyl (DPPH), in which the free electron of nitrogen in DPPH is reduced by hydrogen present in antioxidants, ABTS (2,2′-azinobis (3-ethylbenzothiazoline-6-sulfonic acid)) for testing both hydrophilic and lipophilic antioxidants (Alhawiti 2024). *Arthospira indica, Anabaena variabilis* mediated selenium nanoparticles show significant antioxidant activity (Afzal et al. 2019b).

3.7. Antiparasitic activity of selenium nanoparticles

Due to their ability to spread malaria, Anopheles mosquitoes have emerged as one of the main threats to human life. Thus, using *Penicillium corylophilum* and ascorbic acid as a reducing agent, selenium nanoparticles (Se-NPs) were synthesised for the first time as an anti-victor malaria treatment. By treating with 100 ppm of Se-NPs, 100% larvae mortality was attained as compared with other concentrations which attained 90.6%, 70.3% 50.3%, and 43.3% larval mortality by treating with 75.0, 50.0, 25.0, and 20.0

ppm Se-NPs, respectively. Consequently, it can be concluded evidently that, Se-NPs showed larvicidal activity which increased with Se-NPs dose increases. Additionally, the parameter LC50 of the biosynthesized SeNPs that kill 50% of mosquito larvae was established at a lower value (25.0 ppm). Results demonstrated the high potency of Se-NPs against larvae, pupa and adults of 3rd instar of *Anopheles stephensi* mosquitoes even at low concentrations in which by increasing the concentration of Se-NPs, the larvicidal activities reached 100% at 100 ppm of Se-NPs (Salem et al. 2021).

In many nations, *Leishmania infantum* is an important risk factor for visceral leishmaniasis.

There are different complications for the treatment of leishmaniasis such as toxicity and drug resistance. The anti-leishmanial properties of SeO2 and biosynthesized selenium nanoparticles are dose-dependent. Additionally, compared to SeO2, selenium NPs have less cytotoxic effects and stronger anti-leishmanial activity (Soflaei et al. 2014).

CONCLUSION

Selenium is a vital element for human health, and its consumption varies with geographic location and aliments consumed; however, there are several forms of Se supplementation available today. In the human body, it is used for the production of selenoproteins, which typically incorporate Se in the form of selenocysteine in their active center. As a result of the antioxidant, immunomodulatory, and regulatory properties of selenoproteins, Se plays a crucial role in the human body, influencing the thyroid, liver, brain, and reproduction functions, besides having antitumor and antimicrobial properties. However, because Se has a narrow therapeutic window, both deficiency and excessive intake of Se are associated with severe symptoms and various diseases. The green synthesis of selenium nanoparticles minimizes environmental impact while providing an economical approach to biomedical applications. This synthesis process ensures that nanoparticles possess unique properties that enhance their effectiveness in several medical fields such as drug delivery, cancer therapy, and antimicrobial treatments. In a broad sense, the integration of algal synthesis into the production of nanoparticles represents an innovative advancement in green technology for biomedical solutions. The data given in the review will help researchers rapidly navigate the field of existing research on the functions and therapeutic effects of SeNP and find new directions for their research.

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