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# Selenium oxyanions from harmful environmental pollutants to beneficial selenium nanoparticles

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## ABSTRACT

Selenium, in both organic and inorganic forms, is a necessary trace mineral for human nutrition, it is essential for proper function of the immune system and protection against cancer. Cancer, heart problems, infertility, thyroid conditions, and weakened immune systems are linked to insufficient selenium intake shortage. Selenium is distributed into different environmental compartments by natural and anthropogenic activities, and generally discharged in the form of selenate [$SeO4^{2-}$] and selenite [$SeO3^{2-}$], which are both toxic. Physical-chemical and biological treatment processes have been reported to exhibit good treatment efficiencies for Se from aqueous streams. Moreover, the possibility of the biotic transformation of highly soluble and toxic selenite to less toxic elemental selenium nanoparticles using various bacterial strains and their optimization is a promising and eco-friendly way for its removal from the environment. Especially bacterial conversion is considered one of the best conversion methods for the synthesis of nanoparticles because of their quick growth rate, ease of handling, low cost, and high productivity. Also, selenium nanoparticles have generated interest in medicine as a medicinal agent with negligible side effects. In this review, the beneficial conversion of selenium oxyanions to selenium nanoparticles, their application in the medical field, and various parameters of their biological optimization have been fully discussed and elaborated.

**Keywords:** *Selenate; selenite; toxicity; green synthesis; biogenic selenium nanoparticles*.

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## Introduction

DNA synthesis, the most basic biological process, is one of the many cellular functions that need selenium to be performed. Globally, people are prone to diseases associated with selenium deficiency **[1]**.

With a tiny safety margin, selenium serves as a necessary micronutrient and vital toxin. However, at slightly greater doses or concentrations, selenium becomes toxic. It is dispersed throughout the ecosystem, which includes the atmosphere, mining, water, plants, soils, and wastewater. Se oxyanions have gained more attention, mainly because of their persistence and bioaccumulation effects in aquatic environments **[2]**. To remove selenium's harmful effects and preserve its positive impacts on public health, multi-sector studies are necessary. This would allow for the deployment of different treatment techniques to the contaminated environment **[3]**.

Microorganisms that convert selenium oxyanions or soluble selenium into insoluble elemental selenium play a key role in the natural selenium biogeochemical cycle. This conversion process is essential for maintaining environmental balance. Therefore, microorganisms that facilitate this reduction are highly valuable for bioremediation in selenium-polluted environments **[4]**. This process can be enhanced by manipulating environmental conditions and adding organic amendments **[5]**. Understanding these microbial transformations and transport mechanisms is crucial for developing effective selenium management strategies in water systems and for elucidating selenium's role in biogeochemical cycling **[6,7]**.

Metal nanoparticles have been widely applied in many disciplines, including the material sciences and healthcare. Thus, compared to the chemical synthesis of metal nanoparticles, biogenic metal nanoparticles have gained greater attention because of their low toxicity, economic viability, and environmental friendliness **[8]**. Many types of algae, fungi, plant extracts, and flavonoids which are recognized for their medicinal activities are effective and environmentally benign green nanofactories that are frequently utilized as bio-reductants for the synthesis of nanoparticles **[9]**. Microorganisms are thought to be the ideal source for the biosynthesis of nanomaterials since they can produce nanoparticles. Due to their huge surface areas, resistance to toxicity, ease of handling, and ability to scale up the process in comparison to other microorganisms, fungi are being reexamined as a viable source for the production of metallic nanoparticles **[10]**.

Biogenic selenium nanoparticles have emerged as a promising eco-friendly alternative to chemically synthesized SeNPs, offering numerous applications in agriculture and medicine. These nanoparticles exhibit low toxicity and enhanced bioavailability compared to other selenium forms **[11]**.

The article's goal is to demonstrate the significance of selenium nanoparticles and their uses, as well as the microbial synthesis of selenium nanoparticles, this will include the following topics.

## 1. Role of selenium

Selenium has many fascinating purposes in the human body as shown in **Fig. 1**, including anti-inflammatory, anti-mutagenic, anticarcinogenic, antiviral, antibacterial, and antifungal qualities. Skeletal muscle stores between 28 and 46% of the body's total selenium pool. It was discovered that the kidney has higher quantities of selenium than other organs **[12]**.

In the thyroid gland, Type I 59-deiodinase is an enzyme that contains selenium and is specifically involved in the activation of naturally occurring T4 into physiologically active T3. Transforming growth factors can lead to thyroid tissue injury and fibrosis in low-selenium situations **[13]**.

Selenium is necessary to maintain the body's homeostasis. Pregnant women have a higher demand for selenium, so it's crucial to think about the advantages of supplementing with the mineral. In vitro studies on adult ovaries have shown that selenium controls the proliferation of granulosa cells and the manufacture of 17-estradiol (E2), one of the primary female sex hormones **[1]**.

According to Bai *et al.* **[14]** selenium is a trace element that is vital and controlled by cellular redox homeostasis. It is a key component of selenoproteins, which govern important biological processes like the removal of reactive oxygen species and the modulation of particular enzymes **[15]**. A lack of selenium may make a person more vulnerable to viral infections.

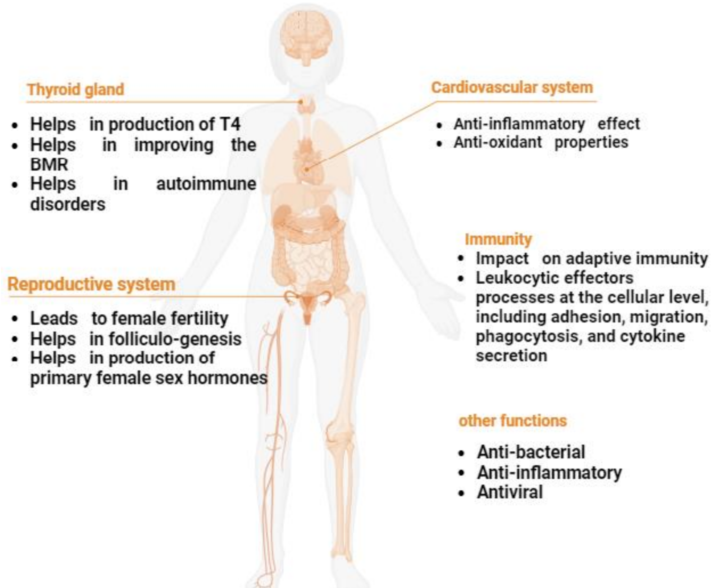


**Fig . 1.** The function of selenium in the human body

Due to its strong relationship to the redox reaction in animals, selenium has anti-disease and anti-immunization properties. Since animals are unable to synthesize selenium on their own, selenium supplements in the proper amounts are required to enhance the quality of livestock and poultry products, encourage selenium enrichment in animals, and create products with selenium enrichment functions **[16]**. In the human diet, eating aquatic animal food is a more cost-effective and efficient way to get selenium **[17]**. Selenium-rich aquatic creatures include salmon and tuna fish, oysters, and shellfish. According to reports, adult British diets supplement about 50% of their selenium from animal tissues **[18]**. Adding selenium-enriched yeast to animal feed is now the most popular way to supplement animals with selenium. SeMet, SeCys, and $SeO_4^{-2}$ are found in livestock and their byproducts, such as meat, organs, milk, and so on **[19]**.

Brazil nuts have the highest selenium level of any plant food source treated with selenium (19.2 μg/g), having been produced in soil rich in selenium in the Brazilian Amazon region. Astragalus, sunflower, cauliflower, some varieties of cabbage, onion, garlic, and cereals (rice, wheat) are excellent sources of selenium accumulation because of the richness of their corresponding derivatives (SeMet, SeCys, and $SeO_3^{2-}$) **[17]**.

## 2. Effect of selenium deficiency

Selenium deficiency is associated with heart failure; in a large European cohort study of patients with rapidly worsening heart failure, 70% had low serum selenium levels. Also reduced ability to exercise, a worsened prognosis with increasing heart failure, and a lower quality of life were associated with these patients' low serum selenium levels **[20]**. Moreover, reduced mitochondrial activity and increased reactive oxygen species (ROS) were seen in human cardiomyocytes derived from human pluripotent stem cells (hPSCs) cultured in low selenium, suggesting impairment of critical metabolic activities **[12]**. Molecular pathways relating selenium insufficiency to cardiovascular disorders are still unclear, despite mounting evidence of selenium's role in the pathophysiology of cardiovascular diseases. Enough selenium must be maintained in the body since excessive or inadequate selenium can be harmful to cardiovascular health. Cardiomyopathies, such as heart failure and Keshan's disease, have been related to selenium deficiency **[21]**.

A shortage of selenium has been connected to a higher risk of getting many infections **[22]**. Selenoprotein S which reduces endoplasmic reticulum stress during macrophage activation, and selenoprotein K, which is essential for immune cell functions like proliferation, migration, cytokine production, and resistance against infections, are two of the selenoproteins that the immune system depends on **[23]**. During viral infections, pathogens produce (ROS) and modify cellular antioxidant defenses, such as selenoproteins like thioredoxin reductases and glutathione peroxidases (GPx), which lead to oxidative stress **[24]**.

The detrimental effects of too much selenium on the endocrine system should be noted. These consequences include reduced synthesis of growth hormone, thyroid hormone, and insulin-like growth factor **[25]**. It has been demonstrated that proper selenium supplementation in conditions such as Grave's disease can slow the disease's progression and enhance the quality of life **[26]**.

## 3. Selenium in the environment and its toxicity

Different environmental compartments contain different types of selenium as shown in **Fig. 2.** Both organic and inorganic, nongaseous forms can be found in nature. However, the accessibility and dispersal of selenium are determined by its speciation, which takes into account a variety of factors **[27]**.

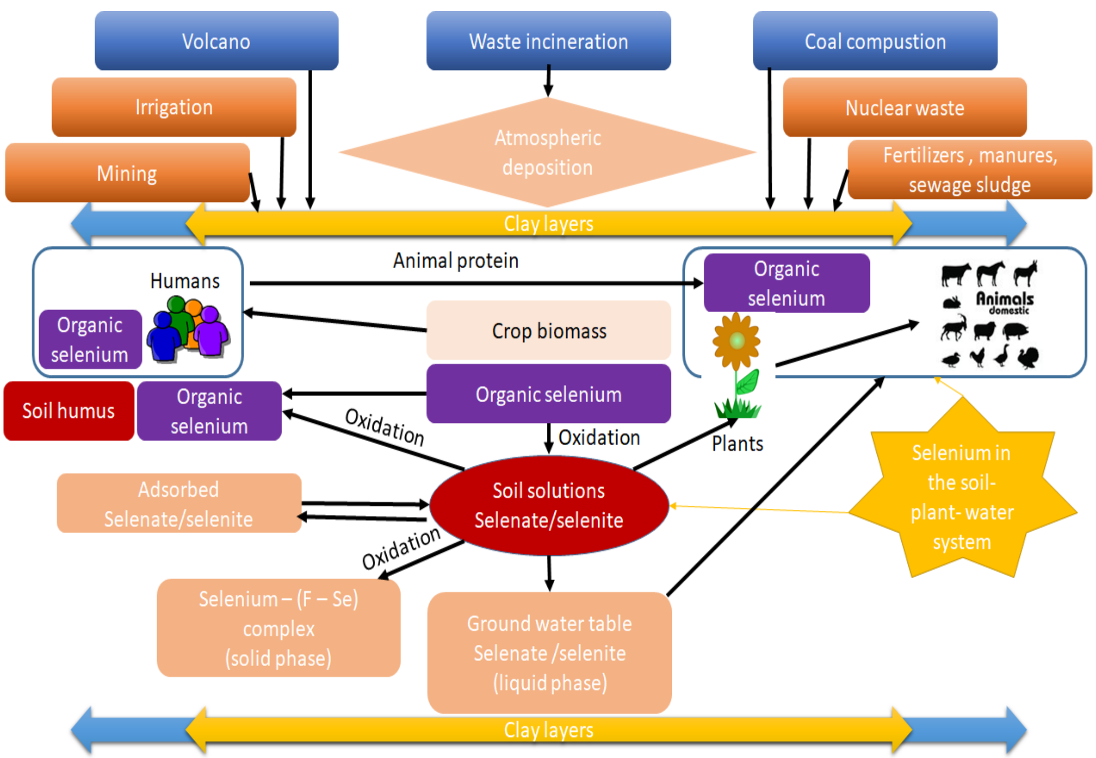


**Fig. 2.** An overview of the environment's Se content and environmental sources of selenium

Selenium oxyanions, primarily selenate ($SeO_4^{2-}$) and selenite ($SeO_3^{2-}$) are toxic environmental pollutants that can be transformed by microorganisms **[7]**. These oxyanions are highly soluble and mobile in water systems **[28]**. Microbial reduction of selenium oxyanions to less toxic elemental selenium ($Se^0$) is a key detoxification mechanism, as demonstrated by Anaeromyxobacter dehalogenans strains **[6]**. This process is significant for bioremediation and potentially for producing selenium nanospheres **[7]**. Other disposal methods include media filtration, chemical treatment, and biomediated removal. An innovative chemical technology has been developed to reduce selenates below EPA recommendations **[29]**.

Numerous researchers are interested in the element selenium. It is present in every area of the natural world as a trace element. It is present in water, rocks, and the atmosphere in both organic and inorganic forms. Because of its toxicity, this element has been classified as a dangerous material for a very long time. The physiological necessity of using it as a vitamin essential to both human and animal health was only discovered in recent years. It is not, however, required for plant growth. Due to selenium is a component of numerous enzymes and has antioxidative and anticarcinogenic activity, it has a substantial impact on human and animal health when taken in proper concentrations. However, excessive selenium can have deleterious effects and induce selenosis. On the other hand, its lack is a far bigger issue. People who live in most parts of the world are susceptible to it. The human body receives its external element, selenium, through food. Since plants are the primary source of this element, raising the plant level is crucial. There are various methods for achieving this. Agronomic biofortification of selenium is one of the most promising strategies to solve the issue of low levels of selenium transfer from soil to the food chain. Utilizing naturally selenium-rich materials and genetic engineering are two more intriguing options. Using nanoparticles to fertilize plants with selenium is a novel method. On the other hand, too much of this element can have harmful effects, including stunted development, dried-out and wilted leaves, decreased protein synthesis, and premature plant death **[30]**.

Ingesting selenium orally has been linked to acute toxicity, which raises the possibility of death. Selenium concentrations in blood and urine samples from non-fatal cases are comparable to those found in instances that result in death. An Indian study found that individuals with high environmental selenium levels had negative health impacts such as nausea, vomiting, foul breath, parasite infestation, dyspnea, chest pain, abnormalities, loss of hair and nails, etc. **[31]**.

Plants mainly absorb selenium in the forms of selenium (IV), selenium (VI), $HSeO_3^-$, and organic selenium, such as selenocysteine (SeCys) and selenomethionine (SeMet), through the sulfur absorption pathway. Many pathways, including major sulfur/nitrogen metabolism, hormone control, redox metabolism, and transcriptome alterations in secondary metabolite production, may be involved in the metabolism of selenium in plants supplemented with the element. These routes influence selenium accumulation as well as the kind and degree of metabolite accumulation, which in turn influences how the body utilizes the mineral. It is commonly known that the effects of accumulation, toxicity, and detoxification in different plant tissues are significantly influenced by the morphology of the plants. The ability of plants to store selenium in their root and stem tissues varies widely **[32]**.

The plants were divided into two groups: those that accumulated selenium (selenium main indicator plants) and those that did not (selenium non-accumulating secondary indicator plants). Primary selenium-accumulating plants often develop in selenium-rich settings, but selenium-non-accumulating plants can survive in both selenium-rich and selenium-deficient soils **[18]**.

From a toxicological perspective, selenium contamination and its natural existence provide serious health dangers in several regions of the world. The build-up of selenium as a result of geological and geothermal activity, exacerbated by human activity, has grown to be a significant environmental issue and public health risk. Due to its simultaneous beneficial and hazardous properties for health, selenium is referred to as the "double-edged sword element" **[33]**. This metalloid is among the most poisonous naturally occurring substances, even with its nutritional advantages. There is a lot of selenium in the environment, and food and water are the two main places where humans are exposed to it **[34]**.

Its quantification is therefore crucial for limit control. The detection and measurement of selenium in environmental conditions are currently improving, thanks in part to the application of a Hydride Generating Atomic Absorption Spectroscopy. This is because different areas have varying excess occurrences of selenium. The two applications of microbiological elimination are in drinking water supplies and the recovery of selenium from wastewater sludge. Despite the fact that sorption research on current selenium removal showed greater efficacy, phytoremediation seems appealing because of its advantage for field-scale use. However, there is still no discussion about what happens to selenium after phytoremediation **[35]**.

## 4. Methods of synthesis of selenium nanoparticles

### 4.1. Physical and chemical methods

One can create nano selenium using physical, chemical, or biological means. Since only a few chemicals can produce nano minerals of uniform size in the laboratory, the chemical technique is the most straightforward and economical **[36]**. Hence, employing chemical processes can result in efficient and regulated bulk manufacturing. However, because dangerous compounds are utilized during synthesis, there is always a risk of toxicity when using the chemical technique **[37]**. Significant drawbacks of employing chemical methods include elevated operational expenses and the production of large quantities of concentrated chemical sludge **[38]**.

In the process of creating SeNPs through physical methods, techniques such as pulsed laser ablation, vapor deposition, hydrothermal, reverse osmosis, nanofiltration, ion exchange, and solvothermal processes were employed. Pulsed laser ablation stands out as superior to other methods due to its ease of NP collection via centrifugation and the exceptional stability of the nanoparticles produced **[39]**.

Physical treatment methods are well-established in the context of drinking water and municipal wastewater treatment, providing a solid foundation of understanding regarding their mechanisms and operational parameters. The use of membrane systems further enhances these processes by minimizing spatial requirements, while ensuring compliance with regulatory limits for selenium. This dual advantage makes physical treatment an effective choice for managing water quality. However, membrane filtration is associated with significant disadvantages, including high energy consumption and substantial capital costs for both operation and maintenance. Additionally, the generation of concentrated waste or brine in ion exchange processes introduces further challenges related to post-treatment and disposal, this process is widely used in various industrial wastewater treatments; however, it has proven to be largely ineffective for selenium removal. This is primarily due to competition from other anions, which are present at significantly higher concentrations than selenium oxyanions. This competition leads to rapid saturation of the resins and results in low selenium removal efficiency. **[38]**.

### 4.2. biological methods

The biosynthesis of nanoparticles can serve as an alternative to existing chemical and physical methods. It provides a greener approach that is not only simpler and more cost-effective but also ensures biocompatibility and safety **[40]**. It offers the benefit of not generating high temperatures, pressures, acidic conditions, or toxic by-products. Unlike physical and chemical methods, they do not require additional functionalization to produce antimicrobial agents with specific properties such as hydrophilic, hydrophobic, conductive, or anticorrosive features for biomedical applications **[41]**.

Green synthesis of nanoparticles offers a sustainable approach that mitigates environmental concerns by facilitating NP production under mild conditions of pressure, temperature, and pH, typically at a lower cost. This eco-friendly method involves utilizing biomass filtrate derived from various biological sources for the synthesis of nanoparticles as shown in **Fig. 3 [42]**.

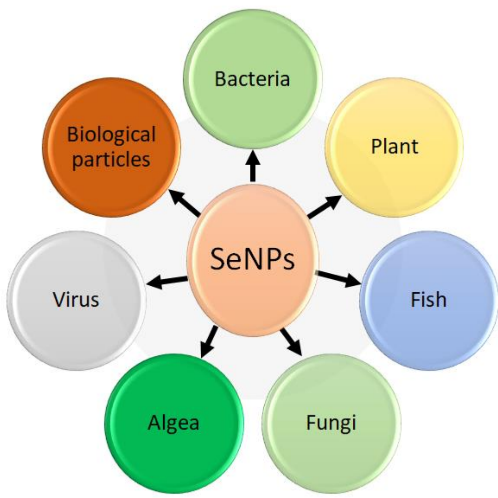


**Fig. 3.** Various modes of biological synthesis of nanoparticles

#### 4.2.1. Selenium reducing plants

It has previously been determined that plants can be useful in producing SeNPs. Fruit peels and other agricultural waste products could be utilized in the procedure. The most promising plant materials are those with significant concentrations of phytochemicals that exhibit stabilizing properties **[43]**.

The process of creating green synthesized SeNPs involves combining sodium hydrogen selenite ($NaHSeO_3$) solution with an extract from *Curcuma longa* leaves. Extract from *Curcuma longa* leaves functions as a capping, stabilizing, and reducing agent. The technique of microwave assistance was used to aid in the creation of selenium nanoparticles. A UV-Vis spectrophotometer was used to confirm the formation of SeNPs. X-ray diffraction (XRD) was used to determine the amorphous nature of the SeNPs, revealing an average size of 251 nm the electrochemical characteristics of the 20 μ SeNPs were utilized to modify the bare glassy carbon electrode (GCE) electro-catalytic process.

Using a cyclic voltammeter, the electro-oxidation of nitrite by SeNPs/GCE was investigated **[44]**.

#### 4.2.2. Selenium-reducing microorganisms

Since certain microbes, including fungi, and bacteria, can grow and survive in certain selenium concentrations and can convert harmful ions into unique nanoparticles, they are utilized to manufacture SeNPs **[45]**.

Microorganisms such as bacteria, fungi, and viruses play a crucial role in nanoparticle synthesis, which can occur either intracellularly or extracellularly. This microbial involvement facilitates the scalable production of nanoparticles **[46]**.

Microbes are also wonderful candidates for food additives because they can convert inorganic selenium into organic selenium with high nutritional value **[**47**]**.

#### 4.2.3. Selenium reducing fungi

The use of fungi for nanoparticle biosynthesis, known as psychosynthesis, is a rapidly developing field at the intersection of multiple scientific disciplines **[48]**.

Examples of Selenium reducing fungi, are *Aspergillus quadrilineatus*, *Fusarium equiseti*, *Aspergillus flavus*, and *Candida albicans* **[40, 49]**.

#### 4.2.4. Selenium reducing bacteria

According to research studies, both Gram-positive and Gram-negative bacteria are capable of synthesizing SeNPs. One method for removing toxic Se oxyanions, such as $SeO_4^{2-}$ and $SeO_3^{2-}$, involves their reduction to Se, which can occur under both aerobic and anaerobic conditions. Bacteria can perform this reduction either intracellularly (in the periplasmic space) or extracellularly, with the latter method being more advantageous due to the easier extraction of the nanoparticles **[50]**.

Both aerobic and anaerobic bacterial reductions of selenate or selenite can be attributed to non-enzymatic or enzymatic processes. The result of this biotransformation is the production of extracellular, periplasmic, or cytoplasmic SeNPs. Bacteria are the best choice among all microbes for the synthesis of nanoparticles because of their quick growth rate, ease of handling, affordability, and high productivity **[45]**.

Javed *et al.* **[51]** found that the biotic transformation of highly soluble and toxic selenite to less toxic elemental selenium using bacterial strains *Bacillus subtilis*, *Exiguobacterium* sp., *Bacillus licheniformis*, and *Pseudomonas pseudoalcaligenes*. The conditions were optimized by changing different physical parameters such as pH, temperature, different selenium concentration levels (200, 400, and 600 μg $ml^{-1}$), aeration, and incubation time for increased selenite reduction. The selenium reduction rate increased with an increase in pH from 28 to 90%. Moreover, the selenite reduction was observed at various temperatures and the results showed that the selenite-reducing bacteria can remediate selenium in both aerobic and anaerobic environments, and their reduction ability decreases as the incubation time increases**.**

El-deeb *et al.* **[52]** identified a bacterial strain *Streptomyces* sp. was evaluated for the capability of SeNP production. The results showed that the bacterial strain could produce stable SeNPs sustainably within a week under optimized conditions (pH 7 and 32 °C) at its extra/intracellular wall. Subsequently, UV-Vis spectra were used to characterize SeNPs produced under different parameters, showing changes in the absorbance around 582 - 620 nm. The antimicrobial effects of SeNPs formed under different pH were also examined against pathogenic *Escherichia coli*. The results showed that SeNPs formed at acidic and basic pH induced substantially less antibacterial activity than those formed at a neutral pH where the diameter of the inhibition zone of SeNPs synthesized at pH 7 was 20 mm, but at pH 4 (13 mm), pH 5 (14 mm) and pH 9 (17 mm).

Studies show that the *Lactobacillus acidophilus* strain bioconverted two inorganic forms of selenium, namely selenite (SeIV) and selenate (SeVI), to an organic form (SeMet). After adding 1, 2, 5, 10, and 20 ppm of selenium ($Na_2SeO_3$, SeIV) or sodium selenate ($Na_2SeO_4$, SeVI) to the culture media (MRS), it was incubated for up to 24 h at 37 °C. At these doses, neither of the selenium forms significantly affected the bacterial growth, suggesting little cytotoxicity. Nevertheless, following a 24 h incubation period, the media supplemented with 5, 10, and 20 ppm of Se (IV), but not Se (VI), turned reddish, with the intensity of the red hue rising as the medium's Se level increased**,** The presence of SeNPs in the media could be detected by the scanning electron microscopy (SEM) analysis **[53]**.

In addition to having a high organic selenium conversion, selenium-enriched *Lactobacillus* can also break down pathogen cell structures, stop their growth, and exhibit greater inhibitory activity. Nearly half of the inorganic selenium may be converted to organic selenium by using bacteria for selenium enrichment. This is sufficient to ensure that the two forms of selenium are equally absorbed, distributed, metabolized, and excreted, which is known as selenium homeostasis **[54]**.

By employing probiotic yogurt bacteria in a fermentation process, Eszenyi *et al.* **[55]** were able to create nano-size (100-500 nm) elemental selenium and developed the laboratory technology of product purification and recovery from bacteria.

A novel strain of *Bacillus subtilis* SE201412 (GenBank accession no OP854680) was identified through isolation from tobacco waste. At a selenite concentration of 66,000 mg $L^{-1}$, this strain exhibited aerobic growth and the capacity to produce biological nano-selenium from 99.19% selenite in less than 18 h. Using strain SE201412, different volumes of fermentation broth with 5000–3000 mg $L^{-1}$ of pure selenium might be produced for commercial use **[56]**.

**5. Using Selenium-reducing bacteria in bioremediation**

Bioremediation, carried out by microorganisms and macroorganisms, is a process designed to clean up environmental pollutants. This technique effectively targets and removes various contaminants, including organic, inorganic, and radioactive substances, from the environment **[57]**.

The microorganisms are described as prospective biofactories for the manufacture of well-defined selenium nanoparticles and use a detoxifying process to reduce selenites/selenates to nano-selenium **[58]**.

Due to the properties of the aqueous solution to be treated and the stringent discharge limitations on the release of selenium and its oxyanions, such as selenium (IV) and selenium (VI), selenium treatment is also frequently expensive**.** The efficiency of treatment techniques used to remove selenium depends critically on the speciation of selenium in groundwater or raw effluent, particularly when selenium is present in low quantities, as is frequently the case (below 1 mg/L). The majority of current research focuses on the removal of selenium (IV) and selenium (VI), with the removal of organic forms of selenium posing an intriguing challenge. Selenium, like other metalloids, is hard to get rid of, notably the oxyanion of selenium (VI), which is found, for instance, in mining wastewater **[59]**.

Studies show that *Bacillus* sp. Selena 3 exhibited exceptional resistance to selenium oxyanions, compared to other bacteria from selenium-contaminated water and soil. The results showed that this bacterium can completely remove 2.5 mM of sodium selenite in just 97 hours. This remarkable ability to effectively reduce selenium makes *Bacillus* sp. Selena 3 is a promising candidate for cleaning up selenium-polluted environments **[57]**.

## 6. Optimization of bacterial reduction of selenium

Optimization of reduction conditions is crucial, with factors such as pH, temperature, initial selenium concentration, and incubation time influencing the process. Generally, pH (6-7), 150-170 rpm, and temperatures around 37 °C favor selenium reduction; Lower initial selenium concentrations typically result in higher reduction rates as shown in **Table 1 [51, 60]**. Some bacteria, like Bacillus sp. Selena 3, can reduce high concentrations of selenite (80 mM) within hours **[57]**.

**Table 1. Microorganisms showing selenium oxyanions reduction and their conditions of conversion**

| Name of the used microorganism | Type of selenium oxyanion used to reduce | Conditions of conversion |
|---|---|---|
| *Bacillus cereus* | Selenite | 170 rpm, 7% inoculum and 33°C **[61]** |
| *Lactobacillus acidophilus* | selenite/selenate | 24 h at 37°C **[53]** |
| *Streptomyces* sp. | Selenite | (pH 7 and 32 °C) **[52]** |
| *Streptococcus thermophilus* | Selenite | pH 6, 6% inoculum and 40°C **[62]** |
| *Lactobacillus delbrueckii* ssp. | Selenite | pH 6, 7% inoculum and 33°C **[62]** |
| *Bacillus subtilis Strain L11* | Selenite | 150 rpm, pH 6 and 37 °C **[63]** |
| *Bacillus licheniformis* F1 | Selenite | 180 rpm, 2% inoculum and 37°C **[64]** |

## 7. Advantages of biogenic selenium nanoparticles

Because of its magnetic qualities, nanoparticle-sized particles ranging from one to 100 nm have drawn attention in the field of nanotechnology. Small size, large surface area, surface energy, solubility, and ease of attachment to medicinal agents are only a few of the numerous advantageous characteristics of nanoparticles **[65]**. Numerous uses for nanoparticles' special qualities can be found in the biological and medical sciences. Physical systems are monitored, treated, diagnosed, and controlled using nanomaterials **[66]**.

Because of their high surface area to volume ratio and electrical characteristics, nanoparticles exhibit the most notable chemical and physical capabilities that can be recognized, and nanoparticles can even function as the reactant in a catalytic reaction **[67]**. However, in addition to being time and money-consuming to produce in large quantities for use in practical applications, nanoparticles also have toxicity issues **[68]**. A growing amount of interest has been ignited by the properties of one of the inorganic nanoparticles that could be employed in biosensors: SeNPs **[69]**. These properties allow SeNPs to bridge the gap between biological recognition events and signal transduction. Because of its low environmental toxicity **[70]**, biocompatibility **[71]**, conductivity, and electro-catalytic qualities **[72]**, SeNPs are frequently employed in poor nations

The unique chemical and physical characteristics of SeNPs stem from their huge surface-to-volume ratio, high surface energy, spatial confinement, and decreased defects. Due to their therapeutic effects, which include lower toxicity, better reactivity, a lower dosage requirement, and excellent bioavailability when compared to other oxidation states of selenium, such as $Se_6^+$ and $Se_4^+$, SeNPs have a wide range of applications, especially in medicine **[73]**. Because of their higher biological activity and lower toxicity, SeNPs are thought to have superior biological activities compared to other forms of selenium **[74]**.

According to Alam *et al***.** **[75]**, the biogenic nanoparticles are deemed to be reasonably safe for usage in both human and animal applications; Biosynthesized SeNPs, in contrast to those produced by other methods, exhibit lower cytotoxicity to normal cells, making them a more suitable choice for use in human studies **[41]**.

Reports indicate that biogenic SeNPs exhibit superior bactericidal activity against resistant bacteria such as *P. aeruginosa* and *K. pneumonia* compared to gentamycin, a synthetic antibiotic. Additionally, biogenic SeNPs have lower minimum inhibitory concentrations and greater bactericidal effectiveness against both Gram-negative bacteria *(S. maltophilia and P. aeruginosa*) and Gram-positive bacteria (*B. mycoides*) than synthetic SeNPs **[76]**.

In contrast to those produced by other, conventional methods, the nanoparticles produced by microorganisms have a wide range of uses and benefits. Because of the biomolecules' inherent coating, biogenic SeNPs are more stable and do not agglomerate **[77]**.

Other studies have indicated that SeNPs exhibit antifungal properties even at lower concentrations. For instance, El-Saadony *et al*. **[78]** used various concentrations of SeNPs (50–150 µg/mL) synthesized through biological and chemical methods to test against *F. graminearum, F. cereales, F. poae, F. avenaceum, and F. culmorum*. Their findings revealed that biogenic SeNPs were more effective than chemical SeNPs against these fungi, and biogenic SeNPs also had a lower minimum inhibitory concentration **[79]**.

## 8. Application of selenium nanoparticles

Selenium supplements that are taken traditionally typically have a low absorption rate and high toxicity. Consequently, novel mechanisms that act as selenium compound transporters to increase this element's bioavailability and enable controlled release within the body are required. Particularly for those who lack selenium, nanoscale selenium has generated a lot of attention as a dietary additive. It has also been used in medicine as a medicinal agent with little adverse effects **[80]**.

It has been found that selenium nanoparticles have low toxicity and significant biological activity. All living organisms require selenium as a vital nutrient, but its use is restricted since higher doses of the mineral become poisonous. It has been demonstrated that selenium nanoparticles are less toxic and have sub-chronic toxicities than other forms of the mineral. The claim that selenium nanoparticles are less hazardous than SeMet has also been validated. Selenium nanoparticles have demonstrated superior selectivity between normal and malignant cells as compared to selenium (IV) nanoparticles at equivalent doses. Also when compared to selenium species, SeNPs exhibit stronger antioxidant properties **[39]**.

According to reports, certain special qualities of selenium nanoparticles make them essential for numerous applications as shown in **Fig. 4**.

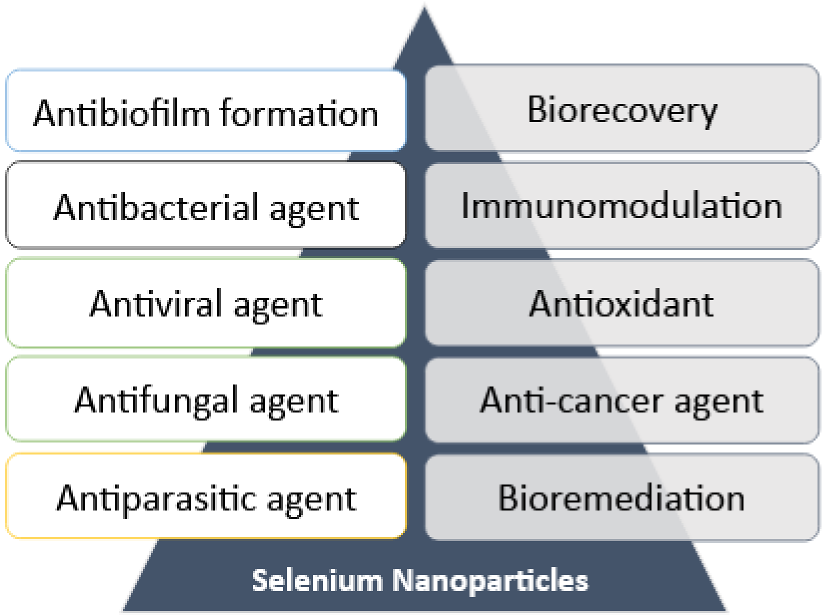


**Fig. 4.** Advantages of selenium nanoparticles in pharmaceutical and biological applications

### 8.1. Antioxidant

In male prepubescent rats, Rashad *et al.* **[81]** study sought to determine if Se-NPs could shield Leyding cells from oxidative damage brought on by di-n-butyl phthalate (DBP). To avoid testicular toxicity caused by DBP (500 mg/kg/d), two dosages of Se-NPs (0.2 and 0.5 mg/kg/d) were given to 42 pregnant female rats from gestation day (GD) 12 to postnatal day (PND) 14. For this reason, SeNPs may be a useful maternal prophylactic medication against the lowered total blood testosterone level and oxidative damage of Leydig cells produced by DBP, as they both lower lipid peroxidation (LPO) and increase antioxidant status in prepubescent male rat pups.

Compared to other chemical forms of selenium, nano-selenium has superior antioxidant capabilities while lowering the possibility of selenium toxicity. According to Wang *et al.* **[82]** SeMet was more hazardous than SeNPs when it came to their antioxidant qualities. Zhang *et al.* **[83]** investigated the impact of elemental nano-selenium versus the inorganic form of selenium on GPx activity in the liver of weanling pigs. When the animals were fed nano-selenium in the form of 0.50 and 1.0 mg selenium·kg$^{-1}$ instead of $Na_2SeO_3$, their GPx activity was much higher.

Lipid peroxidation, a consequence of oxidative stress, reduces spermatozoa's ability to procreate and may cause sperm failure. Goat spermatozoa (109) with aberrant mitochondria develop when selenium levels are low. Testicular and semen GPx activity is raised when selenium levels are supplemented with nano-selenium **[84]**. The Wu *et al.* **[85]** study showed how crucial it is to provide mothers with nanoscale selenium to enhance the formation of hair follicles and encourage fetal growth. This was explained by the fetal skin's regulating antioxidant status. Reactive oxygen species are produced less frequently when antioxidant defense is strengthened. This leads to an increase in the production of IGF-1 and its receptor, IGF-1R, which are essential for the enhancement of both characteristics.

### 8.2. Antibacterial agent

Because of their distinct antibacterial activity, SeNPs have garnered a lot of research

**[80]**.

Ullah *et al.* **[86]** investigated a biosynthetic approach using the probiotic *Bacillus subtilis* BSN313 to produce SeNPs easily and economically. Selenium reduction and SeNP formation increased progressively in the BSN313 up to 200 µg/mL of its surrounding media. Furthermore, 200 µg/mL of SeNPs showed antibacterial reactivity against *Escherichia coli* ATCC 8739, *Staphylococcus aureus* ATCC 9027, and *Pseudomonas aeruginosa* ATCC 25923

### 8.3. Anticancer agent

Selenium nanoparticles also exhibit remarkable anticancer activity and have tremendous promise for use as chemotherapeutic agents and drug carriers **[87]**. Selenium nanoparticles can inhibit cancer cells from developing by inducing cell cycle arrest at the S phase, which gives them anticancer characteristics **[88]**. The induction of cell cycle arrest at the S phase is mediated by the eIF3 protein complex being dysregulated **[89]**. According to a new study, a cell's membrane is crucial for the toxicity that SeNPs cause in cancer cells. The biomechanical characteristics of cancer cells are altered by SeNPs treatment; in particular, the adhesion force and Young's modulus are noticeably reduced **[90]**. It has been demonstrated that, at comparable concentrations, SeNPs exhibit superior selectivity between normal and cancer cells in addition to their distinct anticancer activity **[91]**. Selenium nanoparticles can enter cancer cells specifically by endocytosis and cause cell death by activating signal transduction pathways associated with apoptosis **[92]**.

### 8.4. Antifungal agent

Other research has highlighted the antifungal properties of SeNPs against various fungal species. For example, Gunti *et al.* **[93]** reported that SeNPs, synthesized from *Emblica officinalis* fruit extracts, exhibited broad antimicrobial activity against foodborne fungal pathogens such as *Aspergillus brasiliensis*, *A. flavus, A. oryzae, A. ochraceus, F. anthophilum, and Rhizopus stolonifera* Additionally, another study tested SeNPs against *Pyricularia grisea*, which causes blast disease in pearl millet, and found that even at low concentrations (100 and 200 ppm), SeNPs effectively inhibited fungal growth by the fifth day of a seven-day incubation period **[48, 79]**.

### 8.5. Antiparasitic agent

In vivo and in vitro studies have shown that SeNPs biosynthesized by *Bacillus sp*. Msh-1 is effective in treating *Leishmania's* major parasites, including Promastigote and Amastigote forms. Additionally, in vitro tests have demonstrated that *Bacillus* sp. Msh-1 functionalized SeNPs can combat *Leishmania tropica* and *Leishmania infantum* **[94]**.

### 8.6. Antibiofilm formation

Given their substantial antibacterial properties, biogenic SeNPs have various medical applications. For instance, they can be applied as coatings on orthopedic medical devices to inhibit the growth of biofilm-forming pathogens; The SeNPs synthesized by *Bacillus* sp. demonstrated a strong ability to inhibit the biofilms of *P. aeruginosa, P. mirabilis,* and *S. aureus* **[76]**.

### 8.7. Antiviral agent

Selenium nanoparticles' antiviral potential has garnered more attention lately, along with additional benefits including low toxicity and great activity. Selenium-deficient mice infected with the H1N1 influenza virus had a threefold increased mortality rate when compared to mice receiving 0.5 mg selenium·$kg^{-1}$, and mice with low serum selenium concentrations had a significant decrease in body weight (BW) and lower levels of TNF-α and IFN-γ**.** Administering

SeNPs can also be an effective and feasible way to enhance the body's immunological response **[95]**.

### 8.8. Recent application

Selenium nanoparticles were utilized to create a testing system for virus detection, such as a test strip that identifies anti-SARS-CoV-2 IgM and IgG in human serum and blood **[96]**.

## Conclusion

Selenium is a critical and limited resource with significant applications across various industries. However, it cannot be obtained through conventional ore mining. Due to extensive anthropogenic activities and unregulated natural processes, the rising contamination levels of Se present a unique opportunity for remediation and recovery, particularly in light of the growing demand for pure Se in electronics and medical fields. The microbial recovery of selenium nanoparticles has garnered considerable interest, as these biogenic nanoparticles can be effectively harvested. In addition, the potential for worldwide use of nanoscale selenium in clinical medicine and nutrition is the future perspective. With the potential to alter the physicochemical characteristics of the particles, increase stability in the gastrointestinal tract, and enable controlled release of selenium, the development of new NP systems for selenium transport in the organism holds great dietary and therapeutic potential.

## Declarations

### Ethics Approval and Consent to Participate

Not applicable.

### Consent to Participate

Not applicable.

### Consent for publication

Not applicable.

### Availability of the data and Material

All data generated or analyzed during this study are included in this article.

### Competing interests

The authors declare that there is no conflict of interest.

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### Author contribution

Alaa Amin has collected the data for the manuscript under the supervision and guidance of authors; Nooran S Elleboudy, Mohammad M Aboulwafa, and Nadia A. Hassouna. Nooran S Elleboudy and Mohammad M Aboulwafa have helped in writing and revising this manuscript. All authors have read and approved the final manuscript.

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