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Review

A review on selenium nanoparticles and their biomedical applications

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ABSTRACT

Nanotechnology has enormous promise for a wide range of applications in biology. Nanoparticles (NPs) have the benefit of improving bioactivity, decreasing toxicity, allowing for precision targeting, and modulating the release profile of encapsulated compounds. Nanomaterials' unique qualities, such as their tiny size, biocompatibility, and ability to cross cell membranes for drug administration, make them useful in a variety of biological applications. Selenium (Se), a critical trace element, stands out among these nanoparticles due to its specific bioactivities in nano forms. Selenium is incorporated into Selenoproteins such as selenocysteine (Sec), which play an important role in maintaining physiological redox balance via oxidoreductase activity, a critical enzymatic process. In the field of medication delivery, selenium-based devices have been designed to transport pharmaceuticals to specific locations. Selenium nanoparticles (SeNPs) appear to be a suitable platform for delivering medications to their desired sites. Selenium's medicinal potential has been thoroughly investigated, including its efficacy against various cancer cells, microbial pathogens, viral infections, neuroprotective properties, diabetic control, oxidative stress, and inflammation-mediated illnesses such as rheumatoid arthritis. Notably, due to selenium's extraordinary involvement in immune system regulation, SeNPs have an edge over other nanoparticles. SeNPs phytosynthesis offers an appealing alternative to standard physical and chemical processes, featuring biocompatibility and environmental friendliness. This paper gives an overview of SeNPs' biological uses and emphasizes recent advances in the field.

1. Introduction

Over the last three decades, nanotechnology has greatly altered the landscape of medication research and treatment alternatives [1,2]. Nanotechnology is concerned with minuscule particles having a minimum dimension of 100 nm. Nanoparticles (NPs) are distinguished by their unique qualities, such as their small size and large surface area, and they play an important role in nanotechnology-based drug delivery systems in current therapies. NPs have proven their usefulness as drug carriers, delivering therapeutic compounds with amazing success. The addition of targeting ligands to nanoparticles increases the originality of drug delivery systems and allows for selective administration to target areas [3,4]. Nanomedicine is the use of nanotechnology-based techniques and methodologies in medical research and clinical practice to treat, diagnose, monitor, and regulate biological systems.

Selenium is a necessary ingredient for a healthy immune system and disease prevention [5,6]. Selenium can be classified into various compounds based on its structural characteristics which is demonstrated in the table (Table 1). Selenium (Se) deficiency, discovered by Jöns Jacob Berzelius in 1817 alters the balance between oxidants and antioxidants, resulting in oxidative stress [1,7,8]. Selenium is recognized as a key element that acts as a cofactor and coenzyme in the catalytic-active sites of numerous Selenoproteins and enzymes in the human body, protecting cells and tissues from oxidative damage and stress [7,8]. Selenium is important in selenoenzymes such as GPXs, TXNRDS, and deiodinases (DIO), where it contributes to a variety 55 of biochemical events and physiological antioxidant defense systems [9]. Selenium supplements have been found to reduce the severity of hepatotoxic disorders induced by toxic chemical buildup, alcohol use, and chemotherapy delivery [7, 10]. Numerous studies [11,12] have found that selenium can increase cancer cell apoptosis while not affecting healthy cells. Due to their biological activity, selenium nanoparticles (SeNPs) with diameters ranging

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Table 1
Selenium compound classification based on structural characteristics.

Selenium Compound	Type	Source
Di-selenides	Bis(4-aminophenyl) diselenide	[21]
	Bis (5-phenyl carbamoyl pentyl) diselenide (SelSA-1)	[22]
	Diselenodipropionic acid (DSEPA)	[23]
	2-Selenium-bridged B-cyclodextrin (2-SeCD)	[24]
Selenocyanates	Isatin analogues	[25]
	Diphenylmethylselenocyanate	[26]
	1-4-Phenylenebis (methylene) selenocyanate (*p*-XSC)	[27]
	Temozolomide (TMZ)-Se	[28]
	5-Phenylcarbamoylpentyl selenocyanide (SelSA-2)	[29]
Se-heterocyclic compounds	1,3-Selenazolin-4-one derivatives	[30]
	2-Phenyl-1,2-benzisoselenazol-3(2H)-one (ebselen)	[31]
	2,5-Bis(5-hydroxymethyl-2-selenienyl)-3-hydroxymethyl-*N*-methylpyrrole (D-501036)	[32]
	1,2-[Bis(1,2-benzisoselenazolone-3-(2H)-ketone)] ethane (BBSKE)	[33]
	2-Cyclohexylselenazolidine-4-(R)-carboxylic acid (ChSCA)	[34, 35]
	2-Buthylselenazolidine-4-(R)-carboxylic acid (BSCA)	[35]
Selenides	Methylimidoselenocarbamates	[36]
	5-Phenylselenyl-methyl-2′-deoxyuridine (PhSe-T)	[37]
	5-Methylselenyl-methyl-2′-deoxyuridine (Mese-T)	[37]
	β-Selenium amine derivatives	[38]
	Se −1,4-phenylenebis (1,2-ethanediyl) bisisoselenourea (PBISe)	[39]
Selenoamino acids	Selenomethionine (SeMet)	[40]
	Methyl selenocysteine (MeSeCys)	[41]
	Selenocysteine (SeCys)	[42]
	Selenocystamine	[43]
Se (IV) compounds	Sodium selenite (Na_2SeO3)	[44]
	Selenous acid (H_2SeO3)	[45]
	Methyl selenic acid (MeSeA)	[46]
	Selenium dioxide (SeO2)	[47]

from 5 to 200 nm have gained popularity in recent years.

Nano-selenium is a potential drug delivery carrier for antioxidant or anti-inflammatory effects due to its low toxicity, strong biocompatibility, and antioxidation capacities [13,14]. Selenium (Se) is integrated into Selenoproteins as selenocysteine, where it regulates biological systems such as the antioxidant system [15]. Various research shows that SeNPs have a wide range of medicinal uses, ranging from antioxidant activity to anticancer effects, owing to their redox-balancing function [16]. SeNPs have a lower toxicity profile than elemental selenium, as demonstrated by liver biomarkers [17]. SeNPs synthesized from plants have a high potential for targeted drug delivery, antibacterial activities, and heavy metal detection [18–20]. Several chemical and physical procedures for SeNP formation have been discovered, however, the employment of different chemical compounds and physical approaches can result in hazardous agents that restrict the therapeutic potential of SeNPs in industry. As a result, significant efforts and research have been dedicated towards biosynthesis, namely green synthesis of SeNPs, which is eco-friendly and non-toxic. Plant-derived compounds such as phenolic acids, flavonoids, cinnamic acid, coumarin, sesquiterpenes, and tannins operate as efficient and strong stabilizing agents in the Phyto-synthesis of SeNPs. Selenium based on structural properties is classified in detail in Table 1. The purpose of this study is to provide a thorough assessment of the numerous biological uses, synthesis processes, and pharmacological potentials of SeNPs.

2. Selenoproteins

Selenium is a trace element that is required by the organism, and its incorporation into Selenoproteins leads to a variety of pharmacological activity [48]. There are just a few examples of the known selenoproteins which are listed in the table (Table 2), and their functions are diverse. The enzyme Glutathione peroxidase's action (GPx) stands out among the main selenium-dependent detoxification activities. This enzyme has a selenocysteine (Se-Cys) molecule in its active site and plays an important role in antioxidant defense and oxidative stress reduction [49]. The toxicological characteristics of SeNPs were compared to those of organic and inorganic selenium compounds in a study on SeNPs toxicity.

The toxicity risks of selenium nanostructured were much decreased [50]. Many synthetic selenium compounds with biological activity have been created in recent years, and their therapeutic effects on animal models of mental illnesses and degenerative diseases have been investigated. The seleno-compound 3-[(4-chlorophenyl)-selanyl]-1-methyl-1-H-indole (CMI), for example, has been demonstrated to reduce inflammation and buffer oxidative stress in the brains of post-septic mice with psychological issues including sadness, anxiety, and cognitive impairment [50].

SeNPs are being studied for their possible therapeutic utility in illnesses such as Alzheimer's disease, hepatic damage, and antibiotic resistance [51–53]. It is vital to note that excessive selenium use might have negative consequences. Selenite (Se^{+4}), the major selenium ion responsible for adverse consequences, must be transformed into selenium via biogeochemical cycles. As a result, selenium has a dual nature, it is an antioxidant at sub-nutritional levels and a prooxidant at super-nutritional ones [54].

Our study strives to bridge knowledge gaps by offering a complete review of various pharmacological actions, with an emphasis on the molecular basis of these claimed benefits. Furthermore, we explore the underlying mechanics of selenium toxicity decrease by nano

Table 2
Main kinds of selenoproteins and their functions.

Selenoproteins	Localization	Function	Sources
Extracellular GPX	Plasma and thyroid follicle	Anti-inflammatory activity	[66]
Cytosolic GPXI	Cytoplasm, ubiquitous	Antioxidative defense	[67,68]
Glutathione peroxidase	Cytosol	Protection against oxidative stress. Catalytic reduction of H_2O_2	[69–71]
Cytosolic TrxR	Mainly cytosolic, ubiquitous	The most important antioxidant "weapon" at the cellular level. Apoptosis inhibition and transcription factor redox status	[72,73]
Thioredoxin reductase	Endoplasmic reticulum	Activity of an oxidoreductase using NADPH as a cofactor	[74]
Phospholipid GPx	Mitochondria-l membrane	Membrane mitochondrial Phospholipid hydroperoxides are reduced. Antioxidant in the membrane	[75]
Mitochondrial TrxR	Mitochondrial, ubiquitous	Cell proliferation control	[76]
Mitochondrial TrxR	Mainly mitochondrial, ubiquitous	Apoptosis regulation and signaling pathways	[77]
lodothyronine deiodinase	Plasma membrane	T4 and T3 catalytic conversion	[78,79]
Type III DIO	Placenta, fetus, liver, gravid uterus, fetal and neonatal brain, skin	T2 production from T4 and rT3 production from T4	[80,81]
Type II DIO	Plasma membrane, Endoplasmic reticulum	Local (intracellular) T3 production from T4 and T2 production from rT3	[82]
Type I DIO	Liver, lung, eyes, kidney, thyroid, pituitary, CNS	T4 to T3, T4 to rT3, and T3 to T2 conversions	[83]
Selenoprotein P	Thyroid and blood	Endothelial antioxidant, selenium transport and storage	[84]

particularization, as this phenomenon is unusual given selenium's hazardous nature and small safety margin. In mouse models, the use of SeNPs reduced acute toxicity-related mortality rates by more than twofold [55]. When compared to other selenium species, SeNPs demonstrate significant anticancer efficacy while downregulating toxicological consequences. They have shown potential in treating cancer, diabetes, inflammatory diseases, liver fibrosis, and drug-induced toxicities [56–59]. Yuntao Liu. et, al [60]. used *Catathelasma ventricosum* polysaccharides to biomedically synthesize SeNPs with anti-diabetic properties. Physical, chemical, and biological mechanisms can all be used to create SeNPs. Ultraviolet irradiation, microwave irradiation laser ablation, and ultrasonic field therapy are examples of physical techniques [61]. Various compounds are used in chemical synthesis to convert sodium selenite salt into selenium [62–64]. Polysaccharides as well as common reducing agents such as ascorbic acid, are employed to stabilize the resultant nano-selenium core [65]. Other research has used Quercetin, Gallic acid, and extracellular polymeric molecules to synthesize SeNPs [5]. The physical and chemical approaches of SeNPs production encompass parameters regulating pH, light, sound-assisted procedures, and temperature [64]. Seleno proteins While chemical and physical procedures are time-efficient, they are frequently overlooked owing to cost inefficiency and environmental toxicity concerns. Green synthesis of SeNPs is suggested as an alternate strategy to solve these concerns.

3. Synthesis of SeNPs

To synthesize SeNPs, living organisms such as plants, algae, fungi, and bacteria are used in the biological synthesis of SeNPs. The different methods of synthesis and sources of synthesis of Selenium nanoparticles are illustrated in the figure (Fig. 1). The adoption of biological approaches for SeNPs synthesis has accelerated due to their environmentally benign character, which solves various obstacles such as cost inefficiency, complexity, and safety issues.

In the case of plant-based synthesis, aloe vera leaf extracts are plentiful in secondary metabolites such as sterols, polysaccharides, vitamins, phenolic compounds, lignin, flavonoids, and proteins. These components function as natural reductants and stabilizers, and they play an important role in the green synthesis of SeNPs [85]. Fardsadegh B et al. [86] used the green synthesis method to extract aloe vera leaf extract for SeNPs production to make a 10 mM Na_2SeO_3 solution, 0.263 g of Na_2SeO_3 salt was dissolved in 100 mL of DI water following that, different volumes (1–5 mL) of aloe vera leaf extract were combined with varying amounts (10–30 mL) of Na2SeO3 solution the reaction solution was then put in a laboratory autoclave for 15 min at 121 °C and 1.5 bar pressure. Fourier transform infrared spectroscopy (Shimadzu 8400 S, Shimadzu Co., Kyoto, Japan) using KBr pellets in the 4000-400 cm^{-1} range was used to characterize the synthesized SeNPs. Using a reduction procedure that contained ascorbic acid (VC) and ultrapure water, Sajin Zhou et al. synthesized SeNPs from *Ganoderma lucidum* spore oil. They made a solution of 20 mM sodium selenite, an 80 mM VC solution, and a solution of 2 mg/mL lentinan (LET) for the synthesis, 4 mL of sodium selenite was combined with 12 mL of LET solution for 5 min before adding 4 mL of VC solution dropwise following the dialysis process, the produced SeNPs were gathered within dialysis pouches for a duration of two days [87].

In 2018, Yuntao Liu et colleagues. used *Catathelasmaventricosum* polysaccharides for the biological synthesis of SeNPs with anti-diabetic properties [60]. Moreover, species like methicillin-resistant S. *aureus* (MRSA), *Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli* have been employed for the fabrication of spherical SeNPs ranging from 90 to 150 nm. Researchers such as E. Medina et al. have discovered that SeNPs have antimicrobial capabilities by swiftly synthesizing SeNPs using *C. bulbosa* tuber extract and characterizing them through various techniques [88].

The SeNPs displayed significant cytotoxicity against breast cancer and normal cells, efficient antibacterial activity, and interaction with BRCA2 protein. They also exhibited larvicidal activity against dengue vectors and facilitated MB degradation. The use of plant extract for synthesis is cost-effective, environmentally friendly, and holds potential for biomedical and environmental applications [89]. The study also presents plants used in SeNP preparation and illustrates the synthesis process. While many papers lack explicit rationale for plant selection, it is implied that factors like material availability and traditional or pharmacological uses play a role. Plant materials rich in compounds like polyphenols, flavonoids, and polysaccharides are preferred due to their reducing and stabilizing properties. Some studies have also quantified phytochemical contents, such as phenolic compounds and flavonoids, in the prepared plant extracts, enhancing our understanding of the process [62,90]. The transformation of colorless sodium selenite solution into brick-red with the addition of E. officinalis fruit extract over 24 h. This color change is attributed to the excitation of surface plasmon resonance, indicating the reduction of sodium selenite into elemental selenium. The reduction process involves phenolics, flavonoids, and tannins within the plant extract. Confirmation of PF-SeNPs formation is based on UV–Visible spectroscopy, with an absorption maximum observed at 270 nm, signifying successful reduction and stabilization. This result aligns with prior research, showcasing the consistent absorption patterns for various SeNPs synthesis methods. The study establishes that sodium selenite was effectively converted into PF-SeNPs through the reduction action of E.

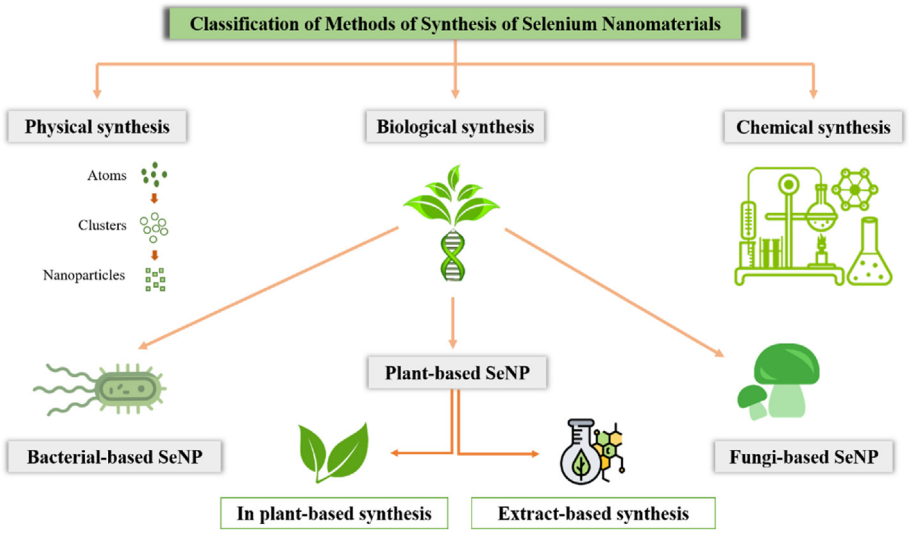

Fig. 1. The different methods of synthesis and sources of synthesis of Selenium nanoparticles.

officinalis fruit extract [90]. The review highlights the use of biological synthesis methods for producing selenium nanoparticles (SeNPs) and their applications across various fields. Plant-based synthesis, employing components like aloe vera leaf extracts has gained attraction due to its environmentally friendly nature. Aloe vera extracts, rich in secondary metabolites, serve as natural reductants and stabilizers in SeNP formation other studies have used different organisms such as *Ganoderma lucidum* spore oil and *Catathelasmaventricosum* polysaccharides for SeNP synthesis, showcasing diverse approaches [87].

The antimicrobial properties of SeNPs have also been explored, particularly against *Staphylococcus aureus*, MRSA, *Escherichia coli*, and *Pseudomonas aeruginosa*. Additionally, the synthesis of SeNPs from sodium selenite using E. officinalis fruit extract is illustrated, with a color change indicating successful reduction. This process is confirmed through UV–visible spectroscopy, aligning with prior research trends [90]. Overall, these studies highlight the versatility and potential of biological synthesis methods for SeNPs across various applications. To make SeNPs, three methods are typically used physical, chemical, and biological. Chemical reduction, which employs chemicals such as vitamin C, sodium sulfite, sodium thiosulfate, and hydrazine, is a popular approach due to its ease of use. SeNPs have also been effectively synthesized via hydrothermal, template, laser ablation, and biosynthetic approaches. Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), Fluorescence Microscopy, X-ray Imaging, Magnetic Resonance Imaging (MRI), and Inductively Coupled Plasma Mass Spectrometry (ICP-MS) can be used to image selenium nanoparticles (SeNPs) in tissue studies. The specific characteristics of SeNPs and the goals of the investigation will define which imaging method is best. By integrating these methodologies, researchers may gain a comprehensive understanding of SeNP distribution and behaviour in biological tissues.

4. Methods of production of selenium nanoparticles

4.1. Chemical methods

Hydrothermal Method Preparation is a low-cost method for producing crystalline selenium nanostructures. Amorphous selenium develops and can change into stable hexagonal Se nanospheres when a polished GeSe3 glass is immersed in water. Se NPs with diameters ranging from 10 to 1000 nm are created. Hydrothermal synthesis demonstrates versatility, with the potential for a wide range of applications [91]. Chemical templates can be used as stabilizers to synthesize selenium nanoparticles (SeNPs). PEG200, (Polyethylene glycol) a surface enhancer and template, was used for this purpose. Grey selenium is dissolved in the PEG200 solution for 15–20 min at 210–220 °C in this procedure. Water is then added, and pure PEG-SeNPs are produced following centrifugation and washing. This methodical technique demonstrates the possibility of employing chemical templates to direct SeNP synthesis, which has applications in a variety of domains [92]. Chemical templates as stabilizers are used to successfully synthesize Se NPs. PEG200, for example, functions as a template and surface enhancer, resulting in monodispersed PEG-Se NPs with a diameter of roughly 5 nm. For the manufacture of Se NP, the template technique, which generally employs chemical reductions, is frequently used. Sulphate polysaccharides (SPS) were used as a template by Hu et al. to generate controlled-size SPS-Se NPs in aqueous solutions. Templates guide the production of nano-sized selenium particles. Various compounds, including chitosan, folate, hyaluronic acid, PEI, and ferulic acid, can act as templates for Se NPs, allowing for cost-effective and customizable size possibilities. Template approaches provide the potential for accurately modifying Se NP properties for diverse applications, hence improving their design and efficacy [93].

4.2. Physical methods

Laser Ablation Method for Selenium Nanoparticles Preparation Perez Tanoira 2017 For laser irradiation to generate selenium nanoparticles (Se NPs) with significant antibacterial activities [94]. They created stable colloidal Se NPs in a microcentrifuge tube by focusing a laser on a selenium pellet. This laser ablation technology demonstrated advantages such as reduced contamination risk, cost-effectiveness, and ease of nanoparticle collection. Using lasers at 248 and 532 nm, similar procedures were used to create Se NPs of various sizes [95].

4.3. Biosynthesis of selenium nanoparticles

Dabei Fan demonstrated the biosynthesis of SeNPs using plant extract in an animal model. The study's clear methodology, from synthesis to purification, underlines its contribution to the field of nanoparticle synthesis, promising valuable applications in research and beyond. The paper describes how to make selenium nanoparticles (Se NPs) using a 50 mM selenious acid solution and a 100 mL plant extract. The mixture was mixed for 5 min before being incubated at 20–22 °C. A UV–Vis spectrophotometer was used to track color changes. Following the reaction, the resultant mixture was centrifuged at 1500 rpm to separate Se NPs, which were then purified with acetone and distilled water before drying overnight. Prior to centrifugation, Se NPs were ultrasonically treated in a pH 7.4 phosphate-buffered saline liquid. The characteristic, red-colored Se NPs were saved for further analysis. The study's clear methodology, from synthesis to purification, underlines its contribution to the field of nanoparticle synthesis, promising valuable applications in research and beyond [96].

5. Biomedical applications of SeNPs

SeNPs have been widely researched in many medical situations due to their superior characteristics when compared to elemental Se as shown in the figure (Fig. 2). SeNPs provide improved bioavailability while also being less harmful. The prooxidant and antioxidant actions open new avenues of investigation in a wide spectrum of pathological diseases. Nanoparticles, particularly SeNPs, exhibit anti-inflammatory, antioxidant, and immune-modulating properties. These characteristics make them appealing as potential treatments for disorders characterized by oxidative stress, inflammation, and immune system dysregulation. All of these problems have been linked to Alzheimer's disease, diabetes, cancer, Rheumatoid arthritis, and viral infections. Here is a full description of the biological features of SeNPs. In addition, we provide an overview of recent improvements in targeted tactics and new applications.

5.1. Role of SeNPs in Alzheimer's disease

Selenium can be found in several forms in foods and supplements, including selenocysteine, selenomethionine, selenite, and selenate. Selenide, a reduced form of sodium selenite, is synthesized in the cytosol through the catalysis of GSH and superoxide radicals [97]. Selenoproteins are highly expressed in the human brain and are thought to be engaged in antioxidant activities, which are important in avoiding the beginning and progression of Alzheimer's disease [98].

Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are examples of free radical species. ROS are biochemically reactive oxygen-rich compounds that include peroxides, superoxides, and singlet oxygen. They emerge in tandem with physiological processes and both ROS and RNS are produced in the brain because of environmental effects [99,100]. If the quantity of ROS is not controlled by antioxidants, it can cause severe, reversible, or permanent damage to a variety of biological components, including nucleic acids, lipids, proteins, and surrounding molecules, triggering a chain reaction [101]. ROS-induced reactions and their significance in the physiology and pathology of Alzheimer's disease have piqued the interest of many researchers as shown in the figure (Fig. 3) [102]. Furthermore, new Selenoproteins and selenium nanoparticles with outstanding physiological properties have been identified [48,55].

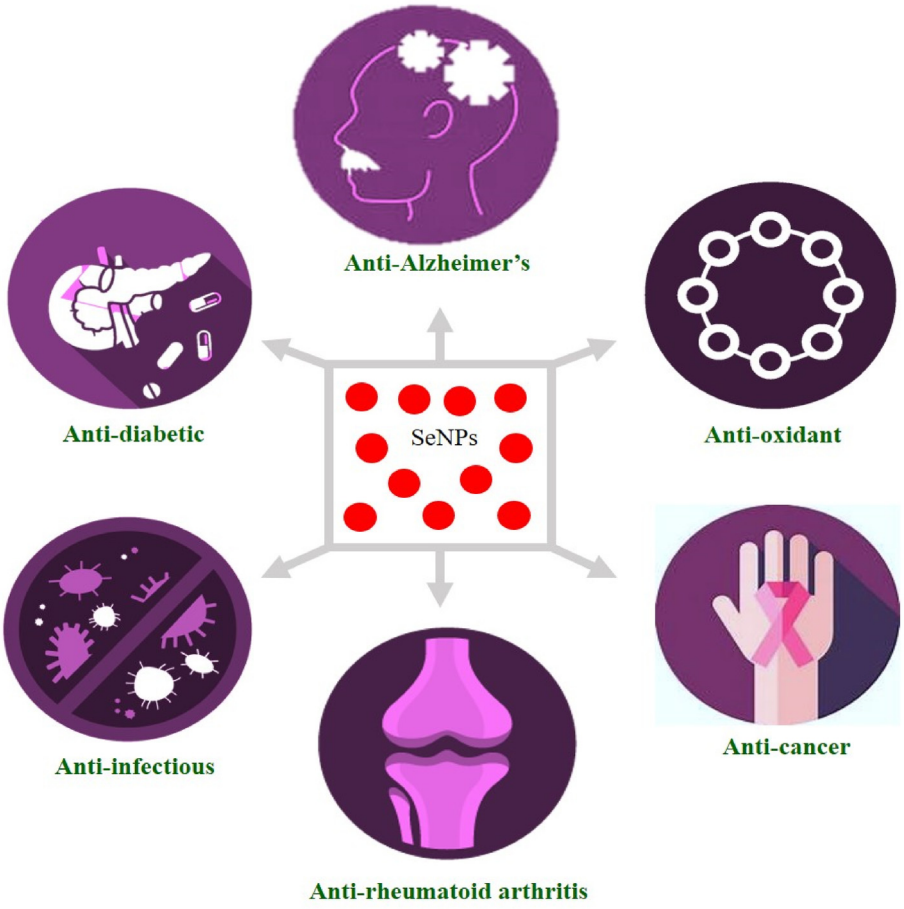

Fig. 2. Different biomedical applications of selenium nanoparticles.

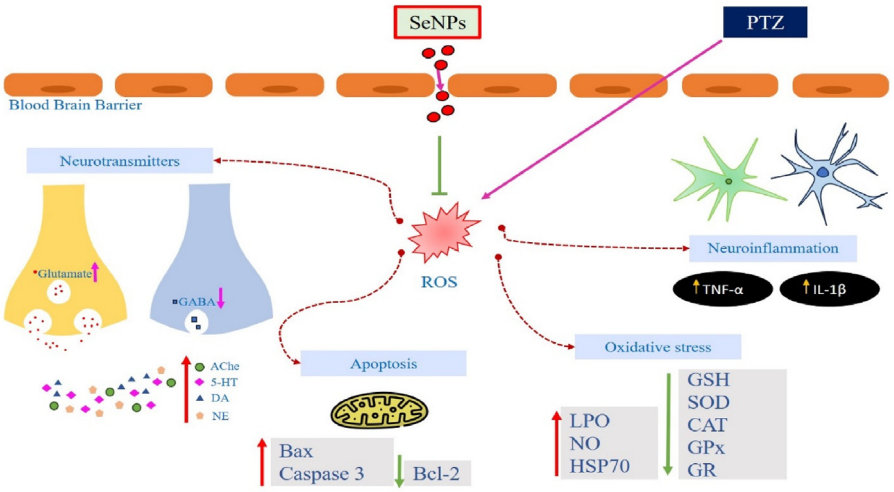

Fig. 3. The mechanism of SeNPs in Alzheimer's disease.

Selenium therapy has also been shown to lower oxidative stress and A formation in the brains of Alzheimer's disease experimental animal models [103,104]. Selenium therapy has also been shown to lower oxidative stress in the brains of Alzheimer's disease experimental animal models [103,104]. Selenium (II), sodium selenite (IV), and sodium selenate (IV) redox cycles have all been identified with ROS suppression being the most important mechanism associated with biological systems in the brain. ROS generation is a natural aspect of our bodies' basic functioning. When antioxidant enzymes and proteins like GSH-Px control the quantities of ROS in the body, they are not hazardous. While the cause of Alzheimer's disease is unknown, oxidative stress may play a role [98]. Furthermore, detecting Alzheimer's disease and regularly monitoring dementia are difficult tasks. As a result, plasma selenium levels and GSH-Px activity may be used to screen older people with Alzheimer's disease. Antioxidant-covered nanoparticles, such as selenium nanoparticles, have been studied for Alzheimer's disease therapy targeting

pathways associated with biological systems in the brain by decreasing ROS [98,105,106].

The function of oxidative stress in neurological illnesses such as dementia [107] and Alzheimer's disease [101] has been widely researched during the last several decades. The performance of selenium can be affected by its various forms and sizes. Elemental selenium nanoparticles, commonly known as red or elemental selenium, with diameters ranging from 20 to 500 nm. The quantity of protein in the redox system influences the magnitude of red elemental selenium produced. The study summarizes the importance of selenium in its many forms, as well as its role in nutrition and brain health. It's worth noting the focus on selenoproteins as brain antioxidants that fight oxidative stress linked with Alzheimer's disease. The possibility of selenium treatment lowering neural oxidative stress and developing adds a therapeutic component. The brief look at selenium nanoparticles as a potential brain-targeted therapeutic option is fascinating. Through this review clearly communicates selenium's relevance in neurodegenerative situations as well as its potential for furthering research and therapies.

5.2. Role of SeNPs in diabetes

Diabetes mellitus (DM) is a common illness characterized by hyperglycemia that affected about 415 million people aged 20–79 in 2015, with this figure expected to climb to 642 million by 2040 [108]. Prolonged hyperglycemia produces free radicals and reactive oxygen species (ROS), raising oxidative stress levels [109]. Notably, the search for a medicine with several bioactivities, including antihyperglycemic, antioxidant, and antihyperlipidemic qualities, is critical for the prevention and treatment of diabetes and its consequences.

Selenium (Se), a trace element and selenoprotein, is essential in many physiological functions in humans. Selenium has been studied for its ability to counteract diabetes-induced structural alterations [110]. Hyperglycemia, the most noticeable feature of diabetes mellitus, promotes oxidative stress by causing ROS overproduction, resulting in an imbalance between free radicals and the cellular antioxidant defense systems as shown in the figure (Fig. 4) [111]. Yuntao Liu [112] discovered that the overproduction of reactive oxygen species (ROS) in diabetes contributes to the development of chronic diabetic lesions in organs such as the liver and kidneys in his research. Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) are key defense mechanisms against ROS that play an important role in limiting oxidative damage [113]. Furthermore, several SeNP preparations were tested, and they were discovered to have better antioxidant activity than other experimental selenium preparations [60].

According to Yuntao Liu's research [60], methane dicarboxylic aldehyde (MDA), a main result of lipid peroxidation, acts as a marker of oxidative damage. The inhibition of MDA production is used to assess antioxidant activity. The combination of CVPs-SeNPs and VE outperformed either CVPs-SeNPs or VE alone in terms of antidiabetic parameters. This shows that CVPs-SeNPs and VE may have a natural synergy in anti-diabetic efficacy. Nonetheless, the fundamental processes are unknown. More chemical and pharmacological research is needed to fully understand the antidiabetic action mechanism of CVPs-SeNPs. The study investigates the mechanism of SeNPs' anti-diabetic actions. The mechanisms of action of selenium nanoparticles (SeNPs) in anti-diabetic actions are complex and include numerous interrelated pathways. We go through some of the primary methods by which SeNPs exert their anti-diabetic characteristics below: Hyperglycemia, a key feature of diabetes mellitus, increases oxidative stress by inducing ROS overproduction, resulting in an imbalance between free radicals and the antioxidant defense mechanisms of the cells [114]. Furthermore, strong data suggests that increased lipid peroxidation plays a key role in diabetes development [115]. According to Quin Zhang. et al. [116], Se increases antioxidant activity, which can help with diabetes management. The study highlighted the worldwide impact of Diabetes Mellitus (DM), emphasizing the growth in cases and the significance of hyperglycemia-induced oxidative stress. The role of selenium in reversing diabetes-induced alterations is investigated, as well as its effect on antioxidant activity. The work focuses on the detailed methods through which Selenium Nanoparticles (SeNPs) may reduce oxidative damage and lipid peroxidation, potentially paving the way for anti-diabetic therapies.

5.3. Role of SeNPs in infectious disease

Infectious disorders caused by direct contact with cellular or acellular microorganisms are intricately linked to a variety of inflammatory and immunological responses. Selenium nanoparticles (Se NPs) have emerged as promising therapeutic agents for both disease prevention and therapy. SeNPs have antibacterial characteristics, efficiently combating multidrug-resistant bacterial infections by destroying bacterial structures, implying possible antibiotic alternatives as in the figure illustrated (Fig. 5) [117]. Furthermore, Se NPs have been shown to slow the course of dengue virus infection, emphasizing their antiviral potential [63,118]. Se NPs interact with biological molecules due to their reduced size and increased surface area, breaking biofilms, compromising cell walls and membranes, and thereby reducing pathogen development [91]. Se NPs' flexibility extends to their ability to combat a wide range of pathogens,

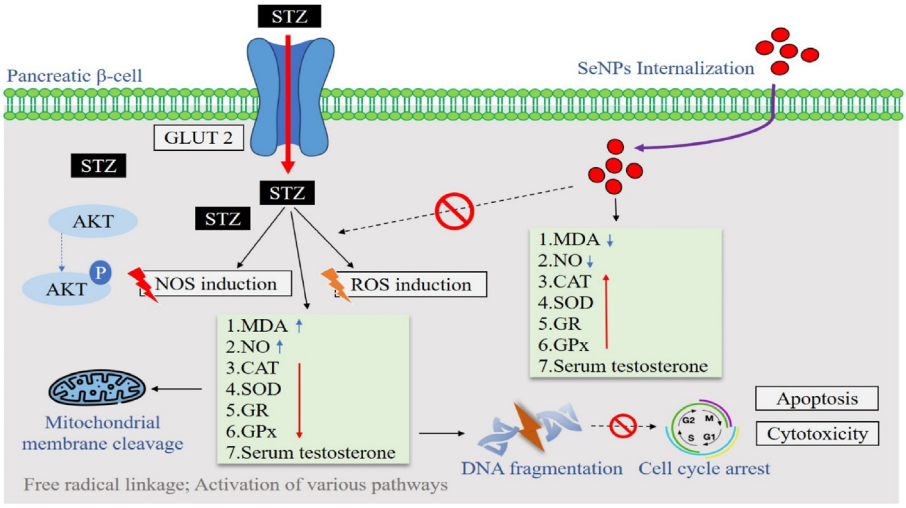

Fig. 4. The mechanism of improving Diabetes by SeNPs.

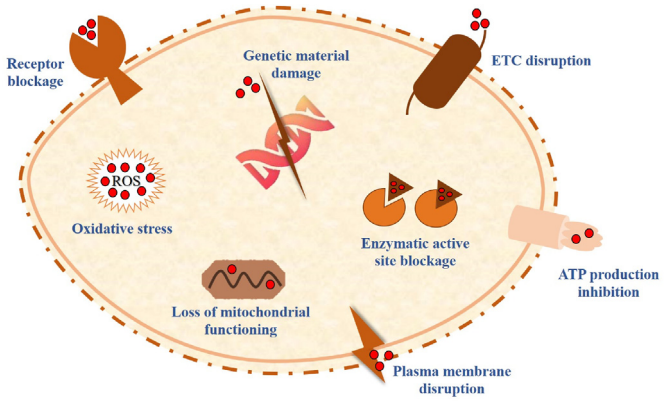

Fig. 5. Antimicrobial activity of SeNPs by penetration of multiple targeting sites of SeNPs.

including bacteria, fungi, viruses, and parasites. This is especially important since microbial resistance frequently originates through the cell wall and membrane defenses. Increased Se ion concentrations not only break cell walls but also undermine cell membrane integrity, altering intracellular homeostasis and eventually leading to microbial cell death [91].

Although most bacteria are harmless, a tiny percentage are capable of displacing helpful bacteria, growing in sterile tissues, and producing toxins, resulting in complex bacterial illnesses, Se NPs offer a potential pathway for avoiding a wide range of nosocomial infections caused by pathogenic bacteria, proving their status as powerful antibacterial agents [91]. A study that looked at the synergy between Se NPs and lysozymes discovered that Se NPs boost the antibacterial activities of lysozymes, which have the potential to fight infections [119]. Furthermore, Se NPs have been shown to improve the antibacterial activities of lysozyme [120]. Concurrently, tuberculosis (TB) caused by *Mycobacterium tuberculosis* (Mtb) has risen to the top of the list of infectious disease-related deaths. The emergence of drug-resistant TB infections in recent decades has fueled the hunt for alternative medicines other than traditional antibiotics, as well as creative techniques to improve the efficacy of existing drugs. Important addition by demonstrating that Se NPs can inhibit Mtb development by impairing cell membrane integrity. This result not only opens a new path for the use of Se nanoparticles as effective antimycobacterial agents but also provides innovative nanosystems that combine the abilities of Se nanoparticles with other therapeutic agents. The study reported on the processes involved in the link between selenium and *Mycobacterium tuberculosis* (MTB) infection. Serum selenium levels in pulmonary tuberculosis (PTB) patients were shown to be lower than in healthy controls, According to the findings, selenium operates via proinflammatory and autophagy mechanisms. The selenium donor methylseleninic acid (MSeA) reduced MTB-infected macrophage M1 polarisation by promoting canonical autophagy and LC3-associated phagocytosis (LAP). The transcription factor *c*-Jun has been discovered as a critical mediator in this process, limiting MTB development within cells [123].

In a study, Se NPs also show promise for broad-spectrum antiviral action, which is backed by selenium's well-established function in fighting viral infections. Se NPs have the potential to be used in direct antibacterial and antiviral therapy [7,121]. Viruses, which are among the most lethal agents, taking millions of lives each year, are presently inflicting a mounting toll because of the ongoing COVID-19 epidemic. A pressing need in the field of human health is to develop more effective medicines to battle viral infections. Selenium has a long history of fighting viral diseases such as influenza. Sabrina Sales Martinez. et, al. state that selenium's potential to control ROS formation, block inflammatory signaling pathways such as NF-, and limit the expression of proinflammatory cytokines including TNF- and IL-6. Inadequate selenium levels have been associated with decreased antioxidant activity, increased oxidative stress, and increased susceptibility to viral infections, potentially increasing virus pathogenicity and causing host injury. stated as emerged as a key figure [122].

Fungi saturate numerous ecosystems, gaining dominance and presenting dangers to human health by infecting a wide range of animals and species. Candida albicans, a dangerous opportunistic fungus, causes a wide range of diseases and poses severe hurdles to eradicate. Its biofilms, which are encased in exopolymeric or extracellular polymeric substance matrices, protect the pathogen against severe environmental conditions, fungicides, and human immunity. The study demonstrated chitosan's microbicidal capabilities, and its efficiency as a result of surface positive charges that facilitate adhesion and interaction with microbial membranes and organelles. This interaction, together with increased intracellular reactive oxygen species (ROS) generation, results in the inhibition of microbial bioactivities and increased cellular membrane permeability. The conversion of chitosan into nanoforms, such as selenium nanoparticles with chitosan, improves these effects by increasing the reactive surface area and decreasing particle size. The shift to nanoforms increases the efficacy of interactions and microbicidal effects, transforming into a powerful and efficient antifungal agent [124].

Se NPs have shown substantial suicidal activities against *Echinococcus granulosus*, bolstering their potency [125]. Furthermore, Se NPs outperform sodium selenite in terms of antioxidant, anti-apoptotic, and anti-inflammatory activity against the Eimeria parasite in the mouse jejunum [126]. Furthermore, Micaela Pescuma et al. [127] show that biogenic Se NPs have significant antifungal efficacy against the wood-rotting fungus *Oligoporus pelliculosus*. Se NPs' broad range of antifungal capabilities broadens the arsenal against diseases caused by many fungi, effectively tackling infectious conditions. Selenium nanoparticles (Se NPs) hold infection-fighting promises. Breaking bacteria's defenses, slowing viruses, and inhibiting tuberculosis, Se NPs disrupt cell structures, enhance immunity, and expand treatment horizons.

The chitosan's powerful antimicrobial capabilities, particularly in its nanoform as selenium nanoparticles (Se NPs). The positive surface charges of chitosan improve its interaction with microbial membranes, resulting in enhanced reactive oxygen species (ROS) production, inhibition of microbial activity, and increased cellular membrane permeability. Se NPs, in particular, have broad-spectrum antifungal activity against a variety of pathogens and show promise in the treatment of bacterial, viral, and parasite illnesses. The synergistic activity of Se NPs with lysozymes increases their efficacy, providing a diverse approach against infectious threats and the possibility for novel treatments.

5.4. Role of SeNPs in rheumatoid arthritis

Rheumatoid arthritis (RA) is a prevalent chronic inflammation-mediated illness with systemic consequences [128]. RA sets off a self-directed inflammatory and immunological cascade that results in joint degeneration. It is a chronic illness characterized by diarthrodial joint inflammation, which leads to symmetrical polyarthritis and synovial hyperplasia (swelling). This process causes increasing cartilage and bone breakdown, resulting in loss of articular function and ultimately joint deformity. While there are several therapeutic options available, none of them are without side effects. As a result, researchers are looking for alternate options. Nanomedicine is one of the most promising RA treatment methods in this area [129]. Many different nanomedicine formulations have been developed and tested throughout the years for a variety of illnesses. Only around 50 of these formulations are now licensed for clinical use, with more nanomedicines in the works [130]. SeNPs have gotten a lot of interest because of their unusual physical and chemical features, such as mechanical, electrical, catalytic, and opto-magnetic capabilities, that arise when this element is scaled down to the nanoscale. This effect is caused by nanoparticles' great spatial confinement, a considerable surface-to-volume ratio, and significant surface energy [131].

Ren et al. [132] found that SeNPs dispersed in 1 % phytochemical coumaric acid (CA) repaired abnormal biochemical markers in rheumatoid arthritis (RA) rat models, indicating a strong therapeutic potential against RA's hallmarks. SeNPs' antioxidant and anti-inflammatory properties resulted in the restoration of GPx1, CAT, and COX-2 mRNA expression, as well as the normalization of TNF-α, IL-1, IL-6, IL-8, and MCP-1 levels. ROS and RNS are useful for studying the pathophysiology of oxidative stress-related diseases as depicted in the figure (Fig. 6) [133]. Inflammation and oxidative stress (OS) both play important roles in the development of RA [134,135]. Selenium (Se) has received a great deal of attention due to its involvement in controlling ROS/RNS and inflammation, as well as its antioxidant and anti-inflammatory properties. TNF- levels were elevated, GPx1 levels were lowered, and NF–B was increased in macrophages grown in a Se-deficient environment [136]. SeNPs have also been the subject of investigation due to their ability to combat oxidative stress and inflammation. Nanoselenium has been shown to increase the production of glutathione peroxidase Se-dependent enzyme—via selenophosphate synthesis, a critical mechanism requiring selenocysteine-specific tRNA [137]. This comprehensive description of the process of nano selenium helps our knowledge of its role in preventing ROS-induced oxidative stress and inflammation, which is pertinent to rheumatoid arthritis.

5.5. Role of SeNPs in cancer

Cancer is defined as the uncontrollable proliferation of abnormal cells, which results in the formation of tumors that can spread to other regions of the body. Cancer is caused by abnormalities in protein function and gene expression, which are frequently the consequence of a more occurrence of epigenetic and genetic events [138]. Epigenetics is the study of gene expression control through heritable alterations unrelated to the DNA sequence. DNA methylation, histone post-translational modifications, and microRNAs are examples of these differences. While not as well studied as DNA methylation, histone acetylation is important in cancer initiation. The acetylation or deacetylation of histone tail amino termini influences the interaction of DNA with histone proteins, hence influencing chromatin structure. Histone acetylation is a chromatin-associated action catalyzed by HATs, which transport acetyl groups from acetyl coenzyme A to residues of lysine. Cancer has been linked to histone acetylation, deacetylation, and ROS elevations [139]. ROS are absorbed by SeNPs in a size-dependent way, with small SeNPs having a higher free radical scavenging capability as shown in the figure (Fig. 7) [140]. Increased solubility, resistance to enzymatic degradation and oxidation, longer residence time, and better bioavailability are all advantages of utilizing nanoparticles [141]. SeNPs-based approaches

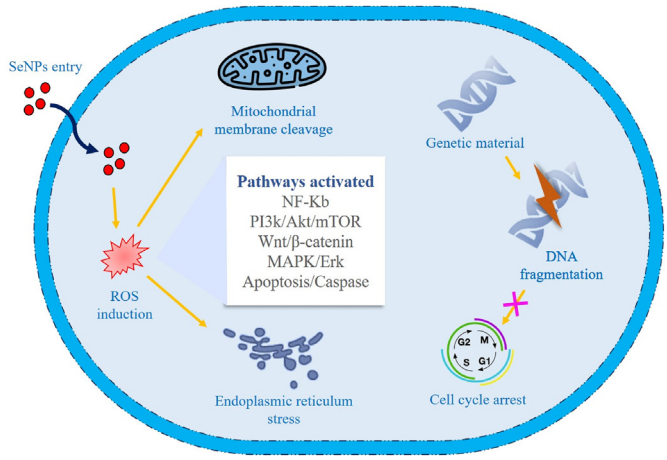

Fig. 7. Indicates the significance of selenium nanoparticles in cancer.

have promise for overcoming drug resistance, reducing toxicity in chemotherapeutic medicines, and enabling targeted distribution of chemotherapy drugs to their intended location [5].

A study suggested that selenium nanoparticles in the size range of 3–20 nm could be a novel therapeutic approach for addressing oxidative stress caused by elevated ROS due to Chromium (VI) exposure. ROS, while playing essential roles as defense mechanisms and signaling agents in biological systems, can become detrimental when produced excessively, leading to cellular damage and adverse effects on various organ systems.

Several mechanisms underpin SeNPs' anticancer properties, to prevent metastasis [142–144]. Apoptosis is the mechanism that has received the most attention for SeNPs' anti-cancer action. There have been instances of RNA made with selenium nanoparticles being used to treat ovarian cancer, (SeNPs) may trigger apoptosis in cancer cells by a variety of methods, including the formation of reactive oxygen species (ROS), modification of mitochondrial pathways, activation of caspases, control of apoptotic proteins, cell cycle arrest, and antioxidant defense. Because of these qualities, SeNPs are being studied for their possible involvement in cancer treatment. However, further study is needed to understand the precise pathways [145].

A Study by boosting the sub-G1 cell population, and chromatin condensation, SeNPs coupled with Spirulina polysaccharides suppress cancer formation. These conjugates also aid in the targeted delivery of SeNPs to cancer cells and the study looks at the potential of fenugreek seed extract for synthesizing selenium nanoparticles (SeNPs) in a green

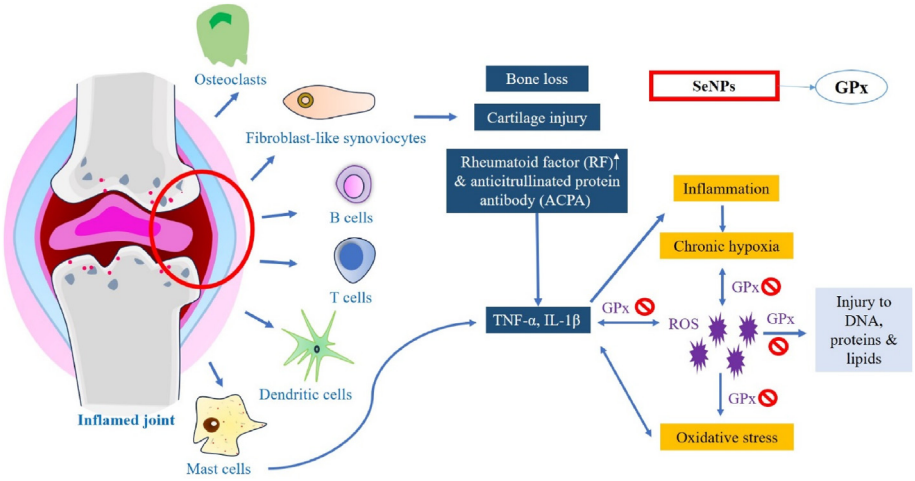

Fig. 6. Depicts the distinct mechanism of SeNP in Rheumatoid Arthritis.

and environmentally friendly way. The presence of alkaloids, flavonoids, amino acids, proteins, glucose, cardiac glycosides, and saponins in fenugreek seed extract is shown by phytochemical screening, indicating its rich biochemical makeup. The galactomannan polysaccharide in fenugreek may be important in the reduction of selenious acids to SeNPs. Furthermore, the chemicals flavanol and phenol function as stabilizers throughout the nanoparticle formation process. The biosynthesis of SeNPs is confirmed by FTIR and UV–Vis spectroscopy, which demonstrate a color change from colourless selenious acid to ruby red SeNPs with absorption peaks in the 200–400 nm range. The study emphasizes the efficiency of fenugreek seed extract as a green and natural agent for SeNP production, providing a promising alternative. In comparison to previous approaches, the review emphasizes the ecologically benign production of selenium nanoparticles (SeNPs) utilizing fenugreek seed extract. UV–Vis spectrophotometer, SEM, and FTIR analysis were used for characterization. Notably, this research is the first to show that phytochemicals found in fenugreek seeds may convert metal complexes into SeNPs. The involvement of different functional groups in selenious acid reduction is shown by FTIR spectra. The study shows considerable cytotoxicity against MCF-7 cancer cells at 6 and 36 h with varied doses. Furthermore, combining SeNPs with doxorubicin boosts the anti-cancer efficacy. The study reveals that SeNPs cause MCF-7 cell death via apoptosis, and it calls for more research to uncover the underlying processes [146].

Selenoenzymes, and thioredoxin reductase, are implicated in enhancing selenium's protective role against conditions like cancer. The potential of selenium nanoparticles to mitigate oxidative stress and its associated risks highlights their potential as regenerative materials with therapeutic applications. SeNPs have been used to successfully cause cytotoxicity in cancer cells. The impact of K2Cr2O7 on the thyroid and assesses the protective effects of selenium nanoparticles (SeNPs). Chromium exposure led to thyroid dysfunction and oxidative damage, as evidenced by altered hormone levels and antioxidant parameters. Selenium nanoparticles effectively mitigated these effects, restoring thyroid function and preventing cellular damage. The study emphasizes the potential of SeNPs as protective agents against chromium toxicity, providing valuable insights for further research and clinical applications [147].

In summary, Selenium nanoparticles (SeNPs) show great potential in cancer treatment and in protecting against oxidative stress-related disorders. Their anticancer strategies include apoptosis induction, ROS modulation, and metastasis suppression. SeNPs have the ability to deliver targeted drugs, overcome drug resistance, and reduce chemotherapy damage. Studies show that they are effective in alleviating oxidative stress caused by Chromium (VI) exposure. Furthermore, when combined with natural chemicals, SeNPs show intriguing anticancer effects. SeNPs' preventive role extends to situations such as thyroid dysfunction induced by chromium exposure. Overall, SeNPs are diverse agents with therapeutic promise, highlighting the importance of future study into their precise mechanisms and uses.

6. SeNPs in combination with drugs

Nanoparticle (NP) and chemotherapeutic drug combinations hold the potential for enhancing drug efficacy through improved cellular internalization. Lower drug doses can combat multidrug-resistant cancers and systemic toxicity. Selenium nanoparticles (SeNPs) have been utilized with drugs like 5-Fluorouracil (5-FU) and irinotecan, displaying enhanced anticancer activity. SeNPs induce apoptosis via intrinsic and extrinsic pathways, involving p53 activation and caspase-mediated routes [148]. Nanotechnology's benefits, including improved bioactivity and controlled release, are promising for diverse biological applications. Selenium-based drug delivery, especially SeNPs, shows transformative potential in cancer therapy and more. SeNPs also offer promise in neurodegenerative diseases and infectious challenges, as well as addressing oxidative stress and inflammation. Integrating SeNPs into biomedicine presents versatile solutions for treatment improvement [10]. The hazards of hexavalent chromium [Cr (VI)] exposure and explores how nano-selenium can mitigate thyroid damage and oxidative stress. This innovative intervention holds promise for addressing Cr (VI)-induced harm. In parallel, the study underscores Cr (VI)'s damaging effects on health and SeNPs' antioxidant properties in countering oxidative stress. SeNPs' potential is demonstrated in preventing Cr (VI)-induced thyroid damage [147]. Overall, the review provides insights into nanotechnology's potential, its applications, and its capacity to mitigate toxic exposures, marking a significant advancement in therapeutic strategies [147].

Nanomedicine has revolutionized modern pharmaceutical applications, particularly through the development of multifunctional nanoparticles (NPs). These NPs have opened new avenues in tailored nanomedicine, including targeted therapies, diagnostics, and combatting multidrug resistance (MDR). Selenium nanoparticles (SeNPs) have rapidly gained prominence in the past few years, serving as drug and gene delivery platforms. They exhibit promise in anticancer drug delivery, gene transportation, and antigen-based active immunization. Selenium activates both cellular and humoral immune responses, triggering proinflammatory cytokines and interferon release from splenocytes. NPs facilitate antigen delivery to the reticuloendothelial system, enhancing immunization [149]. The Study successfully demonstrates the nano complexes exhibit compact sizes, show minimal cytotoxicity, and significantly enhance transfection efficiency by incorporating lactobionic acid (LA) into the SeNPs formulation, active targeting, and cell specificity are achieved, leading to improved transfection in cells treated with Se nano complexes. These nano complexes hold great potential as gene delivery vehicles, particularly for liver cancer treatment, warranting further in vivo exploration [150]. The study presents selenium-based nanocarriers with advantageous characteristics for effective delivery, Minimal toxicity is observed across cell lines, with selective cytotoxicity in cancer cells and low cytotoxicity in non-cancer cells (HEK293). Gene silencing experiments confirm significant suppression by both nanocarriers compared to naked siRNA [151].

Chitosan-coated selenium vector for mRNA delivery, highlighting its potential in tumor vaccination and immunotherapy. The study's focus is to design a functionalized Se carrier for mRNA delivery to tumor cells, specifically for cancer immunotherapy. This marks the first instance of utilizing such a system for mRNA delivery. The functionalized SeNPs demonstrate safe and effective mRNA-based delivery in vitro. The incorporation of a folate receptor-targeting moiety enhances uptake in cells expressing folate receptors. Chitosan-coated selenium nanoparticles exhibit promise for mRNA delivery in tumor vaccination and immunotherapy, suggesting a promising synergy between RNA vaccines and SeNPs with potential implications for cancer therapeutics. The compelling results encourage further investigations to unravel the intricate interaction between mRNA and selenium, especially in the context of gene therapy applications [152]. Nanomedicine advances with versatile nanoparticles (NPs), including selenium nanoparticles (SeNPs), for targeted therapies and diagnostics. SeNPs hold the potential for drug and gene delivery, activating immune responses. Studies showcase stable SeNP formulations for gene delivery, effective siRNA protection, and mRNA distribution. These innovations hint at promising avenues for cancer treatment and immunotherapy.

7. Future perspectives

The future potential of nanotechnology in biology is enormous, because of nanoparticle benefits such as improved bioactivity, decreased toxicity, targeted administration, and controlled release. This study focuses on Selenium Nanoparticles (SeNPs), highlighting their many roles and recent advances, with a particular emphasis on their game-changing influence in biological research and applications. Because of their tiny size and drug delivery compatibility, nanomaterials such as SeNPs are beneficial in a variety of biological applications. Selenium, a trace

element, is notable for its distinct bioactivity in nanoforms. Selenoproteins containing selenium, notably selenocysteine (Sec), play an important role in enzymatic processes that maintain physiological equilibrium. SeNPs have the potential for targeted treatment as a selenium-based medication delivery method. Se's potential in Alzheimer's, diabetes, infectious disease, Rheumatoid arthritis, and cancer is being investigated. SeNPs also make use of selenium's immune-modulating properties, opening new therapeutic options. Sustainability is maintained through ecologically friendly SeNP manufacturing technologies such as phytosynthesis. The intersection of nanotechnology and biology is poised to change medicine, with SeNPs at the vanguard, revolutionizing therapies, diagnostics, and medication delivery for better healthcare outcomes [10]. Selenium nanoparticles may be modified in a variety of ways, including biomolecule conjugation, size control, and surface functionalization. These changes improve their qualities, making them useful in industry, environmental cleanup, and biomedicine. Selenium nanoparticles show promise in a variety of sectors, and scientists are always experimenting with these modifications to optimize them for specific applications.

8. Conclusion

Nanotechnology has enormous promise in a variety of biological applications because of the benefits of nanoparticles such as improved bioactivity, reduced toxicity, precise targeting, and controlled release. This thorough Review summarizes SeNPs' various biological roles and recent advances, emphasizing their transformational potential in biomedical research and applications. These nanomaterials have emerged as valuable tools in a variety of biological situations due to their unique properties such as tiny size and biocompatibility for drug administration. Selenium (Se), a crucial trace element, distinguishes among these nanoparticles due to their unique bioactivities in nanoforms. Selenoproteins containing selenium, namely selenocysteine (Sec), play an important role in maintaining physiological redox equilibrium via oxidoreductase activity, a critical enzymatic function. Selenium, a key component of selenoproteins such as thioredoxin reductases and glutathione peroxidases, protects cells from oxidative damage caused by reactive oxygen and nitrogen species (ROS and RNS) such as superoxide, hydrogen peroxide, hydroxyl radicals, nitric oxide, and peroxynitrite, Selenium by which enhances the antioxidant activity of Selenoproteins which plays a significant role in antioxidant may be responsible for SeNPs' regulatory antioxidant potential.

Selenium-based drug delivery methods, such as selenium nanoparticles (SeNPs), show potential for targeted medication delivery. An extensive study is being conducted to investigate Se's therapeutic potential in the treatment of cancer, pathogens, viruses, neuroprotection, diabetes, oxidative stress, and inflammation-related disorders such as rheumatoid arthritis. SeNPs benefit from selenium's function in immune system modulation. The environmentally favorable nature of SeNPs phytosynthesis provides a long-term solution.

Consuming too much selenium, whether in the form of nanoparticles or other selenium compounds, can result in selenosis, or selenium poisoning. Selenosis symptoms include skin rashes, neurological issues, and gastrointestinal difficulties. The amount or concentration of selenium nanoparticles provided is a crucial concern. A dose that is too high may be hazardous, whereas a dosage that is too low may not provide any therapeutic advantages. Scientists are continuously looking into this area to better understand the safety and efficacy characteristics of selenium nanoparticles in diverse medicinal applications. More comprehensive research, including preclinical and clinical studies, is needed to define the therapeutic window and ensure the safety and efficacy of selenium nanoparticles.

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Data availability

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Code availability

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] D. Peer, J.M. Karp, S. Hong, O.C. Farokhzad, R. Margalit, R. Langer, Nanocarriers as an emerging platform for cancer therapy, Nat. Nanotechnol. 2 (2007) 751–760, https://doi.org/10.1038/nnano.2007.387.
[2] S.S. Davis, Biomedical applications of nanotechnology–implications for drug targeting and gene therapy, Trends Biotechnol. 15 (1997) 217–224, https://doi.org/10.1016/S0167-7799(97)01036-6.
[3] S.M. Moghimi, A.C. Hunter, J.C. Murray, Nanomedicine: current status and future prospects, Faseb. J. 19 (2005) 311–330, https://doi.org/10.1096/fj.04-2747rev.
[4] R.A. Sperling, W.J. Parak, Surface modification, functionalization and bioconjugation of colloidal inorganic nanoparticles, Phil. Trans. Math. Phys. Eng. Sci. 368 (2010) 1333–1383, https://doi.org/10.1098/rsta.2009.0273.
[5] A. Khurana, S. Tekula, M.A. Saifi, P. Venkatesh, C. Godugu, Therapeutic applications of selenium nanoparticles, Biomed. Pharmacother. 111 (2019) 802–812, https://doi.org/10.1016/j.biopha.2018.12.146.
[6] A. Husen, K.S. Siddiqi, Plants and microbes assisted selenium nanoparticles: characterization and application, J. Nanobiotechnol. 12 (2014) 28, https://doi.org/10.1186/s12951-014-0028-6.
[7] B. Hosnedlova, M. Kepinska, S. Skalickova, C. Fernandez, B. Ruttkay-Nedecky, Q. Peng, M. Baron, M. Melcova, R. Opatrilova, J. Zidkova, G. Bjørklund, J. Sochor, R. Kizek, Nano-selenium and its nanomedicine applications: a critical review, Int. J. Nanomed. 13 (2018) 2107–2128, https://doi.org/10.2147/IJN.S157541.
[8] W. Zhang, Z. Chen, H. Liu, L. Zhang, P. Gao, D. Li, Biosynthesis and structural characteristics of selenium nanoparticles by Pseudomonas alcaliphila, Colloids Surf. B Biointerfaces 88 (2011) 196–201, https://doi.org/10.1016/j.colsurfb.2011.06.031.
[9] V.N. Gladyshev, E.S. Arnér, M.J. Berry, R. Brigelius-Flohé, E.A. Bruford, R.F. Burk, B.A. Carlson, S. Castellano, L. Chavatte, M. Conrad, P.R. Copeland, A.M. Diamond, D.M. Driscoll, A. Ferreiro, L. Flohé, F.R. Green, R. Guigó, D.E. Handy, D.L. Hatfield, J. Hesketh, P.R. Hoffmann, A. Holmgren, R.J. Hondal, M.T. Howard, K. Huang, H.-Y. Kim, I.Y. Kim, J. Köhrle, A. Krol, G. V Kryukov, B.J. Lee, B.C. Lee, X.G. Lei, Q. Liu, A. Lescure, A. V Lobanov, J. Loscalzo, M. Maiorino, M. Mariotti, K. Sandeep Prabhu, M.P. Rayman, S. Rozovsky, G. Salinas, E.E. Schmidt, L. Schomburg, U. Schweizer, M. Simonović, R.A. Sunde, P.A. Tsuji, S. Tweedie, F. Ursini, P.D. Whanger, Y. Zhang, Selenoprotein gene nomenclature, J. Biol. Chem. 291 (2016) 24036–24040, https://doi.org/10.1074/jbc.M116.756155.
[10] F. Gao, Q. Yuan, L. Gao, P. Cai, H. Zhu, R. Liu, Y. Wang, Y. Wei, G. Huang, J. Liang, X. Gao, Cytotoxicity and therapeutic effect of irinotecan combined with selenium nanoparticles, Biomaterials 35 (2014) 8854–8866, https://doi.org/10.1016/j.biomaterials.2014.07.004.
[11] S. Skalickova, V. Milosavljevic, K. Cihalova, P. Horky, L. Richtera, V. Adam, Selenium nanoparticles as a nutritional supplement, Nutrition 33 (2017) 83–90, https://doi.org/10.1016/j.nut.2016.05.001.
[12] K.M. Brown, J.R. Arthur, Selenium, selenoproteins and human health: a review, Publ. Health Nutr. 4 (2001) 593–599, https://doi.org/10.1079/phn2001143.
[13] Y. Huang, Y. Fu, M. Li, D. Jiang, C.J. Kutyreff, J.W. Engle, X. Lan, W. Cai, T. Chen, Chirality-driven transportation and oxidation prevention by chiral selenium nanoparticles, Angew Chem. Int. Ed. Engl. 59 (2020) 4406–4414, https://doi.org/10.1002/anie.201910615.

[14] C. Ding, C. Yang, T. Cheng, X. Wang, Q. Wang, R. He, S. Sang, K. Zhu, D. Xu, J. Wang, X. Liu, X. Zhang, Macrophage-biomimetic porous Se@SiO2 nanocomposites for dual modal immunotherapy against inflammatory osteolysis, J. Nanobiotechnol. 19 (2021) 382, https://doi.org/10.1186/s12951-021-01128-4.
[15] M. Wołonciej, E. Milewska, W. Roszkowska-Jakimiec, Trace elements as an activator of antioxidant enzymes, Postepy Hig. Med. Dosw. 70 (2016) 1483–1498, https://doi.org/10.5604/17322693.1229074.
[16] C. Sanmartín, D. Plano, A.K. Sharma, J.A. Palop, Selenium compounds, apoptosis and other types of cell death: an overview for cancer therapy, Int. J. Mol. Sci. 13 (2012) 9649–9672, https://doi.org/10.3390/ijms13089649.
[17] H. Wang, J. Zhang, H. Yu, Elemental selenium at nano size possesses lower toxicity without compromising the fundamental effect on selenoenzymes: comparison with selenomethionine in mice, Free Radic. Biol. Med. 42 (2007) 1524–1533, https://doi.org/10.1016/j.freeradbiomed.2007.02.013.
[18] G. Deng, C. Chen, J. Zhang, Y. Zhai, J. Zhao, A. Ji, Y. Kang, X. Liu, K. Dou, Q. Wang, Se@SiO2 nanocomposites attenuate doxorubicin-induced cardiotoxicity through combatting oxidative damage, Artif. Cells, Nanomed. Biotechnol. 46 (2018) 112–121, https://doi.org/10.1080/21691401.2018.1452250.
[19] H. Alam, N. Khatoon, M. Raza, P.C. Ghosh, M. Sardar, Synthesis and characterization of nano selenium using plant biomolecules and their potential applications, Bionanoscience 9 (2019) 96–104, https://doi.org/10.1007/s12668-018-0569-5.
[20] H. An, Crab shell for the removal of heavy metals from aqueous solution, Water Res. 35 (2001) 3551–3556, https://doi.org/10.1016/S0043-1354(01)00099-9.
[21] D. Plano, Y. Baquedano, D. Moreno-Mateos, M. Font, A. Jiménez-Ruiz, J.A. Palop, C. Sanmartín, Selenocyanates and diselenides: a new class of potent antileishmanial agents, Eur. J. Med. Chem. 46 (2011) 3315–3323, https://doi.org/10.1016/j.ejmech.2011.04.054.
[22] M. Álvarez-Pérez, W. Ali, M.A. Marć, J. Handzlik, E. Domínguez-Álvarez, Selenides, Diselenides, A review of their anticancer and chemopreventive activity, Molecules 23 (2018), https://doi.org/10.3390/molecules23030628.
[23] A. Kunwar, A. Patil, S. Kumar, R. Deshpande, V. Gota, J.S. Goda, V.K. Jain, K. Indira Priyadarsini, Toxicological safety evaluation of 3,3'-diselenodipropionic acid (DSePA), a pharmacologically important derivative of selenocystine, Regul. Toxicol. Pharmacol. 99 (2018) 159–167, https://doi.org/10.1016/j.yrtph.2018.09.019.
[24] Y. Mu, S. Lv, X. Ren, G. Jin, J. Liu, G. Yan, W. Li, J. Shen, G. Luo, UV-B induced keratinocyte apoptosis is blocked by 2-selenium-bridged β-cyclodextrin, a GPX mimic, J. Photochem. Photobiol., B 69 (2003) 7–12, https://doi.org/10.1016/S1011-1344(02)00386-X.
[25] Y. Fu, J. Chen, H. Xu, C. Van Oosterwijck, X. Zhang, W. Dehaen, M. Smet, Fully-branched hyperbranched polymers with a diselenide core as glutathione peroxidase mimics, Macromol. Rapid Commun. 33 (2012) 798–804, https://doi.org/10.1002/marc.201100860.
[26] V. Gandin, P. Khalkar, J. Braude, A.P. Fernandes, Organic selenium compounds as potential chemotherapeutic agents for improved cancer treatment, Free Radic. Biol. Med. 127 (2018) 80–97, https://doi.org/10.1016/j.freeradbiomed.2018.05.001.
[27] T. Tanaka, H. Makita, K. Kawabata, H. Mori, K. El-Bayoumy, 1,4-phenylenebis(methylene)selenocyanate exerts exceptional chemopreventive activity in rat tongue carcinogenesis, Cancer Res. 57 (1997) 3644–3648.
[28] Y. Cheng, U.H. Sk, Y. Zhang, X. Ren, L. Zhang, K.J. Huber-Keener, Y.-W. Sun, J. Liao, S. Amin, A.K. Sharma, J.-M. Yang, Rational incorporation of selenium into temozolomide elicits superior antitumor activity associated with both apoptotic and autophagic cell death, PLoS One 7 (2012) e35104, https://doi.org/10.1371/journal.pone.0035104.
[29] D. Desai, U. Salli, K.E. Vrana, S. Amin, SelSA, selenium analogs of SAHA as potent histone deacetylase inhibitors, Bioorg. Med. Chem. Lett 20 (2010) 2044–2047, https://doi.org/10.1016/j.bmcl.2009.07.068.
[30] Y.-J. Park, M. Koketsu, J.M. Kim, J.-H. Yeo, H. Ishihara, K.-G. Lee, S.Y. Kim, C.-K. Kim, 1,3-Selenazol-4-one derivatives inhibit inducible nitric oxide-mediated nitric oxide production in lipopolysaccharide-induced BV-2 cells, Biol. Pharm. Bull. 26 (2003) 1657–1660, https://doi.org/10.1248/bpb.26.1657.
[31] K. Macegoniuk, E. Grela, J. Palus, E. Rudzińska-Szostak, A. Grabowiecka, M. Biernat, Ł. Berlicki, 1,2-Benzisoselenazol-3(2H)-one derivatives as a new class of bacterial urease inhibitors, J. Med. Chem. 59 (2016) 8125–8133, https://doi.org/10.1021/acs.jmedchem.6b00986.
[32] S.-H. Juang, C.-C. Lung, P.-C. Hsu, K.-S. Hsu, Y.-C. Li, P.-C. Hong, H.-S. Shiah, C.-C. Kuo, C.-W. Huang, Y.-C. Wang, L. Huang, T.S. Chen, S.-F. Chen, K.-C. Fu, C.-L. Hsu, M.-J. Lin, C. Chang, C.L. Ashendel, T.C.K. Chan, K.-M. Chou, J.-Y. Chang, D-501036, a novel selenophene-based triheterocycle derivative, exhibits potent *in vitro* and *in vivo* antitumoral activity which involves DNA damage and ataxia telangiectasia–mutated nuclear protein kinase activation, Mol. Cancer Therapeut. 6 (2007) 193–202, https://doi.org/10.1158/1535-7163.MCT-06-0482.
[33] F. Xing, S. Li, X. Ge, C. Wang, H. Zeng, D. Li, L. Dong, The inhibitory effect of a novel organoselenium compound BBSKE on the tongue cancer Tca8113 in vitro and in vivo, Oral Oncol. 44 (2008) 963–969, https://doi.org/10.1016/j.oraloncology.2007.12.001.
[34] M.R. Franklin, P.J. Moos, W.M. El-Sayed, T. Aboul-Fadl, J.C. Roberts, Pre- and post-initiation chemoprevention activity of 2-alkyl/aryl selenazolidine-4(R)-carboxylic acids against tobacco-derived nitrosamine (NNK)-induced lung tumors in the A/J mouse, Chem. Biol. Interact. 168 (2007) 211–220, https://doi.org/10.1016/j.cbi.2007.04.012.
[35] R.L. Poerschke, P.J. Moos, Thioredoxin reductase 1 knockdown enhances selenazolidine cytotoxicity in human lung cancer cells via mitochondrial dysfunction, Biochem. Pharmacol. 81 (2011) 211–221, https://doi.org/10.1016/j.bcp.2010.09.024.
[36] A. Angeli, M. Ferraroni, A. Capperucci, D. Tanini, G. Costantino, C.T. Supuran, Selenocarbamates as a prodrug-based approach to carbonic anhydrase inhibition, ChemMedChem 17 (2022), https://doi.org/10.1002/cmdc.202200085.
[37] B.M. Kim, A.B. Rode, E.J. Han, I.S. Hong, S.H. Hong, 5-Phenylselenyl- and 5-methylselenyl-methyl-2'-deoxyuridine induce oxidative stress, DNA damage, and caspase-2-dependent apoptosis in cancer cells, Apoptosis 17 (2012) 200–216, https://doi.org/10.1007/s10495-011-0665-2.
[38] F.A.R. Barbosa, R.F.S. Canto, K.F. Teixeira, A.S. de Souza, A.S. de Oliveira, A.L. Braga, Selenium-Derivative compounds: a review of new perspectives in the treatment of alzheimer's disease, Curr. Med. Chem. 30 (2023) 689–700, https://doi.org/10.2174/0929867329666220224161454.
[39] D. Desai, S. V Madhunapantula, K. Gowdahalli, A. Sharma, R. Chandagaludoreswamy, K. El-Bayoumy, G.P. Robertson, S. Amin, Synthesis and characterization of a novel iNOS/Akt inhibitor Se,Se'-1,4-phenylenebis(1,2-ethanediyl)bisisoselenourea (PBISe)–against colon cancer, Bioorg. Med. Chem. Lett 20 (2010), https://doi.org/10.1016/j.bmcl.2009.09.071, 2038–43.
[40] M.J. Nasim, M.M. Zuraik, A.Y. Abdin, Y. Ney, C. Jacob, Selenomethionine: a pink trojan redox horse with implications in aging and various age-related diseases, Antioxidants 10 (2021), https://doi.org/10.3390/antiox10060882.
[41] A.K. Selvam, T. Szekerczés, S. Björnstedt, A. Razaghi, M. Björnstedt, Methods for Accurate and Reproducible Studies of Pharmacological Effects of Selenium in Cancer, 2022, pp. 25–62, https://doi.org/10.1016/bs.mie.2021.10.019.
[42] D. Bartolini, L. Sancineto, A. Fabro de Bem, K.D. Tew, C. Santi, R. Radi, P. Toquato, F. Galli, Selenocompounds in Cancer Therapy: an Overview, 2017, pp. 259–302, https://doi.org/10.1016/bs.acr.2017.07.007.
[43] J. Chaudiere, O. Courtin, J. Leclaire, Glutathione oxidase activity of selenocystamine: a mechanistic study, Arch. Biochem. Biophys. 296 (1992) 328–336, https://doi.org/10.1016/0003-9861(92)90580-p.
[44] S. Zhu, T.E. Gray, P. Nettesheim, The effect of sodium selenite on cell proliferation and transformation of primary rat tracheal epithelial cells, Carcinogenesis 13 (1992) 1725–1729, https://doi.org/10.1093/carcin/13.10.1725.
[45] H.E. Ganther, R.J. Kraus, Chemical stability of selenious acid in total parenteral nutrition solutions containing ascorbic acid, JPEN - J. Parenter. Enter. Nutr. 13 (1989) 185–188, https://doi.org/10.1177/0148607189013002185.
[46] E.G. Varlamova, E.A. Turovsky, The main cytotoxic effects of methylseleninic acid on various cancer cells, Int. J. Mol. Sci. 22 (2021), https://doi.org/10.3390/ijms22126614.
[47] G.R. Waitkins, C.W. Clark, Selenium dioxide: preparation, properties, and use as oxidizing agent, Chem. Rev. 36 (1945) 235–289, https://doi.org/10.1021/cr60115a001.
[48] A.P. Fernandes, V. Gandin, Selenium compounds as therapeutic agents in cancer, Biochim. Biophys. Acta 1850 (2015) 1642–1660, https://doi.org/10.1016/j.bbagen.2014.10.008.
[49] J.T. Rotruck, A.L. Pope, H.E. Ganther, A.B. Swanson, D.G. Hafeman, W.G. Hoekstra, Selenium: biochemical role as a component of glutathione peroxidase, Science 179 (1973) 588–590, https://doi.org/10.1126/science.179.4073.588.
[50] A.M. Casaril, M. Domingues, D. de A. Lourenço, B. Vieira, K. Begnini, C.D. Corcini, R.T. França, A.S. Varela Junior, F.K. Seixas, T. Collares, E.J. Lenardão, L. Savegnago, 3-[(4-chlorophenyl)selanyl]-1-methyl-1H-indole ameliorates long-lasting depression- and anxiogenic-like behaviors and cognitive impairment in post-septic mice: involvement of neuroimmune and oxidative hallmarks, Chem. Biol. Interact. 331 (2020) 109278, https://doi.org/10.1016/j.cbi.2020.109278.
[51] M. Nazıroğlu, S. Muhamad, L. Pecze, Nanoparticles as potential clinical therapeutic agents in Alzheimer's disease: focus on selenium nanoparticles, Expet Rev. Clin. Pharmacol. 10 (2017) 773–782, https://doi.org/10.1080/17512433.2017.1324781.
[52] K.A. Amin, K.S. Hashem, F.S. Alshehri, S.T. Awad, M.S. Hassan, Antioxidant and hepatoprotective efficiency of selenium nanoparticles against acetaminophen-induced hepatic damage, Biol. Trace Elem. Res. 175 (2017) 136–145, https://doi.org/10.1007/s12011-016-0748-6.
[53] X. Huang, X. Chen, Q. Chen, Q. Yu, D. Sun, J. Liu, Investigation of functional selenium nanoparticles as potent antimicrobial agents against superbugs, Acta Biomater. 30 (2016) 397–407, https://doi.org/10.1016/j.actbio.2015.10.041.
[54] E.N. Drake, Cancer chemoprevention: selenium as a prooxidant, not an antioxidant, Med. Hypotheses 67 (2006) 318–322, https://doi.org/10.1016/j.mehy.2006.01.058.
[55] J.S. Zhang, X.Y. Gao, L.D. Zhang, Y.P. Bao, Biological effects of a nano red elemental selenium, Biofactors 15 (2001) 27–38, https://doi.org/10.1002/biof.5520150103.
[56] Y. Huang, L. He, W. Liu, C. Fan, W. Zheng, Y.-S. Wong, T. Chen, Selective cellular uptake and induction of apoptosis of cancer-targeted selenium nanoparticles, Biomaterials 34 (2013) 7106–7116, https://doi.org/10.1016/j.biomaterials.2013.04.067.
[57] G.S. Kumar, A. Kulkarni, A. Khurana, J. Kaur, K. Tikoo, Selenium nanoparticles involve HSP-70 and SIRT1 in preventing the progression of type 1 diabetic nephropathy, Chem. Biol. Interact. 223 (2014) 125–133, https://doi.org/10.1016/j.cbi.2014.09.017.
[58] H. Wang, W. Wei, S.-Y. Zhang, Y.-X. Shen, L. Yue, N.-P. Wang, S.-Y. Xu, Melatonin-selenium nanoparticles inhibit oxidative stress and protect against hepatic injury induced by Bacillus Calmette-Guérin/lipopolysaccharide in mice, J. Pineal Res. 39 (2005) 156–163, https://doi.org/10.1111/j.1600-079X.2005.00231.x.
[59] Y. Li, X. Li, Y.-S. Wong, T. Chen, H. Zhang, C. Liu, W. Zheng, The reversal of cisplatin-induced nephrotoxicity by selenium nanoparticles functionalized with

11-mercapto-1-undecanol by inhibition of ROS-mediated apoptosis, Biomaterials 32 (2011) 9068–9076, https://doi.org/10.1016/j.biomaterials.2011.08.001.
[60] Y. Liu, S. Zeng, Y. Liu, W. Wu, Y. Shen, L. Zhang, C. Li, H. Chen, A. Liu, L. Shen, B. Hu, C. Wang, Synthesis and antidiabetic activity of selenium nanoparticles in the presence of polysaccharides from Catathelasma ventricosum, Int. J. Biol. Macromol. 114 (2018) 632–639, https://doi.org/10.1016/j.ijbiomac.2018.03.161.
[61] A. Kumar, K.S. Prasad, Role of nano-selenium in health and environment, J. Biotechnol. 325 (2021) 152–163, https://doi.org/10.1016/j.jbiotec.2020.11.004.
[62] V. Alagesan, S. Venugopal, Green synthesis of selenium nanoparticle using leaves extract of withania somnifera and its biological applications and photocatalytic activities, Bionanoscience 9 (2019) 105–116, https://doi.org/10.1007/s12668-018-0566-8.
[63] P. Sowndarya, G. Ramkumar, M.S. Shivakumar, Green synthesis of selenium nanoparticles conjugated Clausena dentata plant leaf extract and their insecticidal potential against mosquito vectors, Artif. Cells, Nanomed. Biotechnol. 45 (2017) 1490–1495, https://doi.org/10.1080/21691401.2016.1252383.
[64] A.J. Kora, L. Rastogi, Biomimetic synthesis of selenium nanoparticles by Pseudomonas aeruginosa ATCC 27853: an approach for conversion of selenite, J. Environ. Manag. 181 (2016) 231–236, https://doi.org/10.1016/j.jenvman.2016.06.029.
[65] S.-Y. Zhang, J. Zhang, H.-Y. Wang, H.-Y. Chen, Synthesis of selenium nanoparticles in the presence of polysaccharides, Mater. Lett. 58 (2004) 2590–2594, https://doi.org/10.1016/j.matlet.2004.03.031.
[66] L. Schomburg, Selenium, selenoproteins and the thyroid gland: interactions in health and disease, Nat. Rev. Endocrinol. 8 (2012) 160–171, https://doi.org/10.1038/nrendo.2011.174.
[67] S. Lee, E.-K. Lee, D.H. Kang, J. Lee, S.H. Hong, W. Jeong, S.W. Kang, Glutathione peroxidase-1 regulates ASK1-dependent apoptosis via interaction with TRAF2 in RIPK3-negative cancer cells, Exp. Mol. Med. 53 (2021) 1080–1091, https://doi.org/10.1038/s12276-021-00642-7.
[68] D. Pacitti, T. Wang, M.M. Page, S.A.M. Martin, J. Sweetman, J. Feldmann, C.J. Secombes, Characterization of cytosolic glutathione peroxidase and phospholipid-hydroperoxide glutathione peroxidase genes in rainbow trout (Oncorhynchus mykiss) and their modulation by in vitro selenium exposure, Aquat. Toxicol. 130–131 (2013) 97–111, https://doi.org/10.1016/j.aquatox.2012.12.020.
[69] L. Flohé, S. Toppo, L. Orian, The glutathione peroxidase family: discoveries and mechanism, Free Radic. Biol. Med. 187 (2022) 113–122, https://doi.org/10.1016/j.freeradbiomed.2022.05.003.
[70] Q. Zhao, Y. Tang, L. Zhang, N. Sun, Q. Liu, R. Zhang, Biological functions of selenoprotein glutathione peroxidases (GPXs) and their expression in osteoarthritis, J. Inflamm. Res. 16 (2023) 183–196, https://doi.org/10.2147/JIR.S388934.
[71] H. Steinbrenner, B. Speckmann, L.-O. Klotz, Selenoproteins: antioxidant selenoenzymes and beyond, Arch. Biochem. Biophys. 595 (2016) 113–119, https://doi.org/10.1016/j.abb.2015.06.024.
[72] L. Xia, T. Nordman, J.M. Olsson, A. Damdimopoulos, L. Björkhem-Bergman, I. Nalvarte, L.C. Eriksson, E.S.J. Arnér, G. Spyrou, M. Björnstedt, The mammalian cytosolic selenoenzyme thioredoxin reductase reduces ubiquinone, J. Biol. Chem. 278 (2003) 2141–2146, https://doi.org/10.1074/jbc.M210456200.
[73] KH Lee, D. Jeong, Bimodal actions of selenium essential for antioxidant and toxic pro-oxidant activities: the selenium paradox (Review), Mol Med Rep. 5 (2) (2012 Feb) 299–304, https://doi.org/10.3892/mmr.2011.651. Epub 2011 Oct 31. PMID: 22051937.
[74] R. Gencheva, Q. Cheng, E.S.J. Arnér, Thioredoxin reductase selenoproteins from different organisms as potential drug targets for treatment of human diseases, Free Radic. Biol. Med. 190 (2022) 320–338, https://doi.org/10.1016/j.freeradbiomed.2022.07.020.
[75] R. Schuckelt, R. Brigelius-Flohé, M. Maiorino, A. Roveri, J. Reumkens, W. Strabburger, F. Ursini, B. Wolf, L. Flohé, Phospholipid hydroperoxide glutathione peroxidase is a seleno-enzyme distinct from the classical glutathione peroxidase as evident from cdna and amino acid sequencing, Free Radic. Res. Commun. 14 (1991) 343–361, https://doi.org/10.3109/10715769109093424.
[76] E.I. Biterova, A.A. Turanov, V.N. Gladyshev, J.J. Barycki, Crystal structures of oxidized and reduced mitochondrial thioredoxin reductase provide molecular details of the reaction mechanism, Proc. Natl. Acad. Sci. USA 102 (2005) 15018–15023, https://doi.org/10.1073/pnas.0504218102.
[77] A. Patenaude, M.R. Ven Murthy, M.-E. Mirault, Mitochondrial thioredoxin system: effects of TrxR2 overexpression on redox balance, cell growth, and apoptosis, J. Biol. Chem. 279 (2004) 27302–27314, https://doi.org/10.1074/jbc.M402496200.
[78] M.V. Kasaikina, D.L. Hatfield, V.N. Gladyshev, Understanding selenoprotein function and regulation through the use of rodent models, Biochim. Biophys. Acta Mol. Cell Res. 1823 (2012) 1633–1642, https://doi.org/10.1016/j.bbamcr.2012.02.018.
[79] J. Köhrle, F. Jakob, B. Contempré, J.E. Dumont, Selenium, the thyroid, and the endocrine system, Endocr. Rev. 26 (2005) 944–984, https://doi.org/10.1210/er.2001-0034.
[80] C.A. Bayse, E.S. Marsan, J.R. Garcia, A.T. Tran-Thompson, Thyroxine binding to type III iodothyronine deiodinase, Sci. Rep. 10 (2020) 15401, https://doi.org/10.1038/s41598-020-72243-9.
[81] A. Orozco, C. Valverde-R, A. Olvera, C. García-G, Iodothyronine deiodinases: a functional and evolutionary perspective, J. Endocrinol. 215 (2012) 207–219, https://doi.org/10.1530/JOE-12-0258.
[82] C. Curcio, M.M. Baqui, D. Salvatore, B.H. Rihn, S. Mohr, J.W. Harney, P.R. Larsen, A.C. Bianco, The human type 2 iodothyronine deiodinase is a selenoprotein highly expressed in a mesothelioma cell line, J. Biol. Chem. 276 (2001), https://doi.org/10.1074/jbc.C100325200, 30183–7.
[83] A.L. Maia, I.M. Goemann, E.L.S. Meyer, S.M. Wajner, Type 1 iodothyronine deiodinase in human physiology and disease, J. Endocrinol. 209 (2011) 283–297, https://doi.org/10.1530/JOE-10-0481.
[84] Y. Saito, Selenium transport mechanism via selenoprotein P—its physiological role and related diseases, Front. Nutr. 8 (2021), https://doi.org/10.3389/fnut.2021.685517.
[85] B. Javed, A. Nadhman, Z.-R. Mashwani, Phytosynthesis of Ag nanoparticles from Mentha longifolia: their structural evaluation and therapeutic potential against HCT116 colon cancer, Leishmanial and bacterial cells, Appl. Nanosci. 10 (2020) 3503–3515, https://doi.org/10.1007/s13204-020-01428-5.
[86] B. Fardsadegh, H. Jafarizadeh-Malmiri, Aloe vera leaf extract mediated green synthesis of selenium nanoparticles and assessment of their in vitro antimicrobial activity against spoilage fungi and pathogenic bacteria strains, Green Process. Synth. 8 (2019) 399–407, https://doi.org/10.1515/gps-2019-0007.
[87] S. Zhou, H. Zhu, P. Xiong, L. Shi, W. Bai, X. Li, Spore oil-functionalized selenium nanoparticles protect pancreatic beta cells from palmitic acid-induced apoptosis via inhibition of oxidative stress-mediated apoptotic pathways, Antioxidants 12 (2023) 840, https://doi.org/10.3390/antiox12040840.
[88] D. Medina Cruz, G. Mi, T.J. Webster, Synthesis and characterization of biogenic selenium nanoparticles with antimicrobial properties made by Staphylococcus aureus, methicillin-resistant Staphylococcus aureus (MRSA), Escherichia coli, and Pseudomonas aeruginosa, J. Biomed. Mater. Res. 106 (2018) 1400–1412, https://doi.org/10.1002/jbm.a.36347.
[89] V. Cittrarasu, D. Kaliannan, K. Dharman, V. Maluventhen, M. Easwaran, W.C. Liu, B. Balasubramanian, M. Arumugam, Green synthesis of selenium nanoparticles mediated from Ceropegia bulbosa Roxb extract and its cytotoxicity, antimicrobial, mosquitocidal and photocatalytic activities, Sci. Rep. 11 (2021) 1032, https://doi.org/10.1038/s41598-020-80327-9.
[90] L. Gunti, R.S. Dass, N.K. Kalagatur, Phytofabrication of selenium nanoparticles from emblica officinalis fruit extract and exploring its biopotential applications: antioxidant, antimicrobial, and biocompatibility, Front. Microbiol. 10 (2019) 931, https://doi.org/10.3389/fmicb.2019.00931.
[91] W. Lin, J. Zhang, J.-F. Xu, J. Pi, The advancing of selenium nanoparticles against infectious diseases, Front. Pharmacol. 12 (2021), https://doi.org/10.3389/fphar.2021.682284.
[92] S. Zheng, X. Li, Y. Zhang, Q. Xie, Y.-S. Wong, W. Zheng, T. Chen, PEG-nanolized ultrasmall selenium nanoparticles overcome drug resistance in hepatocellular carcinoma HepG2 cells through induction of mitochondria dysfunction, Int. J. Nanomed. 7 (2012) 3939–3949, https://doi.org/10.2147/IJN.S30940.
[93] X.-D. Shi, Y.-Q. Tian, J.-L. Wu, S.-Y. Wang, Synthesis, characterization, and biological activity of selenium nanoparticles conjugated with polysaccharides, Crit. Rev. Food Sci. Nutr. 61 (2021) 2225–2236, https://doi.org/10.1080/10408398.2020.1774497.
[94] R. Pérez-Tanoira, M. Fernández-Arias, C. Potel, R. Carballo-Fernández, S. Pérez-Castro, M. Boutinguiza, M. Górgolas, F. Lusquiños, J. Pou, Silver nanoparticles produced by laser ablation and Re-irradiation are effective preventing peri-implantitis multispecies biofilm formation, Int. J. Mol. Sci. 23 (2022), https://doi.org/10.3390/ijms231912027.
[95] V. Amendola, M. Meneghetti, Laser ablation synthesis in solution and size manipulation of noble metal nanoparticles, Phys. Chem. Chem. Phys. 11 (2009) 3805, https://doi.org/10.1039/b900654k.
[96] D. Fan, L. Li, Z. Li, Y. Zhang, X. Ma, L. Wu, H. Zhang, F. Guo, Biosynthesis of selenium nanoparticles and their protective, antioxidative effects in streptozotocin induced diabetic rats, Sci. Technol. Adv. Mater. 21 (2020) 505–514, https://doi.org/10.1080/14686996.2020.1788907.
[97] M.P. Rayman, The importance of selenium to human health, Lancet 356 (2000) 233–241, https://doi.org/10.1016/S0140-6736(00)02490-9.
[98] U. Schweizer, A.U. Bräuer, J. Köhrle, R. Nitsch, N.E. Savaskan, Selenium and brain function: a poorly recognized liaison, Brain Res Brain Res Rev 45 (2004) 164–178, https://doi.org/10.1016/j.brainresrev.2004.03.004.
[99] M.C. Kahya, M. Nazıroğlu, B. Çiğ, Selenium reduces mobile phone (900 MHz)-induced oxidative stress, mitochondrial function, and apoptosis in breast cancer cells, Biol. Trace Elem. Res. 160 (2014) 285–293, https://doi.org/10.1007/s12011-014-0032-6.
[100] H.J. Heusinkveld, T. Wahle, A. Campbell, R.H.S. Westerink, L. Tran, H. Johnston, V. Stone, F.R. Cassee, R.P.F. Schins, Neurodegenerative and neurological disorders by small inhaled particles, Neurotoxicology 56 (2016) 94–106, https://doi.org/10.1016/j.neuro.2016.07.007.
[101] C.M. Weekley, H.H. Harris, Which form is that? The importance of selenium speciation and metabolism in the prevention and treatment of disease, Chem. Soc. Rev. 42 (2013) 8870, https://doi.org/10.1039/c3cs60272a.
[102] M. Naziroğlu, New molecular mechanisms on the activation of TRPM2 channels by oxidative stress and ADP-ribose, Neurochem. Res. 32 (2007) 1990–2001, https://doi.org/10.1007/s11064-007-9386-x.
[103] T. Ishrat, K. Parveen, M.M. Khan, G. Khuwaja, M.B. Khan, S. Yousuf, A. Ahmad, P. Shrivastav, F. Islam, Selenium prevents cognitive decline and oxidative damage in rat model of streptozotocin-induced experimental dementia of Alzheimer's type, Brain Res. 1281 (2009) 117–127, https://doi.org/10.1016/j.brainres.2009.04.010.
[104] T. Yin, L. Yang, Y. Liu, X. Zhou, J. Sun, J. Liu, Sialic acid (SA)-modified selenium nanoparticles coated with a high blood-brain barrier permeability peptide-B6

peptide for potential use in Alzheimer's disease, Acta Biomater. 25 (2015) 172–183, https://doi.org/10.1016/j.actbio.2015.06.035.
[105] Z. Wang, Y. Wang, W. Li, F. Mao, Y. Sun, L. Huang, X. Li, Design, synthesis, and evaluation of multitarget-directed selenium-containing clioquinol derivatives for the treatment of Alzheimer's disease, ACS Chem. Neurosci. 5 (2014) 952–962, https://doi.org/10.1021/cn500119g.
[106] A. Vedagiri, S. Thangarajan, Mitigating effect of chrysin loaded solid lipid nanoparticles against Amyloid β25-35 induced oxidative stress in rat hippocampal region: an efficient formulation approach for Alzheimer's disease, Neuropeptides 58 (2016) 111–125, https://doi.org/10.1016/j.npep.2016.03.002.
[107] H. Balaban, M. Nazıroğlu, K. Demirci, İ.S. Övey, The protective role of selenium on scopolamine-induced memory impairment, oxidative stress, and apoptosis in aged rats: the involvement of TRPM2 and TRPV1 channels, Mol. Neurobiol. 54 (2017) 2852–2868, https://doi.org/10.1007/s12035-016-9835-0.
[108] K. Ogurtsova, J.D. da Rocha Fernandes, Y. Huang, U. Linnenkamp, L. Guariguata, N.H. Cho, D. Cavan, J.E. Shaw, L.E. Makaroff, IDF Diabetes Atlas: global estimates for the prevalence of diabetes for 2015 and 2040, Diabetes Res. Clin. Pract. 128 (2017) 40–50, https://doi.org/10.1016/j.diabres.2017.03.024.
[109] F. Yang, B. Li, X. Dong, W. Cui, P. Luo, The beneficial effects of zinc on diabetes-induced kidney damage in murine rodent model of type 1 diabetes mellitus, J. Trace Elem. Med. Biol. 42 (2017) 1–10, https://doi.org/10.1016/j.jtemb.2017.03.006.
[110] R. Gurbanov, M. Bilgin, F. Severcan, Restoring effect of selenium on the molecular content, structure and fluidity of diabetic rat kidney brush border cell membrane, Biochim. Biophys. Acta 1858 (2016) 845–854, https://doi.org/10.1016/j.bbamem.2016.02.001.
[111] T. Zhang, J. Gao, Z.-Y. Jin, X.-M. Xu, H.-Q. Chen, Protective effects of polysaccharides from Lilium lancifolium on streptozotocin-induced diabetic mice, Int. J. Biol. Macromol. 65 (2014) 436–440, https://doi.org/10.1016/j.ijbiomac.2014.01.063.
[112] A.A. Ahmed, J.S. Fedail, H.H. Musa, T.H. Musa, A.Z. Sifaldin, Gum Arabic supplementation improved antioxidant status and alters expression of oxidative stress gene in ovary of mice fed high fat diet, Middle East Fertil. Soc. J. 21 (2016) 101–108, https://doi.org/10.1016/j.mefs.2015.10.001.
[113] P. Sharma, A.B. Jha, R.S. Dubey, M. Pessarakli, Reactive oxygen species, oxidative damage, and antioxidative defense mechanism in plants under stressful conditions, J. Bot., Le (2012) 1–26, https://doi.org/10.1155/2012/217037, 2012.
[114] Y. Zhang, K.L. Ma, Y.X. Gong, G.H. Wang, Z.B. Hu, L. Liu, J. Lu, P.P. Chen, C.C. Lu, X.Z. Ruan, B.C. Liu, Platelet microparticles mediate glomerular endothelial injury in early diabetic nephropathy, J. Am. Soc. Nephrol. 29 (2018) 2671–2695, https://doi.org/10.1681/ASN.2018040368.
[115] R. Kakkar, J. Kalra, S. V Mantha, K. Prasad, Lipid peroxidation and activity of antioxidant enzymes in diabetic rats, Mol. Cell. Biochem. 151 (1995) 113–119, https://doi.org/10.1007/BF01322333.
[116] Q. Zhang, L. Chen, K. Guo, L. Zheng, B. Liu, W. Yu, C. Guo, Z. Liu, Y. Chen, Z. Tang, Effects of different selenium levels on gene expression of a subset of selenoproteins and antioxidative capacity in mice, Biol. Trace Elem. Res. 154 (2013) 255–261, https://doi.org/10.1007/s12011-013-9710-z.
[117] H.-W. Han, K.D. Patel, J.-H. Kwak, S.-K. Jun, T.-S. Jang, S.-H. Lee, J.C. Knowles, H.-W. Kim, H.-H. Lee, J.-H. Lee, Selenium nanoparticles as candidates for antibacterial substitutes and supplements against multidrug-resistant bacteria, Biomolecules 11 (2021), https://doi.org/10.3390/biom11071028.
[118] O.M. Guillin, C. Vindry, T. Ohlmann, L. Chavatte, Selenium, selenoproteins and viral infection, Nutrients 11 (2019), https://doi.org/10.3390/nu11092101.
[119] N.E. Eleraky, A. Allam, S.B. Hassan, M.M. Omar, Nanomedicine fight against antibacterial resistance: an overview of the recent pharmaceutical innovations, Pharmaceutics 12 (2020), https://doi.org/10.3390/pharmaceutics12020142.
[120] M. Vahdati, T. Tohidi Moghadam, Synthesis and characterization of selenium nanoparticles-lysozyme nanohybrid system with synergistic antibacterial properties, Sci. Rep. 10 (2020) 510, https://doi.org/10.1038/s41598-019-57333-7.
[121] J. Kopel, J. Fralick, T.W. Reid, The potential antiviral effects of selenium nanoparticles and coated surfaces, Antibiotics 11 (2022) 1683, https://doi.org/10.3390/antibiotics11121683.
[122] S.S. Martinez, Y. Huang, L. Acuna, E. Laverde, D. Trujillo, M.A. Barbieri, J. Tamargo, A. Campa, M.K. Baum, Role of selenium in viral infections with a major focus on SARS-CoV-2, Int. J. Mol. Sci. 23 (2021), https://doi.org/10.3390/ijms23010280.
[123] W. Chen, Z. Liu, Y. Zheng, B. Wei, J. Shi, B. Shao, D. Wang, Selenium donor restricts the intracellular growth of Mycobacterium tuberculosis through the induction of c-Jun-mediated both canonical autophagy and LC3-associated phagocytosis of alveolar macrophages, Microb. Pathog. 161 (2021) 105269, https://doi.org/10.1016/j.micpath.2021.105269.
[124] M.F. Salem, W.A. Abd-Elraoof, A.A. Tayel, F.M. Alzuaibr, O.M. Abonama, Antifungal application of biosynthesized selenium nanoparticles with pomegranate peels and nanochitosan as edible coatings for citrus green mold protection, J. Nanobiotechnol. 20 (2022) 182, https://doi.org/10.1186/s12951-022-01393-x.
[125] H. Mahmoudvand, M. Fasihi Harandi, M. Shakibaie, M.R. Aflatoonian, N. ZiaAli, M.S. Makki, S. Jahanbakhsh, Scolicidal effects of biogenic selenium nanoparticles against protoscolices of hydatid cysts, Int. J. Surg. 12 (2014) 399–403, https://doi.org/10.1016/j.ijsu.2014.03.017.
[126] A.A. Alkhudhayri, M.A. Dkhil, S. Al-Quraishy, Nanoselenium prevents eimeriosis-induced inflammation and regulates mucin gene expression in mice jejunum, Int. J. Nanomed. 13 (2018) 1993–2003, https://doi.org/10.2147/IJN.S162355.
[127] M. Pescuma, F. Aparicio, R.D. Zysler, E. Lima, C. Zapata, J.A. Marfetán, M.L. Vélez, O.F. Ordoñez, Biogenic selenium nanoparticles with antifungal activity against the wood-rotting fungus Oligoporus pelliculosus, Biotechnol Rep (Amst). 37 (2023) e00787, https://doi.org/10.1016/j.btre.2023.e00787.
[128] B.M. Köhler, J. Günther, D. Kaudewitz, H.-M. Lorenz, Current therapeutic options in the treatment of rheumatoid arthritis, J. Clin. Med. 8 (2019), https://doi.org/10.3390/jcm8070938.
[129] I. Rubinstein, G.L. Weinberg, Nanomedicines for chronic non-infectious arthritis: the clinician's perspective, Nanomedicine 8 (Suppl 1) (2012) S77–S82, https://doi.org/10.1016/j.nano.2012.05.004.
[130] D. Bobo, K.J. Robinson, J. Islam, K.J. Thurecht, S.R. Corrie, Nanoparticle-based medicines: a review of FDA-approved materials and clinical trials to date, Pharm. Res. (N. Y.) 33 (2016) 2373–2387, https://doi.org/10.1007/s11095-016-1958-5.
[131] G. Cao, NANOSTRUCTURES and NANOMATERIALS - Synthesis, Properties and Applications, Imperial College Press, London, 2004, https://doi.org/10.1142/9781860945960.
[132] S.-X. Ren, B. Zhan, Y. Lin, D.-S. Ma, H. Yan, Selenium nanoparticles dispersed in phytochemical exert anti-inflammatory activity by modulating catalase, GPx1, and COX-2 gene expression in a rheumatoid arthritis rat model, Med. Sci. Mon. Int. Med. J. Exp. Clin. Res. 25 (2019) 991–1000, https://doi.org/10.12659/MSM.912545.
[133] S. Di Meo, T.T. Reed, P. Venditti, V.M. Victor, Role of ROS and RNS sources in physiological and pathological conditions, Oxid. Med. Cell. Longev. (2016) 1245049, https://doi.org/10.1155/2016/1245049, 2016.
[134] N. Qamar, P. John, A. Bhatti, Toxicological and anti-rheumatic potential of trachyspermum ammi derived biogenic selenium nanoparticles in arthritic balb/c mice, Int. J. Nanomed. 15 (2020) 3497–3509, https://doi.org/10.2147/IJN.S243718.
[135] S. Ponist, M. Zloh, K. Bauerova, Impact of oxidative stress on inflammation in rheumatoid and adjuvant arthritis: damage to lipids, proteins, and enzymatic antioxidant defense in plasma and different tissues, in: Animal Models in Medicine and Biology, IntechOpen, 2020, https://doi.org/10.5772/intechopen.89480.
[136] H. Vunta, F. Davis, U.D. Palempalli, D. Bhat, R.J. Arner, J.T. Thompson, D.G. Peterson, C.C. Reddy, K.S. Prabhu, The anti-inflammatory effects of selenium are mediated through 15-deoxy-Delta12,14-prostaglandin J2 in macrophages, J. Biol. Chem. 282 (2007) 17964–17973, https://doi.org/10.1074/jbc.M703075200.
[137] H. Vunta, B.J. Belda, R.J. Arner, C. Channa Reddy, J.P. Vanden Heuvel, K. Sandeep Prabhu, Selenium attenuates pro-inflammatory gene expression in macrophages, Mol. Nutr. Food Res. 52 (2008) 1316–1323, https://doi.org/10.1002/mnfr.200700346.
[138] B. Sadikovic, K. Al-Romaih, J.A. Squire, M. Zielenska, Cause and consequences of genetic and epigenetic alterations in human cancer, Curr. Genom. 9 (2008) 394–408, https://doi.org/10.2174/138920208785699580.
[139] C. Wang, Y. Xia, S. Huo, D. Shou, Q. Mei, W. Tang, Y. Li, H. Liu, Y. Zhou, B. Zhu, Silencing of MEF2D by siRNA loaded selenium nanoparticles for ovarian cancer therapy, Int. J. Nanomed. 15 (2020) 9759–9770, https://doi.org/10.2147/IJN.S270441.
[140] A. Ullah, X. Yin, F. Wang, B. Xu, Z.A. Mirani, B. Xu, M.W.H. Chan, A. Ali, M. Usman, N. Ali, M. Naveed, Biosynthesis of selenium nanoparticles (via Bacillus subtilis BSN313), and their isolation, characterization, and bioactivities, Molecules 26 (2021), https://doi.org/10.3390/molecules26185559.
[141] S. Sonkaria, S.-H. Ahn, V. Khare, Nanotechnology and its impact on food and nutrition: a review, Recent Pat. Food, Nutr. Agric. 4 (2012) 8–18, https://doi.org/10.2174/2212798411204010008.
[142] T. Chen, Y.-S. Wong, W. Zheng, Y. Bai, L. Huang, Selenium nanoparticles fabricated in Undaria pinnatifida polysaccharide solutions induce mitochondria-mediated apoptosis in A375 human melanoma cells, Colloids Surf. B Biointerfaces 67 (2008) 26–31, https://doi.org/10.1016/j.colsurfb.2008.07.010.
[143] H. Luo, F. Wang, Y. Bai, T. Chen, W. Zheng, Selenium nanoparticles inhibit the growth of HeLa and MDA-MB-231 cells through induction of S phase arrest, Colloids Surf. B Biointerfaces 94 (2012) 304–308, https://doi.org/10.1016/j.colsurfb.2012.02.006.
[144] M.S. Ahmad, M.M. Yasser, E.N. Sholkamy, A.M. Ali, M.M. Mehanni, Anticancer activity of biostabilized selenium nanorods synthesized by Streptomyces bikiniensis strain Ess_amA-1, Int. J. Nanomed. 10 (2015) 3389–3401, https://doi.org/10.2147/IJN.S82707.
[145] J.S. Song, Y.S. Kim, D.K. Kim, S. Il Park, S.J. Jang, Global histone modification pattern associated with recurrence and disease-free survival in non-small cell lung cancer patients, Pathol. Int. 62 (2012) 182–190, https://doi.org/10.1111/j.1440-1827.2011.02776.x.
[146] C. Ramamurthy, K.S. Sampath, P. Arunkumar, M.S. Kumar, V. Sujatha, K. Premkumar, C. Thirunavukkarasu, Green synthesis and characterization of selenium nanoparticles and its augmented cytotoxicity with doxorubicin on cancer cells, Bioproc. Biosyst. Eng. 36 (2013) 1131–1139, https://doi.org/10.1007/s00449-012-0867-1.
[147] K.M.A. Hassanin, S.H. Abd El-Kawi, K.S. Hashem, The prospective protective effect of selenium nanoparticles against chromium-induced oxidative and cellular damage in rat thyroid, Int. J. Nanomed. 8 (2013) 1713–1720, https://doi.org/10.2147/IJN.S42736.
[148] W. Liu, X. Li, Y.-S. Wong, W. Zheng, Y. Zhang, W. Cao, T. Chen, Selenium nanoparticles as a carrier of 5-fluorouracil to achieve anticancer synergism, ACS Nano 6 (2012) 6578–6591, https://doi.org/10.1021/nn202452c.
[149] P. Mezhenny, S. Staroverov, A. Fomin, A. Volkov, I. Domnitsky, S. Kozlov, V. Laskavy, L. Dykman, Study of immunogenic properties of transmissible

gastroenteritis virus antigen conjugated to gold nanoparticles, J Biomed Photonics Eng 2 (2016) 040308, https://doi.org/10.18287/JBPE16.02.040308.
[150] S. Naidoo, A. Daniels, S. Habib, M. Singh, Poly-L-lysine-lactobionic acid-capped selenium nanoparticles for liver-targeted gene delivery, Int. J. Mol. Sci. 23 (2022), https://doi.org/10.3390/ijms23031492.
[151] F. Maiyo, M. Singh, Polymerized selenium nanoparticles for folate-receptor-targeted delivery of anti-luc-siRNA: potential for gene silencing, Biomedicines 8 (2020) 76, https://doi.org/10.3390/biomedicines8040076.
[152] F. Maiyo, M. Singh, Folate-targeted mRNA delivery using chitosan-functionalized selenium nanoparticles: potential in cancer immunotherapy, Pharmaceuticals 12 (2019), https://doi.org/10.3390/ph12040164.