Egyptian Journal of Animal Health

P-ISSN: 2735-4938 On Line-ISSN: 2735-4946
Journal homepage: https://ejah.journals.ekb.eg/

Article Review

Possible application of nano-selenium and the associated safety in the veterinary field: a summary overview

Dalia M. Azab [*]; Lamya A. Ateya [**] and Hemat S. EL-Sayed [***]

[*] Biochemistry Department (Pharmacology), Animal Health Research Institute, Benha -Branch, Agriculture Research Center (ARC), Egypt.

[**] Virology Department, Animal Health Research Institute, Benha-Branch, Agriculture Research Center (ARC), Egypt.

[***] Poultry Diseases Department Animal Health Research Institute, Benha-Branch, Agriculture Research Center (ARC), Egypt.

Received in 9/10/2024
Received in revised from 23/10/2024
Accepted in 24/11/2024

Keywords:

Antioxidant
Drug delivery
Green synthesis
Immunomodulator and selenium nanoparticles (SeNPs)

ABSTRACT

Selenium is a crucial micronutrient for maintaining animal health, playing a vital role in combating bacterial, viral, fungal, and parasitic diseases. However, concerns have been raised about its toxicity. Selenium nanoparticles (SeNPs) present a solution to this issue, offering higher biocompatibility and bioavailability, and lower toxicity compared to bulk selenium. The synthesis of selenium nanoparticles can be achieved through three primary methods: physical, chemical, and biological. Among these, biological methods have garnered interest due to their superior compatibility and reduced toxicity compared to the other two methods. This Review summarizes the synthetic methods for selenium and provides an overview of the biological activity of selenium nanoparticles against bacteria, viruses, fungi, and parasites. This review also discusses the immunomodulatory and antioxidant activities of selenium nanoparticles in various animal models as well as the safety and toxicity of selenium nanoparticles.

Review methodology

Various databases have been used to collect original articles on selenium nanoparticle synthesis, biomedical applications, and experimental studies using different animal models. The antioxidant properties, safety, and possible toxicities were also considered. Databases included the Web of Science, PubMed, Academia, and Google Scholar. The review includes research results from more than three decades.

Corresponding author: Dalia M. Azab , Biochemistry Department (Pharmacology), Animal Health Research Institute, Benha-Branch, Agriculture Research Center (ARC), Egypt.
Email address: drdaliamahfouz@yahoo.con
DOI: 10.21608/ejah.2025.399709

INTRODUCTION

Selenium (Se) is a crucial element in nature. Its deficiency can lead to cardiovascular disorders, liver dysfunction, weakened immunity, and diseases such as Kashin–Beck disease **(Tan et al. 2010).** Selenium exists in two forms: inorganic (selenite and selenate) and organic (selenomethionine and selenocysteine). The organic form is vital for functions related to reproduction, DNA synthesis, thyroid hormone metabolism, and protection against infection and oxidative damage **(Zhu et al. 2019).**

Selenium supplementation can be beneficial in preventing viral diseases and alleviating immune disorders. However, its use has limited toxicity at high doses. Interestingly, selenium nanoparticles (SeNPs) exhibit lower cytotoxicity than other forms such as organic and inorganic selenium (Zhang et al., 2008; Zhang et al., 2001). Moreover, compared to other oxidation states (Se^{+IV} and Se^{+VI}), SeNPs demonstrate excellent bioavailability **(Torres et al. 2012).** The bioavailability of nanoparticles improves due to their resistance to unfavorable pH values, digestion, and enzymatic cleavage **(Yao et al. 2015).** This has led to increased interest in the use of selenium nanoparticles in biomedical research. In many clinical studies, selenium nanoparticles have been used as alternatives to traditional forms of selenium. They confirmed a decrease in cytotoxicity with increasing size of selenium nanoparticles (**Skalickova et al. 2017).** This nanoform of selenium is biologically highly active **(Zhang et al. 2005)** has a stronger detoxifying effect on heavy metal exposure **(Ikemoto et al. 2004),** and can prevent DNA oxidation (**Huang et al. 2003).**

The focus of this review is on studies on the synthesis of selenium nanoparticles using various chemical and biological methods. In addition, we discuss the biological applications of SeNPs in the animal field and investigate the antioxidant properties and safety issues related to the use of selenium nanoparticles in animal models.

Synthesis of selenium nanoparticles

There have been various methods for producing selenium nanoparticles, including physical methods, Chemical and green synthesis using microorganisms or plant extracts.

Physical synthesis

Physical methods use a top-down approach in which larger molecules are either crushed or ground into smaller ones (Harris et al., 2019). Physical methods include hydrothermal treatment, irradiation, and pulsed laser ablation **(Dhawan et al. 2021).** The deposition method, or pulsed laser ablation (PLA), is a well-known physical method for synthesizing selenium nanoparticles. This method controls the size of nanoclusters using laser parameters, such as wavelength and pulse duration **(Marine et al. 2000).**

Chemical synthesis

In chemical methods, the synthesis is bottom-up. In this method, selenium nanoparticles were produced by reducing a selenic acid solution with ascorbic acid, in the presence of polysaccharides. Polysaccharides influence the formation and stabilization of Se nanoparticles **(S. Y. Zhang et al. 2004).** Chemically produced selenium nanoparticles have several advantages such as biocompatibility, biodegradability, and nontoxicity **(Bezerra et al. 2008; Saini et al. 2015).** These advantages allow selenium nanoparticles to be used in nutritional and biomedical applications as well as in drug delivery systems (**Rinaudo, 2006).**

Biological synthesis (Green synthesis)

A green synthesis approach for selenium nanoparticles has recently attracted attention. It offers improved biocompatibility and stability compared with chemical methods that require reducing and stabilizing agents that can be toxic and hamper their use in biological systems **(Bisht et al. 2022).**

Selenium nanoparticles have been synthesized using a variety of organisms, including bacteria, fungi, algae, and plant extracts. These organisms convert toxic metal ions into nontoxic ones **(Bhainsa & D'Souza, 2006; Song**

& Kim, 2009). Thus, they act as both bio-reductants and stabilizers for SeNP nanoparticles.

Recent studies have highlighted the advantages of green synthesis of SeNPs using plant extracts, ease of synthesis, and feasibility for biological applications (Ikram **et al. 2021; Korde et al. 2020).** Therefore, there is an enormous body of literature on the biosynthesis of SeNPs **(Shoeibi & Mashreghi, 2017; Tugarova et al. 2020; Wang et al. 2019; Xu et al. 2019).**

Antibacterial

Selenium nanoparticles have been found to exhibit significant antibacterial activity against a variety of bacteria. Studies have confirmed their role in inhibiting the growth of E. coli, Streptococcus *pyogenes, P. aeruginosa, and S. aureus*. For instance, selenium coatings on polycarbonate medical devices significantly inhibited S. aureus growth by 27% after 72 hours compared with an uncoated polycarbonate surface **(Wang & Webster, 2012).** Green synthesized selenium nanoparticles in the 100–150 nm size range showed potent inhibition of five microbes, including *S. aureus* and *Proteus sp. E. coli, Klebsiella sp., Pseudomonas sp.* **(Menon et al. 2019).**

Other studies have also explored the antibacterial effect of Se nanoparticles. **Stevanović et al. (2015)** showed that SeNPs exhibited significant antibacterial activity against gram-positive bacteria, *S. aureus* and *S. epidermidis*.

Alagawany et al. (2021) tested chemically synthesized selenium nanoparticles against three gram-negative bacteria (*E. coli, P. aeruginosa, and S. enterica*) and three positive strains (*L. monocytogenes, B. cereus,* and *S. aureus*). They observed the maximum inhibition zones in three gram-positive bacterial strains. In same context, **Filipovi et al. (2021)** investigated the antimicrobial activity of SeNPs on eight standard bacterial strains. They proved that SeNPs provide better antimicrobial activity against Gram-positive bacteria.

SeNPs also show anti-biofilm activity against pathogens such as *Bacillus cereus, Enterococcus faecalis, Staphylococcus aureus, and Escherichia coli* **(Khiralla & El-Deeb, 2015).** In same context, SeNPs have been proposed as an alternative to eradicate bacterial biofilms, reducing the possibility of bacterial antibiotic resistance **(Hernández-Díaz et al. 2021).** Selenium nanoparticles were also tested against antibiotic-resistant bacteria, multidrug-resistant *E. coli* (MDR), and methicillin-resistant *S. aureus* (MRSA), with SeNP concentrations of□25 ppm effectively inhibiting the growth of antibiotic-resistant bacteria **(Geoffrion et al. 2020).**

Antifungal activity

Selenium nanoparticles show broad antifungal activity against various fungi, suggesting that they are good weapons against fungal infectious diseases (**W Lin et al. 2021**). In a recent study, chemically synthesized selenium nanoparticles were tested against animal pathogenic Candida strains using the disk diffusion method. Chemically synthesized selenium nanoparticles (Che-SeNPs) demonstrated satisfactory antifungal activity against all tested fungal strains, with concentrations ranging from 50 to 800 μg/mL. Among the strains tested, C. albicans was found to be the most sensitive to Che-SeNP **(Alagawany et al. 2021).**

Moreover, **Shakibaie et al. (2015**) showed that Se NPs exerted a potent inhibitory effect on Aspergillus fumigatus and Candida albicans. In the context of Candida albicans biofilms, a study investigated the mechanism by which Se NPs inhibit Candida albicans. Selenium nanoparticles penetrate pathogens and destroy the cell structure by substitution with sulfur (**Guisbiers et al. 2017).**

Anti parasitic activity

Various studies have highlighted the role of SeNPs in controlling several parasites such as leishmania, coccidia, intestinal schistosomiasis, and Toxoplasma gondii **(Beheshti et al. 2013; Dkhil et al. 2019; Alkhudhayri et al. 2020 and Shakibaie et al. 2020).** These findings suggest that SeNPs could be used as dietary supplements with strong antiparasitic effects (**Lin et al. 2021).**

Anti-aflatoxin

However, little research has been conducted on the alleviating effects of selenium nanoparticles on aflatoxicosis. A recent study has shown promising results in using selenium nanoparticles to counteract the harmful effects of aflatoxicosis in male albino rats. The study found that a higher dosage of Se-NPs (0.5 mg/kg) was more effective in eliminating aflatoxin B1 from the liver tissues of the affected rats compared to a lower dosage (0.3 mg/kg) **(Hassan et al. 2020).**

Antiviral

Research has shown that selenium is effective against a number of viruses, including influenza virus and hepatitis C virus **(Beck et al. 1995; Li & Beck, 2007; Verma et al. 2008; Stone et al. 2010; Himoto et al. 2011 and Wang et al. 2012)**

As for influenza viruses, selenium nanoparticles showed antiviral activity against influenza viruses. SeNPs inhibit H1N1-induced apoptosis in MDCK cells **(Y. Li et al. 2018).** Moreover, it has been found that it inhibits ROS-mediated p53 signaling pathways in lung tissue (**Wang et al. 2020).** In contrast, SeNPs did not significantly inhibit H9N2 infection **(Hossein et al. 2015).**

Recently, few studies have examined the role of NanoSe in COVID-19. This is due to the proven effect of selenium intake in the treatment of COVID-19 **(Moghaddam et al. 2020).** A significant disinfection activity of 87.5% against SARS-CoV-2 coronavirus was observed using SeNP-printed polyester fabric (**Elmaaty et al. 2022).**

While Selenium has been found to be effective against a variety of viruses, its toxicity raises significant concerns. This makes nano-selenium a preferred choice as an antiviral agent due to its lower toxicity compared to bulk selenium. The median lethal dose (LD50) of NanoSe in mice is less than that of organic selenium and selenite **(Wang et al. 2007; Zhang et al. 2001)**. The low toxicity and biocompatibility of nano-selenium make it a promising candidate for antiviral applications. For instance, surface-modified SeNPs containing oseltamivir (OTV) have shown potential as effective anti-H1N1 antiviral drugs. They interfere with the H1N1 influenza virus in host cells by inhibiting the activity of hemagglutinin and neuraminidase, and their superior antiviral properties help limit drug resistance **(Li et al. 2017).** Furthermore, Se-NPs are used as drug delivery systems against EV71 virus infections and provide opportunities to control EV71 infections **(Lin et al. 2020).**

Immunomodulatory effects

Immunity is severely compromised by the lack of selenium in the diet. Selenium deficiency can weaken the immune response of calves infected with foreign pathogens. In contrast, selenium supplementation increases IgG and IgM levels in calves and supports their immunity **(Reffett et al. 1988**).

Recent studies have explored the impact of adding selenium nanoparticles to the diet and its potential effects on humeral immunity in response to vaccination in broilers. It was found that dietary supplementation with selenium nanoparticles at concentrations of 0.15 ppm positively affected humeral immunity in broilers, with the birds showing HI titers compared to those in the Newcastle control-vaccinated group (**Azab et al. 2019**). Moreover, supplementing the diet with SeNPs at a dosage of 0.1 mg/dose significantly increased the expression of interleukin 2 (IL2), interleukin 6 (IL6), and interferon (IFN) in blood cells, which was accompanied by a significantly high antibody titer against HPAI H5N1 **(Yehia et al. 2022).** Similarly, glycine nano-selenium was found to enhance the effectiveness of the H9N2 avian influenza vaccine by significantly increasing immunoglobin indices and mRNA levels of certain interleukins in the liver, lungs and spleen **(Ren et al. 2022**).

Selenium nanoparticles have been shown to modulate both innate and adaptive immunity, suggesting their potential use in treating various immunological responses associated with infectious diseases. For instance, dietary chitosan-selenium nanoparticles were found to boost immunity against Aeromonas hydrophila infection in zebrafish **(Xia et al. 2019).** In a similar vein, another study demonstrated that Se NPs enhances intracellular Mtb-killing efficiency by promoting host antibacterial immunity and inducing apoptosis, autophagy, and antibacterial M1 polarization of host cells **(Pi et al. 2020).**

Vaccines adjuvants

Selenium nanoparticles have recently attracted attention and have been used as adjuvants in vaccines. Few studies on this topic have investigated their possible immune-boosting effects. Selenium nanoparticles serve as novel adjuvants to enhance the immune response against killed whole-cell *Vibrio cholerae* in a mouse cholera model. The addition of selenium nanoparticles to this vaccine elicited strong protective immune responses in a mouse model **(Raahati et al. 2020).**

Ranjbariyan et al. (2023) added synthetic SeNPs as a co-adjuvant to the vaccine formulation against MRSA infection. The SeNPs showed a significant increase in cellular and humoral immunity. Higher levels of total IgG and increased levels of cytokines were observed. This suggests that selenium nanoparticles, as good co-adjuvants, enhance the immune response against methicillin-resistant *Staphylococcus aureus*.

Selenium nanoadjuvants have been used in SARS-CoV-2 vaccines. Se nano-adjuvant-based vaccines induce the activation of innate immune cells. Nanoadjuvant-based Se vaccines can induce Th1-dependent immunity and superior antigen-specific neutralizing antibodies with a high titer and potency to fight pseudovirus infections. Selenium nano-adjuvants are universal drug candidates that can boost the immune response against serious diseases **(Lai et al. 2023).**

Drug delivery

Se NPs is considered a promising option for drug delivery. They can carry drugs at high concentrations, significantly enhancing their effects **(Guan et al. 2018)** and increasing drug potency (**Chen et al. 2008).** In line with this, an injectable Se NP nanosystem has been developed to load anticancer drugs like sorafenib **(Zheng et al. 2019**) and boost solubility of oridonin **(Pi et al. 2017).**

Selenium-lipid nanocarriers loaded with ciprofloxacin have proven to be effective drug delivery systems for preventing pulmonary infections in interstitial lung diseases **(Liu et al. 2019).** They also improve isoniazid intracellular Mtb killing efficiency and aid in intracellular pathogen clearance **(Pi et al. 2020).**

Growth performance and body weight gain

The high surface area to volume ratio of selenium nanoparticles provides a large surface area for interaction with mucosal tissues and cells. This property improves their absorption into the mucosal surface, thereby extending the residence time of these particles in the intestine **(Kassim et al. 2022).** Thus, selenium nanoparticles showed improved growth performance and feed conversion ratio compared with the bulk forms of selenium. This has been demonstrated in various animal models; for example, poultry supplemented with nano-selenium had a higher body weight and a lower feed conversion rate ($P<0.05$) than poultry fed inorganic or organic selenium **(A.A. Abdel-Wareth et al. 2022; Ahmadi et al. 2018; Jayanthi et al. 2018; Azab et al. 2019; Zhou & Wang, 2011).**

In fish, Se nanoparticles are required for the optimal growth of striped catfish (Pangasianodon hypophthalmus). Based on the regression analysis of the FCR data, Se nanoparticles are recommended at a level of 1.02 to1.11 mg/kg diet **(El-Sharawy et al. 2021).**

Furthermore, fish fed dietary Se nanoparticles at 1 mg/kg daily, every other day showed improved growth rates and feeding efficiencies **(Abd El-Kader et al. 2020).**

Studies have shown that the performance of growing rabbits can be significantly improved by supplementing their diet with 0.3 mg nano-Se/kg **(Abd Allah et al. 2020; Qin et al. 2016),** and 25 and 50 mg nano-selenium/kg **(Sheiha et al. 2020).** Similarly, the inclusion of Che-SeNP in rabbit diets has been found to significantly enhance feed intake and feed conversion ratio **(Abdel-Wareth et al. 2019; Sheiha et al. 2020).**

In the case of ruminants such as goats and lambs, supplementation with Se nanoparticles has been observed to have a positive impact on body weight and average body weight gain, as demonstrated in studies by **Shi et al. (2011) and Yaghmaie et al. (2017).**

Antioxidant activity of selenium nanoparticles

Various abiotic stresses can induce the overproduction of toxic reactive oxygen species (ROS), leading to the destruction of vital nutrients such as carbohydrates, proteins, and lipids, and consequently causing a range of diseases **(Kumar et al. 2020).** The cellular and tissue-level benefits of selenium nanoparticles have piqued the interest of researchers globally due to their biomedical applications. They also play a crucial role in reducing free radical concentrations, thereby preventing oxidative DNA damage under both in vivo and in vitro conditions (**Battin et al. 2011**). This review outlines the impact of nano-selenium on antioxidant levels and lipid profiles across various animal models.

Rabbits.

El-Badry et al. (2019) found that the use of nanoselenium in rabbits significantly enhanced the total antioxidant capacity in their blood and mitigated the negative effects of heat stress by lowering the levels of blood malondialdehyde. Similarly, **Sheiha et al. (2020)** observed that New Zealand rabbits subjected to heat stress for 56 days showed marked improvements when fed a diet enriched with biologically synthesized nano-selenium at feeding rates of 25 or 50 mg/kg (50–400 nm). The selenium nanoparticles (SeNPs) led to a reduction in glutathione and catalase activities compared to the heat stress group. Furthermore, both nitric oxide and malondialdehyde levels saw a significant decrease in the groups treated with selenium nanoparticles compared to other groups.

Broilers

Boostani et al. (2015) found that broilers supplemented with 0.3 mg/kg of nano selenium showed a significant increase in the levels of reduced glutathione and the activity of glutathione peroxidase (GSH-Px), and a decrease in malondialdehyde levels compared to both controls and stressed birds. Similarly, **El-Deep et al. (2017)** observed that poultry consuming a diet with nano selenium (0.2–0.3 mg/kg) showed a significant improvement in serum-reduced glutathione (GSH) activity.

Shirsat et al. (2016) supplemented chickens under oxidative stress with biogenic selenium nanoparticles (100 nm) for 42 days along with enrofloxacin. The selenium nanoparticles (SeNPs) had beneficial effects on cellular and humoral immune response activities, and there was an evident increase in enzymatic and non-enzymatic antioxidants after reduced EFX treatment.

Di-(2-ethylhexyl) phthalate (DEHP), a common artificial pollutant found in the environment, can cause biological damage to various organs through oxidative stress, enhancing the degree of oxidative damage and apoptosis in chicken liver cells. However, adding 1 mg/kg of nano-selenium to the feed reversed these changes. Experimental results indicated that nano-selenium counteracts the toxic effects of DEHP via the PI3K/AKT pathway **(Li et al. 2021).**

Quails

Alagawany et al. (2021) reported that in quail, groups fed a diet supplemented with 0.4 g/kg of selenium chemical nanoparticles during the fattening period (15 weeks of age) experienced a significant improvement in performance, lipid profile, antioxidant indices and immunity. and a reduction in intestinal pathogens.

Goats

(Shi et al. 2011) showed improvements in the antioxidant status of male goats fed SeNPs compared with those fed selenium yeast and sodium selenite. Elevated levels of serum superoxide dismutase, catalase (CAT) and glutathione peroxidase (GSH-Px).

Pigs

A previous study found that feeding selenium nanoparticles (30-70 nm) at a rate of 0.5 mg/kg over a period of 25 days led to an increase in the levels of superoxide dismutase, catalase, immunoglobulin G, and immunoglobulin A, and a decrease in malondialdehyde in both serum and liver **(Liu et al. 2022) .**

Rats

Amin et al. (2017) found that selenium nanoparticles can protect against liver damage caused by an overdose of paracetamol. This protection is achieved through the enhancement of liver function and oxidative stress mediated by catalase, SOD, and GSH, and a reduction in hepatic DNA fragmentation, a marker of cell death in rats. In a another study, **Kokila et al. (2017)** highlighted the antioxidant properties of selenium nanoparticles. It's worth noting that the shape and size of nanoparticles can significantly influence these properties. For instance, hollow spherical selenium nanoparticles have been shown to exhibit antioxidant properties (**Wang et al. 2007).** Therefore, plant-derived selenium nanoparticles are more effective in preventing ROS-mediated diseases caused by oxidative stress.

Donkeys

The impact of selenium nanoparticles on heat shock proteins (HSPs) and the gene expression of HSP90, which are additional indicators of oxidative stress, was examined. Enhanced oxygen metabolism leads to the production of reactive oxygen species (ROS), and intense training in trotting horses can result in oxidative stress, ROS generation, and subsequent damage to lipids, proteins, and DNA. Besides adaptive changes in protective enzymes like SOD, catalase, and GPx, oxidative stress in cells is known to boost the production of stress proteins or HSPs. The expression of HSPs is a defensive mechanism against disturbances in cellular homeostasis and integrity during physical activity. A study was conducted on the effect of orally administering selenium nanoparticles (0.5 mg kg − 1) for 10 days on the gene expression of HSP90 during intense training in donkeys **(Kinnunen et al. 2005; Kojouri et al. 2013).**

Kojouri & Sharifi. (2013) investigated the influence of selenium nanoparticles on blood urea nitrogen in donkeys. High concentrations of urea are known to induce oxidative stress and DNA damage in cells. The study revealed that oral administration of selenium nanoparticles led to changes in blood urea nitrogen, creatinine, and total protein during intense exercise in donkeys, significantly increasing the serum selenium concentration after supplementation with selenium nanoparticles. The creatinine concentration in both the experimental and control groups significantly increased at 2 hours post-exercise rest and rapidly decreased in the experimental group after 72 hours of post-exercise rest. A similar pattern was observed with changes in blood urea nitrogen in the control group; its concentration significantly increased at 2 hours of rest post-exercise compared to the group dosed with selenium nanoparticles. These findings may elucidate the positive effects of dietary supplementation with selenium nanoparticles on serum changes in blood urea nitrogen levels and blood creatinine in response to intensive training of donkeys. The beneficial effects of selenium nanoparticles could be attributed to the integration of selenium into proteins such as selenocysteine and its protective role against oxidative tissue damage.

Fish

Li et al. (2023) suggested that Nano-Se has a protective effect against gut damage caused by heat stress in rainbow trout. This is achieved by enhancing the activity of antioxidant enzymes (catalase, GPX, thioredoxins (TRX)), promoting protein repair, reducing inflammatory responses, and restoring the composition of the intestinal microbiota. In a similar vein, **Sun et al. (2022)** showed that 5.0 µg/mL SeNPs could potentially serve as hepatocyte-protective therapeutic agents. They found that these nanoparticles synergistically boost the expression of GSH-Px and SOD activity, thereby protecting hepatocytes from heat stress in rainbow trout.

Toxicity and **safety of selenium nanoparticles:**

Selenium nanoparticles have recently garnered significant interest due to their lower toxicity compared to dissolved ionic selenium species **(Ikram et al. 2021).** The toxicity of these nanoparticles can be further reduced through green synthesis or modification. While numerous animal studies have been conducted to assess the toxicity of selenium nanoparticles, our understanding of their toxicological effects remains limited **(Bisht et al. 2022).** For instance, in vivo toxicity studies based on LD50 data have shown that the toxicity of selenium nanoparticles is approximately four to six times lower than that of SeMet, Se-Met, and SeCys (**Wang et al. 2007, Zhang et al. 2005; Zhang et al. 2008).** The higher toxicity of selenite, SeCys2, and SeO2 is attributed to their ability to initiate the oxidation of thiol groups in proteins **(Kim et al. 2003),** which can disrupt the activity of essential enzymes containing sulfhydryl groups. In comparison to selenite, Nano-Se has proven to be superior as it significantly increases hepatic glutathione peroxidase levels, reduces the production of malondialdehyde (a product of lipid peroxidation), and enhances the activity of antioxidant liver enzymes such as superoxide dismutase and catalase **(Zhang et al. 2005).**

Nanoselenium, when compared to sodium selenite, is less toxic and more biocompatible, exhibiting a range of beneficial properties such as catalytic performance, adsorption strength, surface activity, chemical stability, and high antioxidant activity **(Boostani et al. 2015; Skalickova et al. 2017).** Furthermore, the majority of studies comparing the toxicity of Se and nano-selenium concur with the lower toxicity of nano-selenium. In same context, **Qin et al. (2016)** discovered that a low dose of nano-selenium at a dose of 0.3 mg/kg body weight administered over a 48-day period in rabbits did not have any harmful effects and did not significantly alter blood biochemistry or liver enzyme activity. Moreover, **Hosnedlova et al. (2018)** noted that comprehensive toxicological studies demonstrated that 20-60 nm nano-selenium and Se-methionine in supranational amounts (30 and 70 µg Se/kg bw) reduced Se accumulation in whole blood, liver, and kidneys in a dose-dependent manner compared to controls. However, at diet-related Se concentrations (1000 mg Se/kg body weight), no improvement in bioaccumulation in blood and tissue was observed with nano-selenium, unlike with the Se-methionine form.

Abbas, (2021) pointed out that various animal species exhibit different responses to the effects of selenium and selenium nanoparticles. Given the sensitivity of these species to water pollutants, the toxicity of nanoparticles has been primarily studied in aquaculture. The toxicity of Se nanoparticles in aquaculture is well-documented and validated in recent research, suggesting that nanoforms of Se are notably less toxic than inorganic Se salts. **Dawood et al. (2021)** noted that selenium nanoparticles can accumulate in the environment and be ingested by fish, leading to significant bioaccumulation. However, controlled studies have also shown that nano-selenium can enhance the productivity of aquatic animals and improve their health. Similar to mammals, the toxicological effects in fish are also dependent on the dose, chemistry of the nanoparticles, and duration of exposure.

Mohammadinejad et al. (2015) emphasized the need for extensive research to devise less toxic and cost-effective synthetic methods, and to comprehend the role of nanoselenium in cancer therapy, chemotherapy, and radiotherapy to modulate their efficiency and cytotoxicity. Bionic or green-synthesized and modified nanoparticles have been reported to enhance health effects in animal models and reduce toxicity, owing to the unique properties of bionic selenium. Biogenic nano-selenium holds potential for use as an anti-TB and antiviral agent, as well as a drug delivery system. The toxicity of nanoselenium is influenced by several interrelated parameters such as nanoparticle size, nanoselenium chemistry, dose, and exposure time, which collectively affect the biological response of the organism. In a related study, **Mal et al. (2017)** examined the toxicity of biogenic nanoselenium formed by anaerobic granular sludge biofilms on zebrafish embryos in comparison with selenite and chemogenic nanoselenium. The biogenic nano-Se exhibited an LC50 value of 1.77 mgL−1, making it 3.2 times less toxic than selenite and 10 times less toxic to zebrafish embryos. Nano -Se stabilized with bovine serum albumin was found to be less toxic than chemogenic. In this context, biogenic methods offer greater advantages over chemical reduction methods due to their higher biocompatibility and lower cytotoxicity. Therefore, they are considered promising therapeutic agents for cancer treatment and antioxidant and antimicrobial applications (**Bisht et al. 2022).**

However, there is limited literature on the interaction of nanoselenium with the immune system, gastrointestinal tract, bioaccumulation in muscle, and other indirect targets of selenium. **Jia et al. (2005)** conducted a study on the sub-chronic toxicity of different forms of Se in Sprague-Dawley rats (both sexes). The rats were fed diets containing varying concentrations of individual compounds (0, 2, 3, 4, and 5 mg kg^{-1} Se) for a duration of 13 weeks. Significant abnormal changes were observed in body weight, hematology, clinical chemistry, relative organ weights, and histopathological parameters at Se doses of 4 and 5 mg kg^{-1}. The toxicological evaluation of SeNPs has primarily focused on the performance of the antioxidant system in terms of body weight and bioaccumulation in the liver, kidneys, and heart.

Due to its large surface area and small size, nanoselenium appears to be more reactive and exhibits better biodistribution in organisms compared to other forms of selenium. Rats that ingested 0.5, 1.5, 3.0 and 5.0 mg Se/kg (sublethal doses of nanoselenium) for 28 days with a size of 100 nm showed damage to the liver parenchyma and intestinal epithelium and reduced ALT activity (**Urbankova et al. 2021).**

The toxicity of selenium nanoparticles has been examined in various animal models. **Han et al. (2021)** studied the effects of sublethal doses of nano-selenium (100 nm) at doses of 0.3 mg/kg diet during a 30-day treatment in lactating dairy cows, which resulted in increased plasma Se and GPx levels and decreased mRNA expression levels of several enzymes and selenoproteins. **Li et al. (2021)** found that sheep taking 5 mg nanoselenium/kg bw for 30 days exhibited changes in various blood parameters and immune markers, with the nano-selenium group (40 nm) showing lower values than the control. **Xun et al. (2012)** reported changes in rumen chemistry when sheep were fed selenium nanoparticles at 4 mg/kg b.w. for 25 days.

Gangadoo et al. (2020) found that broilers fed inorganic selenium at various doses for 29 days showed lower bioavailability of selenium in certain tissues and increased accumulation in detoxification organs when compared to organic selenium.

Li et al. (2008) discovered that medaka fish (Oryzias latipes) exposed to nano-selenium for 10 days at a dose of 100 µg Se L^{-1} showed greater toxicity due to hyperaccumulation compared to those exposed to the same amount of Na_2SeO_3.

Gallego-Gallegos et al. (2013) conducted a study on the toxicity of nano-selenium using a 10-day exposure to aquatic and dietary larvae of Chironomus dilutus. They found that even the lowest concentrations of Se^0 and nano-selenium tested resulted in selenium bioaccumulation, particularly as SeMet. Inhibition of larval growth was also observed at higher concentrations due to dietary and aquatic exposure. However, these studies primarily used chemically produced nanoparticles. Recent research indicates that the toxicity of selenium is dependent on its method of production, with biogenic nano-selenium being less toxic than chemogenic selenium. For instance, **Khiralla and El-Deeb (2015)** found no significant toxicity of nano-selenium biosynthesized by B. licheniformis when tested using Artemia salina larvae as a model organism in the toxicity assessment of nanoparticles. Similarly, **Rajabi et al. (2015**) observed no toxicity in Artemia larvae exposed to nano-selenium up to 100 $\mu g mL^{-1}$.

Conclusion and future prospects

Selenium is a vital trace mineral with many antimicrobial biological activities; however, its use to combat microbes has been restricted owing to toxicity concerns. Selenium nanoparticles are predominantly biologically synthesized. Thus, nano-selenium is an excellent option for overcoming this limitation. Additionally, they are both bioavailable and biocompatible. This review highlights the importance of selenium nanoparticles in fighting many types of bacterial, viral, fungal, parasitic, and animal infections. It also plays a role in increasing body weight and enhancing antioxidant parameters in various animal models. It is also used as a drug delivery agent, vaccine adjuvant, and immunomodulatory. Toxicity issues related to selenium nanoparticles are also discussed in this review. Extensive research is needed in the near future to develop synthetic methods to obtain more biocompatible and less toxic selenium nanoparticles. In addition, the urgent need for Further clinical studies using animal models are required to investigate the toxicological effects of selenium nanoparticles.

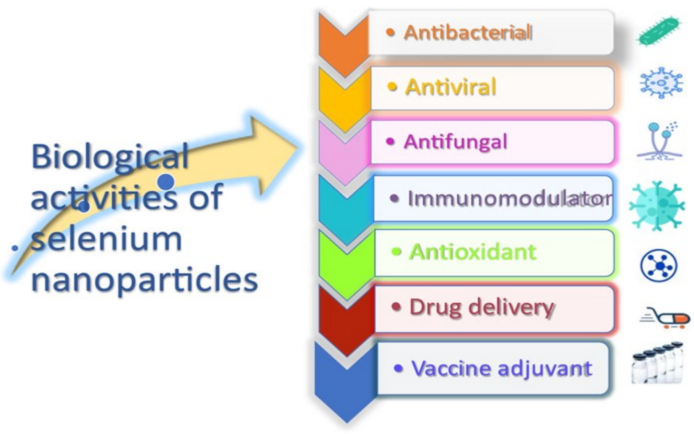

Figure 1.The graphic shows the various biomedical applications of selenium nanoparticles in the veterinary field

Figure 2. The graphic showed the antioxidant abilities of selenium nanoparticles in different animal models

REFERENCES

Abbas WT. 2021. Advantages and prospective challenges of nanotechnology applications in fish cultures: a comparative review. In Environmental Science and Pollution Research (Vol. 28, Issue 7). https://doi.org/10.1007/s11356-020-12166-0

Abd Allah DA, Tawfeek MI, El Kerdawy D. A, Rashwan A. 2020. IMPACT OF DIETARY SUPPLEMENTATION WITH NANO AND ORGANIC SELENIUM WITHOUT OR WITH VITAMIN E ON GROWTH PERFORMANCE AND SELENIUM METABOLISM IN GROWING RABBITS. In J. Product. & Dev (Vol. 25, Issue 3).

Abd El-Kader MF, Fath El-Bab AF, Shoukry M, Abdel-Warith AWA, Younis EM, Moustafa EM, El-Sawy HB, Ahmed HA, Van Doan H, Dawood MAO. 2020. Evaluating the possible feeding strategies of selenium nanoparticles on the growth rate and wellbeing of European seabass (Dicentrarchus labrax). Aquaculture Reports, 18. https://doi.org/10.1016/j.aqrep.2020.100539

Abdel-Wareth AAA, Ahmed AE, Hassan HA, Abd El-Sadek MS, Ghazalah AA, Lohakare J. 2019. Nutritional impact of nano -selenium, garlic oil, and their combination on growth and reproductive performance of male Californian rabbits. Animal Feed Science and Technology, 249, 37–45. https://doi.org/10.1016/j.anifeedsci.2019.01.016

Abdel-Wareth AA, Elkhateeb FS, Ghazalah A, Abdel-Wareth A. 2022. Effect of selenium sources on growth performance, carcass criteria and physical meat quality of broiler chickens. SVU-International Journal of Agricultural Sciences, 4(4), 207–217. https://doi.org/10.21608/svuijas.2022.186986.1265

Ahmadi M, Ahmadian A, Seidavi AR. 2018. Effect of different levels of nano-selenium on performance, blood parameters, immunity and carcass characteristics of broiler chickens. Poultry Science Journal, 6(1): 99–108. https://doi.org/10.22069/psj.2018.13815.1276

Alagawany M, Qattan SYA, Attia YA, El-Saadony MT, Elnesr SS, Mahmoud MA, Madkour M, Abd El-Hack ME, Reda FM. 2021. Use of chemical nano-selenium as an antibacterial and antifungal agent in quail diets and its effect on growth, carcasses, antioxidant, immunity and caecal microbes. Animals, 11(11). https://doi.org/10.3390/ani11113027

Alkhudhayri A, Al-Shaebi EM, Qasem MAA, Murshed M, Mares MM, Al-Quraishy S, Dkhil MA. 2020. Antioxidant and anti-apoptotic effects of selenium nanoparticles against murine eimeriosis. Anais Da Academia Brasileira de Ciencias, 92(2):1–9. https://doi.org/10.1590/0001-3765202020191107

Amin KA, Hashem KS, Alshehri FS, Awad ST, Hassan MS. 2017. Antioxidant and Hepatoprotective Efficiency of Selenium Nanoparticles Against Acetaminophen-Induced Hepatic Damage. Biological Trace Element Research, 175(1). https://doi.org/10.1007/s12011-016-0748-6

Azab DM, Hemat El-Sayed S, El-Habbaa AS. 2019. ANTIOXIDANT AND IMMUNOMODULATORY EFFECTS OF NANO-SELENIUM ON RESPONSE OF BROILERS TO ND VACCINE. In Assiut Veterinary Medical Journal Assiut Vet. Med. J (Vol. 65, Issue 161). www.aun.edu.eg

Battin EE, Zimmerman MT, Ramoutar RR, Quarles CE, Brumaghim JL. 2011. Preventing metal-mediated oxidative DNA damage with selenium compounds. Metallomics, 3(5). https://doi.org/10.1039/c0mt00063a

Beck MA, Shi Q, Morris VC, Levander OA. 1995. Rapid genomic evolution of a non-virulent Coxsackievirus B3 in selenium-deficient mice results in selection of identical virulent isolates. Nature Medicine, 1 (5). https://doi.org/10.1038/nm0595-433

Beheshti N, Soflaei S, Shakibaie M, Yazdi MH, Ghaffarifar F, Dalimi A, Shahverdi AR. 2013. Efficacy of biogenic selenium nanoparticles against Leishmania major: In vitro and in vivo studies. Journal of Trace Elements in Medicine and Biology, 27(3). https://doi.org/10.1016/j.jtemb.2012.11.002

Bezerra MA, Santelli RE, Oliveira EP, Villar LS, Escaleira LA. 2008. Response surface methodology (RSM) as a tool for optimization in analytical chemistry. In Talanta (Vol. 76, Issue 5, pp. 965–977). Elsevier. https://doi.org/10.1016/j.talanta.2008.05.019

Bhainsa KC, D'Souza SF. 2006. Extracellular biosynthesis of silver nanoparticles using the fungus Aspergillus fumigatus. Colloids and Surfaces B: Biointerfaces, 47(2). https://doi.org/10.1016/j.colsurfb.2005.11.026

Bisht N, Phalswal P, Khanna PK. 2022. Selenium nanoparticles: A review on synthesis and biomedical applications. In Materials Advances (Vol. 3, Issue 3). https://doi.org/10.1039/d1ma00639h

Boostani A, Sadeghi AA, Mousavi SN, Chamani M, Kashan N. 2015. Effects of organic, inorganic, and nano-Se on growth performance, antioxidant capacity, cellular and humoral immune responses in broiler chickens exposed to oxidative stress. Livestock Science, 178. https://doi.org/10.1016/j livsci. 2015. 05.004

Chen T, Wong YS, Zheng W, Bai Y, Huang, L. 2008. Selenium nanoparticles fabricated in Undaria pinnatifida polysaccharide solutions induce mitochondria-mediated apoptosis in A375 human melanoma cells. Colloids and Surfaces B: Biointerfaces, 67 (1). https://doi.org/10.1016/j.colsurfb.2008.07.010

Dawood MAO, El Basuini MF, Yilmaz S, Abdel-Latif HMR, Kari ZA, Abdul Razab MKA, Ahmed HA, Alagawany M, Gewaily MS. 2021. Selenium nanoparticles as a natural antioxidant and metabolic regulator in aquaculture: A review. In Antioxidants (Vol. 10, Issue 9). https://doi.org/10.3390/antiox10091364

Dhawan G, Singh I, Dhawan U, Kumar P. 2021. Synthesis and Characterization of Nanoselenium: A Step-by-Step Guide for Undergraduate Students. Journal of Chemical Education, 98(9). https://doi.org/10.1021/acs.jchemed.0c01467

Dkhil MA, Khalil MF, Diab MSM, Bauomy AA, Santourlidis S, Al-Shaebi EM, Al-Quraishy S. 2019. Evaluation of nanoselenium and nanogold activities against murine intestinal schistosomiasis. Saudi Journal of Biological Sciences, 26 (7). https://doi.org/10.1016/j.sjbs.2018.02.008

El-Badry ASO, Mahrousa Hassanane M, Mosalm GAG, Ekram Ahmed S, El-Aasar TA. 2019. INFLUENCE OF INGESTION OF NANO-SELENIUM ON GROWTH PERFORMANCE, ANTIOXIDATIVE AND MUTAGENICITY STATUS IN SOMATIC CELLS OF NEW ZEALAND WHITE RABBITS. In Egyptian Journal of Rabbit Science (Vol. 29, Issue 1).

El-Deep M, Shabaan M, Assar M, Attia Kh, Sayed M. 2017. Comparative Effects of Different Dietary Selenium Sources on Productive Performance, Antioxidative Properties And Immunity in Local Laying Hens Exposed to High Ambient Temperature. Journal of Animal and Poultry Production, 8(9). https://doi.org/10.21608/jappmu.2017.45998

Elmaaty TA, Sayed-Ahmed K, Elsisi H, Ramadan SM, Sorour H, Magdi M, Abdeldayem SA. 2022. Novel Antiviral and Antibacterial Durable Polyester Fabrics Printed with Selenium Nanoparticles (SeNPs). Polymers, 14(5). https://doi.org/10.3390/polym14050955

El-Sharawy ME, Hamouda M, Soliman AA, Amer AA, El-Zayat AM, Sewilam H, Younis EM, Abdel-Warith AWA, Dawood MAO. 2021. Selenium nanoparticles are required for the optimum growth behavior, antioxidative capacity, and liver wellbeing of Striped catfish (Pangasianodon hypophthalmus). Saudi Journal of Biological Sciences, 28(12), 7241–7247. https://doi.org/10.1016/j.sjbs.2021.08.023

Filipović N, Ušjak D, Milenković MT, Zheng K, Liverani L, Boccaccini AR, Stevanović M. M. 2021. Comparative Study of the Antimicrobial Activity of Selenium Nanoparticles With Different Surface Chemistry and Structure. Frontiers in Bioengineering and Biotechnology, 8. https://doi.org/10.3389/fbioe.2020.624621

Gallego-Gallegos M, Doig LE, Tse JJ, Pickering IJ, Liber K. 2013. Bioavailability, toxicity and biotransformation of selenium in midge (Chironomus dilutus) larvae exposed via water or diet to elemental selenium particles, selenite, or selenized algae. Environmental Science and Technology, 47(1). https://doi.org/10.1021/es300828r

Gangadoo S, Dinev I, Willson NL, Moore R. J, Chapman J, Stanley D. 2020. Nanoparticles of selenium as high bioavailable and non-toxic supplement alternatives for broiler chickens. Environmental Science and Pollution Research, 27(14). https://doi.org/10.1007/s11356-020-07962-7

Geoffrion LD, Hesabizadeh T, Medina-Cruz D, Kusper M, Taylor P, Vernet-Crua A, Chen, J, Ajo A, Webster TJ, Guisbiers G. 2020. Naked Selenium Nanoparticles for Antibacterial and Anticancer Treatments. ACS Omega, 5(6):2660–2669. https://doi.org/10.1021/acsomega. 9b03172

Guan B, Yan R, Li, R, Zhang X. 2018. Selenium as a pleiotropic agent for medical discovery and drug delivery. In International Journal of Nanomedicine (Vol. 13, pp. 7473–7490). Dove Medical Press Ltd. https://doi.org/10.2147/IJN.S181343

Guisbiers G, Lara HH, Mendoza-Cruz R, Naranjo G, Vincent BA, Peralta XG, Nash KL. 2017. Inhibition of Candida albicans biofilm by pure selenium nanoparticles synthesized by pulsed laser ablation in liquids. Nanomedicine: Nanotechnology, Biology, and Medicine, 13(3). https://doi.org/10.1016/j. nano. 2016. 10.011

Han L, Pang K, Fu, T, Phillips CJC, Gao T. 2021. Nano-selenium Supplementation Increases Selenoprotein (Sel) Gene Expression Profiles and Milk Selenium Concentration in Lactating Dairy Cows. Biological Trace Element Research, 199(1). https://doi.org/10.1007/s12011-020-02139-2

Harris C, Gaster C, Gelabert MC. 2019. Reverse Micelles as Templates for the Fabrication of Size-Controlled Nanoparticles: A Physical Chemistry Experiment. Journal of Chemical Education, 96(3). https://doi.org/10.1021/acs.jchemed.8b00630

Hernández-Díaz JA, Garza-García Jo, JO, León-Morales JM, Zamudio-Ojeda A, Arratia-Quijada J, Velázquez-Juárez G, López-Velázquez JC, García-Morales S. 2021. Antibacterial activity of biosynthesized selenium nanoparticles using extracts of calendula officinalis against potentially clinical bacterial strains. Molecules, 26(19). https://doi.org/10.3390/molecules26195929

Himoto T, Yoneyama H, Kurokohchi K, Inukai M, Masugata H, Goda F, Haba R, Watababe S, Kubota S, Senda S, Masaki T. 2011. Selenium deficiency is associated with insulin resistance in patients with hepatitis C virus-related chronic liver disease. Nutrition Research, 31(11). https://doi.org/10.1016/j.nutres.2011.09.021

Hassan AA, Mansour M, K, Elahl RS, Tag El-Din HA, Awad M, EA, Younis E. 2020. Influence of Selenium Nanoparticles on The Effects of Poisoning with Aflatoxins. Advances in Animal and Veterinary Sciences, 8(s2). DOI: 10.17582/journal.aavs/2020/8.s2.64.73.

Hosnedlova B, Kepinska M, Skalickova S, Fernandez C, Ruttkay-Nedecky B, Peng Q, Baron M, Melcova M, Opatrilova R, Zidkova J, Bjørklund G, Sochor J, Kizek R. 2018. Nano-selenium and its nanomedicine applications: A critical review. In International Journal of Nanomedicine (Vol. 13). https://doi.org/10.2147/IJN.S157541

Hossein A, Najjari A, Rajabi Z, Marandi MV, Dehghan G, Dvm ZR. 2015. The effect of the hexanic extracts of fig (Ficus carica) and olive (Olea europaea) fruit and nanoparticles of selenium on the immunogenicity of the inactivated avian influenza virus subtype H9N2. In ARTICLE Veterinary Research Forum (Vol. 6, Issue 3).

Huang B, Zhang J, Hou J, Chen C. 2003. Free radical scavenging efficiency of Nano-Se in vitro. Free Radical Biology and Medicine, 35(7), 805–813. https://doi.org/10.1016/S0891-5849(03)00428-3

Ikemoto T, Kunito T, Tanaka H, Baba N, Miyazaki N, Tanabe S. 2004. Detoxification mechanism of heavy metals in marine mammals and seabirds: Interaction of selenium with mercury, silver, copper, zinc, and cadmium in liver. Archives of Environmental Contamination and Toxicology, 47(3), 402–413. https://doi.org/10.1007/s00244-004-3188-9

Ikram M, Javed B, Raja NI, Mashwani ZUR. 2021. Biomedical potential of plant-based selenium nanoparticles: A comprehensive review on therapeutic and mechanistic aspects. In International Journal of Nanomedicine (Vol. 16, pp. 249–268). Dove Medical Press Ltd. https://doi.org/10.2147/IJN.S295053

Jayanthi K, Kumanan K, Om Prakash AV, Vijayarani K. Ramesh J. 2018. Cost effective inclusion of nano selenium in broiler feed for their performance. Indian Veterinary Journal, 95(5).

Jia X, Li, N, Chen J. 2005. A subchronic toxicity study of elemental Nano-Se in Sprague-Dawley rats. Life Sciences, 76(17). https://doi.org/10.1016/j.lfs.2004.09.026

Kassim A, Ali AHH, Marwan T, Abdel-Wareth AAA. 2022. Selenium nanoparticles in rabbit nutrition. a review. SVU-International Journal of Agricultural Sciences, 4(1), 90–98. https://doi.org/10.21608/svuijas.2022.117298.1171

Khiralla GM, El-Deeb BA. 2015. Antimicrobial and antibiofilm effects of selenium nanoparticles on some foodborne pathogens. LWT, 63(2). https://doi.org/10.1016/j. lwt. 2015. 03.086

Kim TS, Yun BY, Kim IY. 2003. Induction of the mitochondrial permeability transition by selenium compounds mediated by oxidation of the protein thiol groups and generation of the superoxide. Biochemical Pharmacology, 66(12). https://doi.org/10.1016/j.bcp.2003.08.021

Kinnunen S, Hyyppä S, Lappalainen J, Oksala N, Venojärvi M, Nakao C, Hänninen O, Sen CK, Atalay M. 2005. Exercise-induced oxidative stress and muscle stress protein responses in trotters. European Journal of Applied Physiology, 93(4). https://doi.org/10.1007/s00421-004-1162-x

Kojouri GA, Faramarzi P, Ahadi AM, Parchami A. 2013. Effect of Selenium Nanoparticles on Expression of HSP90 Gene in Myocytes after an Intense Exercise. Journal of Equine Veterinary Science, 33(12), 1054–1056. https://doi.org/10.1016/J.JEVS.2013.04.001

Kojouri GA, Sharifi S. 2013. Preventing effects of nano-selenium particles on serum concentration of blood urea nitrogen, creatinine, and total protein during intense exercise in donkey. Journal of Equine Veterinary Science, 33(8). https://doi.org/10.1016/j.jevs.2012.09.008

Kokila K, Elavarasan N, Sujatha V. 2017. Diospyros Montana leaf extract-mediated synthesis of selenium nanoparticles and their biological applications. New Journal of Chemistry, 41(15). https://doi.org/10.1039/c7nj01124e

Korde P, Ghotekar S, Pagar T, Pansambal S, Oza R, Mane D. 2020. Plant Extract Assisted Eco-benevolent Synthesis of Selenium Nanoparticles- A Review on Plant Parts Involved, Characterization and Their Recent Applications. Journal of Chemical Reviews, 2(3).

Kumar H, Bhardwaj K, Nepovimova E, Kuča K, Dhanjal DS, Bhardwaj S, Bhatia Verma R, Kumar D. 2020. Antioxidant functionalized nanoparticles: A combat against oxidative stress. In Nanomaterials (Vol. 10, Issue 7). https://doi.org/10.3390/nano10071334

Lai H, Xu, L, Liu, C, Shi, S, Jiang Y, Yu, Y, Deng B, Chen T. 2023. Universal selenium nanoadjuvant with immunopotentiating and redox-shaping activities inducing high-quality immunity for SARS-CoV-2 vaccine. In Signal Transduction and Targeted Therapy (Vol. 8, Issue 1). Springer Nature. https://doi.org/10.1038/s41392-023-01371-1

Li, H, Zhang J, Wang T, Luo W, Zhou Q, Jiang G. 2008. Elemental selenium particles at nano-size (Nano-Se) are more toxic to Medaka (Oryzias latipes) as a consequence of hyper-accumulation of selenium: A comparison with sodium selenite. Aquatic Toxicology, 89(4). https://doi.org/10.1016/j. aquatox. 2008. 07.008

Li, H, Zhang J, Xia Y, Pan W, Zhou D. 2021. Antagonistic effect of nano-selenium on hepatocyte apoptosis induced by DEHP via PI3K/AKT pathway in chicken liver. Ecotoxicology and Environmental Safety,

218. https://doi.org/10.1016/j.ecoenv.2021.112282

Li, L, Liu Z, Quan J, Sun J, Lu, J, Zhao G. 2023. Dietary nano-selenium alleviates heat stress-induced intestinal damage through affecting intestinal antioxidant capacity and microbiota in rainbow trout (Oncorhynchus mykiss). Fish and Shellfish Immunology, 133. https://doi.org/10.1016/j.fsi.2023.108537

Li, W, Beck MA. 2007. Selenium deficiency induced an altered immune response and increased survival following influenza A/Puerto Rico/8/34 infection. Experimental Biology and Medicine, 232(3).

Li, Y, Lin Z, Guo M, Xia Y, Zhao M, Wang, C, Xu T, Chen T, Zhu, B. 2017. Inhibitory activity of selenium nanoparticles functionalized with oseltamivir on H1N1 influenza virus. International Journal of Nanomedicine, (12):5733–5743. https://doi.org/10.2147/IJN. S140939

Li, Y, Lin Z, Guo M, Zhao M, Xia Y, Wang, C, Xu T, Zhu B. 2018. Inhibition of H1N1 influenza virus-induced apoptosis by functionalized selenium nanoparticles with amantadine through ROS-mediated AKT signaling pathways. International Journal of Nanomedicine, 13. https://doi.org/10.2147/IJN.S155994

Lin, W, Zhang J, Xu, JF, Pi, J. 2021. The Advancing of Selenium Nanoparticles Against Infectious Diseases. In Frontiers in Pharmacology (Vol. 12). Frontiers Media S.A. https://doi.org/10.3389/fphar.2021.682284

Lin Z, Li, Y, Xu, T, Guo, M, Wang C, Zhao M, Chen H, Kuang J, Li, W, Zhang Y, Lin T, Chen Y, Chen H, Zhu B. 2020. Inhibition of Enterovirus 71 by Selenium Nanoparticles Loaded with siRNA through Bax Signaling Pathways. ACS Omega, 5(21), 12495–12500. https://doi.org/10.1021/acsomega.0c01382

Liu C, Li, Y, Li, H, Wang Y, Zhao K. 2022. Nano-Selenium and Macleaya cordata Extracts Improved Immune Functions of Intrauterine Growth Retardation Piglets under Maternal Oxidation Stress. Biological Trace Element Research, 200(9). https://doi.org/10.1007/s12011-021-03009-1

Liu J, Meng J, Cao L, Li, Y, Deng P, Pan P, Hu, C, Yang H. 2019. Synthesis and investigations of ciprofloxacin loaded engineered selenium lipid nanocarriers for effective drug delivery system for preventing lung infections of interstitial lung disease. Journal of Photochemistry and Photobiology B: Biology, 197. https://doi.org/10.1016/j.jphotobiol.2019.05.007

Mal J, Veneman WJ, Nancharaiah YV, van Hullebusch ED, Peijnenburg WJGM, Vijver, MG, Lens PNL. 2017. A comparison of fate and toxicity of selenite, biogenically, and chemically synthesized selenium nanoparticles to zebrafish (Danio rerio) embryogenesis. Nanotoxicology, 11 (1). https://doi.org/10.1080/17435390.2016.1275866

Marine W, Patrone L, Luk'Yanchuk B, Sentis M. 2000. Strategy of nanocluster and nanostructure synthesis by conventional pulsed laser ablation. Applied Surface Science, 154. https://doi.org/10.1016/S0169-4332(99)00450-X

Menon S, Shrudhi SD, Agarwal H, Shanmugam VK. 2019. Efficacy of Biogenic Selenium Nanoparticles from an Extract of Ginger towards Evaluation on Anti-Microbial and Anti-Oxidant Activities. Colloids and Interface Science Communications, 29. https://doi.org/10.1016/j.colcom.2018.12.004

Moghaddam A, Heller RA, Sun Q, Seelig J, Cherkezov A, Seibert L, Hackler J, Seemann P, Diegmann J, Pilz M, Bachmann M, Minich WB, Schomburg L. 2020. Selenium deficiency is associated with mortality risk from COVID-19. Nutrients, 12(7), 1–13. https://doi.org/10.3390/nu12072098

Mohammadinejad R, Karimi S, Iravani S, Varma RS. 2015. Plant-derived nanostructures: types and applications. In Green Chemistry (Vol. 18, Issue 1). https://doi.org/10.1039/c5gc01403d

Pi, J, Jiang J, Cai H, Yang F, Jin H, Yang P, Cai J, Chen ZW. 2017. Ge11 peptide conjugated selenium nanoparticles for egfr targeted oridonin delivery to achieve enhanced anticancer efficacy by inhibiting egfr-mediated pi3k/akt and ras/raf/mek/erk pathways. Drug Delivery, 24(1), 1549–1564. https://doi.org/10.1080/10717544.2017.1386729

Pi, J, Shen L, Yang E, Shen H, Huang D, Wang R, Hu, C, Jin H, Cai H, Cai J, Zeng G, Chen ZW. 2020. Macrophage-Targeted Isoniazid–Selenium Nanoparticles Promote Antimicrobial Immunity and Synergize Bactericidal Destruction of Tuberculosis Bacilli. Angewandte Chemie - International Edition, 59(8). https://doi.org/10.1002/anie.201912122

Qin SY, Chen F, Zhao FH, Jin TM, Ma JF. 2016. Effects of Nano-selenium on Blood Biochemistry, Liver Antioxidant Activity and GPx-1 mRNA Expression in Rabbits.

Raahati Z, Bakhshi B, Najar-Peerayeh S. 2020. Selenium Nanoparticles Induce Potent Protective Immune Responses against Vibrio cholerae WC Vaccine in a Mouse Model. Journal of Immunology Research, 2020. https://doi.org/10.1155/2020/8874288

Rajabi S, Ramazani A, Hamidi M, Naji T. 2015. Artemia salina as a model organism in toxicity assessment of nanoparticles. DARU, Journal of Pharmaceutical Sciences, 23(1). https://doi.org/10.1186/s40199-015-0105-x

Ranjbariyan A, Haghighat S, Yazdi MH, Arbabi Bidgoli S. 2023. Synthetic selenium nanoparticles as co-adjuvant improved immune responses against methicillin-resistant Staphylococcus aureus. World Journal of Microbiology and Biotechnology, 39(1). https://doi.org/10.1007/s11274-022-03455-6

Reffett JK, Spears JW, Brown TT. 1988. Effect of dietary selenium on the primary and secondary immune response in calves challenged with infectious bovine rhinotracheitis virus. Journal of Nutrition, 118(2), 229–235. https://doi.org/10.1093/jn/118.2.229

Ren Z, Okyere SK, Zhang M, Zhang X, He H, Hu, Y. 2022. Glycine Nano-Selenium Enhances Immunoglobulin and Cytokine Production in Mice Immunized with H9N2 Avian Influenza Virus Vaccine. International Journal of Molecular Sciences, 23(14). https://doi.org/10.3390/ijms23147914

Rinaudo M. 2006. Chitin and chitosan: Properties and applications. In Progress in Polymer Science (Oxford) (Vol. 31, Issue 7). https://doi.org/10.1016/j.progpolymsci.2006.06.001

Saini D, Fazil M, Ali MM, Baboota S, Ameeduzzafar A, Ali J. 2015. Formulation, development and optimization of raloxifene-loaded chitosan nanoparticles for treatment of osteoporosis. Drug Delivery, 22(6), 823–836. https:/doi.org/10.3109/10717544.2014.900153

Shakibaie M, Ezzatkhah F, Gabal E, Badparva E, Jahanbakhsh S, Mahmoudvand H. 2020. Prophylactic effects of biogenic selenium nanoparticles on acute toxoplasmosis: An in vivo study. Annals of Medicine and Surgery, 54. https://doi.org/10.1016/j. amsu. 2020. 04. 010

Shakibaie M, Mohazab NS, Ayatollahi Mousavi SA. 2015. Antifungal activity of selenium nanoparticles synthesized by bacillus species Msh-1 against Aspergillus fumigatus and Candida albicans. Jundishapur Journal of Microbiology, 8(9). https://doi.org/10.5812/jjm. 26381

Sheiha AM, Abdelnour SA, Abd El-Hack M. E, Khafaga AF, Metwally KA, Ajarem JS, Maodaa SN, Allam, AA, El-Saadony MT. 2020. Effects of dietary biological or chemical-synthesized nano-selenium supplementation on growing rabbits exposed to thermal stress. Animals, 10(3). https://doi.org/10.3390/ani10030430

Shi L, Xun W, Yue W, Zhang C, Ren Y, Shi L, Wang Q, Yang R, Lei F. 2011. Effect of sodium selenite, Se-yeast and nano-elemental selenium on growth performance, Se concentration and antioxidant status in growing male goats. Small Ruminant Research, 96(1). https://doi.org/10.1016/j. smallrumres. 2010.11.005

Shirsat S, Kadam A, Mane RS, Jadhav VV, Zate MK, Naushad M, Kim KH. 2016. Protective role of biogenic selenium nanoparticles in immunological and oxidative stress generated by enrofloxacin in broiler chicken. Dalton Transactions, 45(21). https://doi.org/10.1039/c6dt00120c

Shoeibi S, Mashreghi M. 2017. Biosynthesis of selenium nanoparticles using Enterococcus faecalis and evaluation of their antibacterial activities. Journal of Trace Elements in Medicine and Biology, 39. https://doi.org/10.1016/j.jtemb.2016.09.003

Skalickova S, Milosavljevic V, Cihalova K, Horky P, Richtera L, Adam V. 2017. Selenium nanoparticles as a nutritional supplement. In Nutrition (Vol. 33). https://doi.org/10.1016/j.nut.2016.05.001

Song JY, Kim BS. 2009. Rapid biological synthesis of silver nanoparticles using plant leaf extracts. Bioprocess and Biosystems Engineering, 32(1), 79–84. https://doi.org/10.1007/s00449-008-0224-6

Stevanović M, Filipović N, Djurdjević J, Lukić M, Milenković M, Boccaccini A. 2015. 45S5Bioglass®-based scaffolds coated with selenium nanoparticles or with poly (lactide-co-glycolide)/selenium particles: Processing, evaluation and antibacterial activity. Colloids and Surfaces B: Biointerfaces, 132. https://doi.org/10.1016/j.colsurfb.2015.05.024

Stone CA, Kawai K, Kupka R, Fawzi WW. 2010. Role of selenium in HIV infection. Nutrition Reviews, 68(11): 671–681. https://doi.org/10.1111/j.1753-4887.2010.00337.x

Sun J, Liu Z, Quan J, Li, L, Zhao G, Lu, J. 2022. Protective effects of different concentrations of selenium nanoparticles on rainbow trout (Oncorhynchus mykiss) primary hepatocytes under heat stress. Ecotoxicology and Environmental Safety, 230. https://doi.org/10.1016/j.ecoenv.2021.113121

Tan Q, Li, J, Yin, HW, Wang LH, Tang WC, Zhao F, Liu XM, Zeng HH. 2010. Augmented antitumor effects of combination therapy of cisplatin with ethaselen as a novel thioredoxin reductase inhibitor on human A549 cell in vivo. Investigational New Drugs, 28(3), 205–215. https://doi.org/10.1007/s10637-009-9235-7

Torres SK, Campos VL, León CG, Rodríguez-Llamazares SM, Rojas SM, González M, Smith C, Mondaca MA. 2012. Biosynthesis of selenium nanoparticles by pantoea agglomerans and their antioxidant activity. Journal of Nanoparticle Research, 14(11). https://doi.org/10.1007/s11051-012-1236-3

Tugarova AV, Mamchenkova PV, Khanadeev VA, Kamnev AA. 2020. Selenite reduction by the rhizobacterium Azospirillum brasilense, synthesis of extracellular selenium nanoparticles and their characterisation. New Biotechnology, 58. https://doi.org/10. 1016/j.nbt. 2020. 02.003

Urbankova L, Skalickova S, Pribilova M, Ridoskova A, Pelcova P, Skladanka J, Horky P. 2021. Effects of sub-lethal doses of selenium nanoparticles on the health status of rats. Toxics, 9(2). https://doi.org/10.3390/toxics9020028

Verma S, Molina Y, Lo, YY, Cropp B, Nakano C, Yanagihara R, Nerurkar, VR. 2008. In vitro effects of selenium deficiency on West Nile virus replication and cytopathogenicity. Virology Journal, 5. https://doi.org/10.1186/1743-422X-5-66

Wang A, Yu, K, Zou W, Song K. 2012. Anti-herpes simplex virus type 1 activity of trace element selenium In vitro. J Nanchang Univ, 52(9), 1–4.

Wang C, Chen H, Chen D, Zhao M, Lin Z, Guo M, Xu T, Chen Y, Hua L, Lin T, Tang Y, Zhu B, Li, Y. 2020. The Inhibition of H1N1 Influenza Virus-Induced Apoptosis by Surface Decoration of Selenium Nanoparticles with β-Thujaplicin through Reactive Oxygen Species-Mediated AKT and p53 Signaling Pathways. ACS Omega, 5(47), 30633–30642. https://doi.org/10.1021/acsomega.0c04624

Wang H, Zhang J, Yu, H. 2007. Elemental selenium at nano size possesses lower toxicity without compromising the fundamental effect on selenoenzymes: Comparison with selenomethionine in mice. Free Radical Biology and Medicine, 42(10). https://doi.org/10.1016/j.freeradbiomed.2007.02.013

Wang Q, Webster TJ. 2012. Nanostructured selenium for preventing biofilm formation on polycarbonate medical devices. Journal of Biomedical Materials Research - Part A, 100 A(12), 3205–3210. https://doi.org/10.1002/jbm.a.34262

Wang X, Pan X, Gadd GM. 2019. Immobilization of elemental mercury by biogenic Se nanoparticles in soils of varying salinity. Science of the Total Environment, 668. https://doi.org/10.1016/j.scitotenv.2019.02.457

Xia IF, Cheung JS, Wu M, Wong K, Sen Kong HK, Zheng XT, Wong KH, Kwok KW. 2019. Dietary chitosan-selenium nanoparticle (CTS-SeNP) enhance immunity and disease resistance in zebrafish. Fish and Shellfish Immunology, 87. https://doi.org/10.1016/j. fsi. 2019.01.042

Xu, C, Qiao L, Ma, L, Guo, Y, Dou, X, Yan, S, Zhang B, Roman A. 2019. Biogenic selenium nanoparticles synthesized by lactobacillus casei ATCC 393 alleviate intestinal epithelial barrier dysfunction caused by oxidative stress via nrf2 signaling-mediated mitochondrial pathway. International Journal of Nanomedicine, 14. https://doi.org/10.2147/IJN.S199193

Xun, W, Shi, L, Yue, W, Zhang C, Ren Y, Liu, Q. 2012. Effect of high-dose nano-selenium and selenium-yeast on feed digestibility, rumen fermentation, and purine derivatives in sheep. Biological Trace Element Research, 150(1–3). https://doi.org/10.1007/s12011-012-9452-3

Yaghmaie P, Ramin A, Asri-Rezaei S, Zamani A, Dvm PY. 2017. Evaluation of glutathion peroxidase activity, trace minerals and weight gain following administration of selenium compounds in lambs. In ARTICLE Veterinary Research Forum (Vol. 8, Issue 2).

Yao, M, McClements DJ, Xiao H. 2015. Improving oral bioavailability of nutraceuticals by engineered nanoparticle-based delivery systems. In Current Opinion in Food Science (Vol. 2). https://doi.org/10.1016/j.cofs.2014.12.005

Yehia N, AbdelSabour MA, Erfan AM, Mohammed Ali Z, Soliman RA, Samy A, Mohamed Soliman M, Abd El-Hack ME, El-Saadony MT, Ahmed KA. 2022. Selenium nanoparticles enhance the efficacy of homologous vaccine against the highly pathogenic avian influenza H5N1 virus in chickens. Saudi Journal of Biological Sciences, 29(4), 2095–2111. https://doi.org/10.1016/j. sjbs. 2021. 11.051

Zhang JS, Gao XY, Zhang L, De, Bao YP. 2001. Biological effects of a nano red elemental selenium. BioFactors, 15(1). https://doi.org/10.1002/biof.5520150103

Zhang J, Wang H, Yan X, Zhang L. 2005. Comparison of short-term toxicity between Nano-Se and selenite in mice. Life Sciences, 76(10). https://doi.org/10.1016/j. lfs. 2004. 08.015

Zhang J, Wang X, Xu TT. 2008. Elemental selenium at nano size (Nano-Se) as a potential chemopreventive agent with reduced risk of selenium toxicity: Comparison with se-methylselenocysteine in mice. Toxicological Sciences, 101(1), 22–31. https://doi. org/10. 1093/toxsci/kfm221

Zhang SY, Zhang J, Wang HY, Chen HY. 2004. Synthesis of selenium nanoparticles in the presence of polysaccharides. Materials Letters, 58(21). https://doi.org/10.1016/j. matlet. 2004.03.031

Zheng L, Li, C, Huang X, Lin X, Lin W, Yang F, Chen T. 2019. Thermosensitive hydrogels for sustained-release of sorafenib and selenium nanoparticles for localized synergistic chemoradiotherapy. Biomaterials, 216. https://doi.org/10.1016/j.biomaterials.2019.05.031

Zhou X, Wang Y. 2011. Influence of dietary nano elemental selenium on growth performance, tissue selenium distribution, meat quality, and glutathione peroxidase activity in Guangxi Yellow chicken. Poultry Science, 90(3). https://doi.org/10.3382/ps.2010-00977

Zhu M, Niu G, Tang J. 2019. Elemental Se: Fundamentals and its optoelectronic applications. In Journal of Materials Chemistry C (Vol. 7, Issue 8, pp. 2199–2206). Royal Society of Chemistry. https://doi.org/10.1039/c8tc05873c