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Nano-Selenium as a Key Supplement in Rabbit Nutrition: Physiological and Productive Benefits-A Review

A. Abd El-Aziz[a,*], A. Noreldin[b], A. Elbaz[c], B. Mishra[d], G. Buonaiuto[e,†], & K. El-Sabrout[f,*,†]
[a]Department of Animal Wealth Development, Faculty of Veterinary Medicine, Damanhour University, Damanhour 22511, Egypt;
[b]Department of Histology and Cytology, Faculty of Veterinary Medicine, Damanhour University, Damanhour 22511, Egypt;
[c]Department of Animal and Poultry Nutrition, Desert Research Center, Mataria, Cairo, Egypt;
[d]Department of Human Nutrition Food and Animal Sciences, University of Hawaii at Manoa, 1955 East-West Road, Honolulu, HI, 96822, USA;
[e]Department of Veterinary Medical Sciences, University of Bologna, Ozzano dell'Emilia, Bologna, 40064, Italy;
[f]Department of Poultry Production, Faculty of Agriculture, Alexandria University, Alexandria 21545, Egypt
*Corresponding authors: ayman.sadaka@vetmed.dmu.edu.eg; kareem.badr@alexu.edu.eg
[†]These authors contributed equally to this work.
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ABSTRACT

Nutrition is a vital component of health, productivity, and performance. During the last decades, nanotechnology has been highlighted as an innovative technique in the area of animal nutrition, which is used for improving nutrient utilization/supply and maintaining the health of the animal. Among the nano-minerals, selenium nano-particles (Nano-Se) have been of exceptional interest because of higher bioavailability and biological activity than the traditional sources of Se. Nano-Se is essential for growth performance, gut health, and immunity in rabbits. The absorption of trace elements is essential for an animal's growth and productivity. Nano-Se has exhibited visible potential in advancing physiological processes, functioning as an effective antioxidant and anti-inflammatory agent. These attributes result in better immune response, healthier guts, and proper organ function. Moreover, selenium is well known for its vital role in immune regulation, digestion, and metabolism. Several reports are available on the beneficial effects of Nano-Se supplementation on production performance, reproductive performance, carcass characteristics, and meat quality in rabbits. By modulating the expression of tight junction proteins, Nano-Se safeguards gut barrier function, improves hematobiochemical profiles, and supports tissue histology. Therefore, Nano-Se not only enhances biological performance but also the economic efficiency of rabbit production. The review provides a comprehensive and updated overview of the action mechanisms, effective dosage levels, and physiological effects of Nano-Se on rabbit growth, nutrient digestibility, reproduction, immunity, and intestinal health. It also stresses the necessity of precise selenium supplementation and indicates the range of optimum dietary selenium levels between 0.05 and 0.3 mg/kg, depending on the diet composition. Further research is needed to establish proper and safe Nano-Se supplementation guidelines for sustainable rabbit production.

Keywords: antioxidant; gut health; nutraceuticals; immune function; rabbit production; selenium nanoparticles

INTRODUCTION

Rabbit health and productivity are significantly influenced by environmental along with nutritional factors (Abd El-Aziz *et al*., 2024; Elsayed *et al*., 2024). Nanotechnology in the past few years has been a developing and hopeful approach in the arena of animal nutrition and agriculture with the capability to revolutionize nutrient delivery systems and support animal health (El-Sabrout *et al*., 2023 and 2025). Nano particles possess some advantages over their traditional mineral counterparts due to their unique physicochemical properties, which include nanoscale size (1–100 nm), large surface area-to-volume ratio, improved stability, and enhanced bioactivity. Among them, Nano-Se particles are particularly outstanding with their enhanced bioavailability, reduced toxicity, and improved biological efficacy relative to their conventional selenium supplements. Nano-Se has improved adsorption, better stability, and reduced toxicity in animal systems, which is appropriate for growth improvement, immune response, reproductive performance, and metabolic activity (Surai *et al*., 2017; Moustafa *et al*., 2024). Selenium is itself an essential trace element with many roles in biological processes, such as immune and endocrine regulation, organ function maintenance, and antioxidant defense (Mahima *et al*., 2012). Selenium can be administered in nanoparticulate, organic, or inorganic forms, with Nano-Se having an additional benefit due to its bioavailability and lesser toxicity risk (Wang *et al*., 2021).

Recently, Nano-Se has come to the spotlight as a nutraceutical identified as a novel form of dietary supplement for rabbits possessing antioxidant and antimicrobial activities to aid in nutrient utilization, intestinal integrity, and overall physiological functions (Sheiha *et al*., 2020; Wang *et al*., 2021). Experimental studies have revealed that the supplementation of rabbits with Nano-Se significantly enhanced the growth of rabbits and carcass quality. For instance, Sheiha *et al*. (2020) reported a significant increase and improvement in carcass quality in rabbits that were fed diets supplemented with 50 mg/kg Nano-Se over the control group. Baseline selenium intake in the diet of rabbits has been found to be in the range 0.05-0.4 mg/kg, and supplementation has been found to increase selenium intake up to a maximum of 1 mg/kg when selenium yeast or sodium selenite is supplemented at a level of 0.6 mg/kg of diet (Abdel-Wareth *et al*., 2019; Amer *et al*., 2019). While promising, the enormous variability in effective doses of selenium speaks to the rationale for further research to customize and optimize supplementation. Nano-Se has been shown to have a beneficial impact not only on growth performance (Kassim *et al*., 2022; El-Shobokshy *et al*., 2022; Abdel-Wareth *et al*., 2024; Bashar *et al*., 2024; Moustafa *et al*., 2024), but also reproductive performance (Abdel-Wareth *et al*., 2019; El-Ratel *et al*., 2023; Bashar *et al*., 2024), carcass and meat quality (Sheiha *et al*., 2020; Abdel-Wareth *et al*., 2024; Moustafa *et al*., 2024), and blood biochemical indices (Sheiha *et al*., 2020; El-Ratel *et al*., 2023; Bashar *et al*., 2024). Moreover, it controls the expression of tight junction proteins, the significance of which is to preserve gut barrier function and maximum nutrient uptake (Liu *et al*., 2023). These physiological gains are also passed on in the form of increased economic efficiency on the basis of enhanced feed conversion as well as reproductive efficiency (Abdel-Wareth *et al*., 2024).

However, while a growing body of evidence exists, there are few existing studies of Nano-Se on rabbit nutrition focusing on single results in isolation, without regard to a full consideration of its multifaceted impacts on biological processes and profitability and productivity consequences. This review attempts to cover this shortfall through the presentation of a synthesis of the existing knowledge concerning Nano-Se, including its physicochemical characteristics, mechanisms of action, and documented outcomes in the context of key performance metrics. Additionally, this review puts the role of Nano-Se in sustainable animal agriculture and the emerging field of nutraceuticals into perspective, providing a roadmap for future applied work and research.

METHODOLOGY

Electronic databases of published scientific literature, as many as 59 references, were the main source for this review, with a range of publication years: 2007–2025; except for one earlier reference (Štruklec *et al*., 1994). Scopus/Web of Science (approximately 33), PubMed (approximately 10), and Google Scholar (approximately 16) were searched for Nano-selenium as a key supplement in rabbit nutrition. Additional articles of interest were obtained through cross-referencing of published literature. The primary key terms used were "nano-selenium", "synthesis and characterization", "physicochemical properties", "recommended levels", "production", "carcass", "reproduction", "blood parameters", "immunity", "economics", and "rabbits". Papers not related to rabbit production, health, and physiology were excluded. Only English-language papers were taken into consideration.

SYNTHESIS AND CHARACTERIZATION OF NANO SELENIUM PARTICLES

Nano-Se can be synthesized through various approaches, including chemical and biological synthesis. Understanding these methods is essential to harness the full therapeutic and nutritional potential of Nano-Se in both medical and agricultural contexts. Chemical synthesis employs reducing agents to reduce selenium salt to elemental selenium, enabling the formation and stabilization of nanoparticles. The conventional method has the advantage of high reproducibility and nanoparticle shape and size control. Conventional production methods frequently rely on highly toxic reagents, generating hazardous waste that poses a long-term threat to ecosystems (Anu *et al*., 2017). Many of these chemical routes also operate at elevated temperatures, restricting scale-up and driving up capital and operational costs due to reactor and environment containment necessities (Jadhav & Khanna, 2015). By contrast, the biological synthesis of nanoparticles offers a markedly greener pathway. Living systems, including higher plants, algae, and various microbes, serve as biological factories that sequentially reduce selenium oxyanions and stabilize the resultant nanostructures. Among these, plant extracts are particularly attractive, since they act simultaneously as reductants and capping agents; phenolic compounds, flavonoids, and terpenoids within the extracts limit particle size and prevent agglomeration (Pyrzynska & Sentkowska, 2022; Ren *et al*., 2021; Chandran *et al*., 2023). Such biomimetic fabrication not only circumvents toxic reagent use and excessive thermal stress, but it also yields nanoparticles with inherently favorable biocompatibility and minimal cytotoxicity. Cost advantages arise from the availability and low-energy processing of biomass, rendering the technology economically viable for applications in medicine and sustainable agriculture (Ren *et al*., 2021; Pyrzynska & Sentkowska, 2022; Behera *et al*., 2024).

One of the branches of biological methods, green synthesis specifically utilizes plant materials and has drawn widespread attention due to its potential in enhancing the antioxidant capacity of Nano-Se. Citrus fruits and garlic extracts, for example, have been successfully used for the synthesis of Nano-Se with proven antioxidant and antibacterial activities (Alvi *et* *al*., 2021; Behera *et al*., 2024). These extracts supply the phytochemicals as natural reducing and stabilizing agents, improving the biological activity along with the safety profile of the nanoparticles (Sivakumar & Jeganathan, 2018; Dimitriu *et al*., 2020). Nano-Se via green synthesis has been reported to be less cytotoxic compared to those synthesized via chemical routes and is being promoted as more compatible for biomedical applications (Safaei *et al*., 2022). The recent advancement in green and biological synthesis shows the potential of these methods for synthesizing Nano-Se with low toxicity and high bioavailability. The nanoparticles have also been shown to provide significant benefits for regulating antioxidant systems and oxidative stress in living organisms (Azeem & Abd El Megid, 2023; Huang *et al*., 2023). For instance, Garcinia mangostana extracts have been used to synthesize nano-Se with excellent anticancer activity and reduced toxicity to normal cells (Benitha *et al*., 2021; BenithaJ *et al*., 2023).

The microbial route, particularly through the use of *Bacillus spp*. and other selenium oxyanion reductive bacteria, has also been successful in synthesizing stable bioactive nano-Se. The approach holds great promise in the development of therapeutic agents with high biological activity and excellent biocompatibility (Greeshma & Mahesh, 2019). Regardless of the synthesis method, full characterization of the physicochemical characteristics of Nano-Se is necessary to determine its potential applications. Some parameters include size, shape, surface charge, and crystal structure that can significantly influence the reactivity, cellular uptake, and biological interactions of nanoparticles (Wang *et al*., 2022; Sampath *et al*., 2024). The typical techniques used in the characterization of Nano-Se include transmission electron microscopy (TEM) and scanning electron microscopy (SEM), which reveal that most of the nano-Se are spherical in shape and in the nanometer scale (Cavalu *et al*., 2017; Adebayo-Tayo *et al*., 2021).

The potential applications of Nano-Se synthesized by different methods are wide, extending from medicine, agriculture, and biotechnology to the nutraceutical industry. Their biosafety, biocompatibility, and structural versatility render Nano-Se great candidates for drug delivery systems, biosensors, and dietary supplements (Satarzadeh *et al*., 2023; Zhang *et al*., 2023). As nanobiotechnology continues to evolve, nano-Se will undoubtedly play an increasingly important role in addressing the world's health, nutrition, and food security-related problems.

PHYSICOCHEMICAL PROPERTIES, BIOAVAILABILITY, AND MODE OF ACTION

Physicochemical properties of Nano-Se, including particle size, morphology, surface charge, and solubility, are key determinants of their bioavailability and biological activity (Abdel-Wareth *et al*., 2022; El-Sabrout *et al*., 2023). Among them, the particle size is particularly critical, with smaller nanoparticles more readily absorbed in the gastrointestinal tract, thus resulting in greater systemic bioavailability and activity in cross-linking biological systems (Saffari *et al*., 2017). Additionally, Nano-Se formulations can be engineered to maximize their structural stability and controlled release in the gut environment, thereby further improving their bio-accessibility and utilization (Ali *et al*., 2021; Petrovic *et al*., 2024).

Nano-Se is characterized by a high surface-area-to-volume ratio, which facilitates its rapid diffusion across cellular membranes and promotes superior absorption compared to larger particles (Hassan *et al*., 2020). This property not only extends residence time in the gastrointestinal tract but also enhances the transport and uptake of selenium at the cellular level. Particulates of diameters less than <0.1 μm are particularly efficacious, with studies showing that they are better absorbed and are more bioactive than larger counterparts (Adamo *et al*., 2017). Aside from its bioavailability, Nano-Se exhibits a variety of physiological roles through its antioxidant, immunomodulatory, and metabolic activities. Physiologically, Nano-Se is a potent scavenger of reactive oxygen species (ROS), which helps to mitigate oxidative stress and maintain cellular integrity. It takes part in the action of principal antioxidant enzymes, viz. glutathione peroxidase (GPx) and superoxide dismutase (SOD), which play key roles in the protection of cellular components from oxidative damage (Shi *et al*., 2011; Hassanin *et al*., 2013). This antioxidative effect is of particular significance to reproductive performance, thyroid status, muscle strength, and even cancer prevention because Nano-Se is a cofactor for various selenoproteins, being involved in these functions (Hozyen *et al*., 2024; Sampath *et al*., 2024). Moreover, it was revealed that the intestinal microbiota of monogastric animals, i.e., rabbits, can convert Nano-Se into bioactive selenium metabolites, such as selenite, which are further incorporated into essential selenoproteins. They have a fundamental role in metabolic homeostasis, immune regulation, and antioxidant status (Surai *et al*., 2017). Nano-Se also modulates the gut microbiota composition, promoting the generation of short-chain fatty acids and particularly butyrate, resulting in enhanced gut barrier function and immune competency (Abdel-Wareth *et al*., 2019; Oraby *et al*., 2022). These mechanisms are illustrated in Figure 1. Collectively, these effects explain the improvements in growth performance, immunity, and gut health in Nano-Se supplemented animals (Figure 2). Particularly important is the ability of Nano-Se to modulate the expression of tight junction proteins and influence intestinal permeability, as this guarantees its role in the maintenance of gut integrity and nutrient absorption.

However, despite its many positive aspects, Nano-Se supplementation must be well managed. Excessive selenium intake, even in nanoparticulate form, has the potential to trigger tissue accumulation, selenium toxicity, and increased oxidative stress rather than relief (Peng *et al*., 2007). Therefore, determination of optimal dosage levels is necessary to allow for maximum beneficial effects without leading to unwanted outcomes. There is ongoing evidence supporting additional research for the identification of optimal, safe, and effective dosing regimens for Nano-Se in

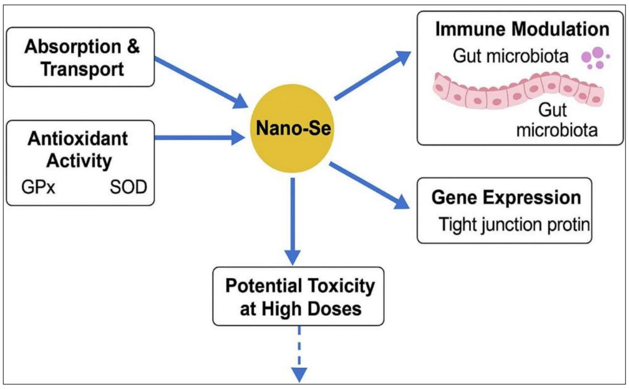

Figure 1. The mode of action of Nano-Se in rabbits

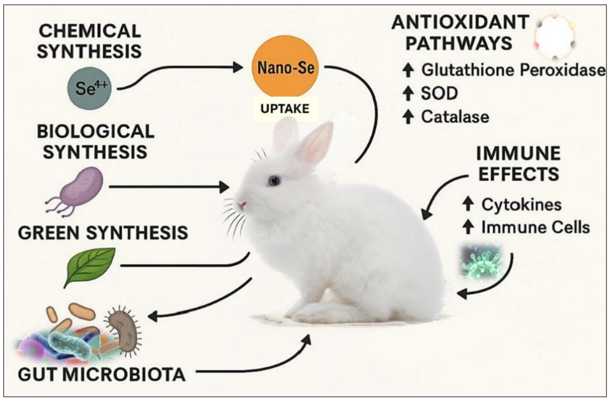

Figure 2. The potential effects of Nano-Se in rabbits

feeding rabbits. It is necessary to define the relationship between the physicochemical properties of Nano-Se and its biological function to design safe supplementation protocols and unlock its highest potential to improve rabbit health, welfare, and production efficiency.

RECOMMENDED SELENIUM LEVELS IN RABBIT DIETS

Selenium is a trace mineral required for the health, growth, and physiological function of rabbits. The recommended dietary levels of selenium for rabbits differ considerably, primarily depending on the composition of the basal diet and the supplemental selenium form. Experiments reveal that unsupplemented diets typically contain levels of selenium between 0.05 and 0.4 mg/kg, whereas selenium-fortified diets of approximately 1 mg/kg are attained after supplementing 0.6 mg/kg of selenium yeast or sodium selenite (Štruklec *et al*., 1994; Blas & Mateos, 2010; Amer *et al*., 2019). Various methodologies have been adopted in recent work to optimize selenium supplementation, particularly through the use of Nano-Se with apparently increased bioavailability and biological activity. A new approach was introduced by Emara (2019), wherein weekly intramuscular injection of 4 ml Nano-Se solution elicited important growth performance gains, showing that possible different routes of administration could be effective too. Reaffirming the beneficial role of dietary Nano-Se, Abdel-Wareth *et al*. (2019) documented enhanced performance in growing rabbits given 400 µg/kg of Nano-Se with or without supplementation with 700 mg/kg of garlic oil. Consistent with this, Abd Allah *et al*. (2020) documented enhanced growth in diets supplemented with 0.3 mg/kg of Nano-Se with or without 250 mg/kg of vitamin E. Further evidence is provided by Sheiha *et al*. (2020), who reported significant improvement in performance as Nano-Se/kg was supplemented in the diets of rabbits in the interval between 25 mg and 50 mg/kg. Likewise, Qin *et al*. (2016) showed that 0.3 mg/kg Nano-Se enhanced growth performance tremendously in growing rabbits. All these pieces of work categorically confirm the implication of Nano-Se supplementation in enhancing growth performance in rabbits. But the extensive differential in dose and administration, from oral diet inclusion to injective, justifies the need for setting standard guidelines. The dose administered and how it will interact with the rest of the food matrix (i.e., vitamin E or ZnO) all bear an important role in effectiveness. Therefore, there is a need to carry out further studies to ascertain the optimal levels of selenium, particularly in nanoparticulate state, to enable maximum performance, minimize toxicity risk, and contribute to the sustainable production of rabbits. Future guidance must also take into account the stage of production, breed, environment, and target health or productivity effects.

POSSIBLE BENEFITS OF INCORPORATING NANO-SE INTO RABBIT NUTRITION

Selenium is a critical trace mineral involved in various biological processes that support immunity, digestion, and metabolic regulation in rabbits (El-Ratel *et al*., 2023; Hozyen *et al*., 2024). When provided in its nanoparticulate form, Nano-Se exhibits superior bioavailability and enhanced biological activity compared to conventional inorganic and organic selenium sources. These properties make Nano-Se a valuable tool in optimizing rabbit nutrition and overall productivity (Table 1).

The following subsections provide a comprehensive overview of the effects of Nano-Se supplementation in rabbits, with specific focus on production and reproductive performance, blood and biochemical parameters, immune and antioxidant responses, gene expression, and economic efficiency (Table 1). Each aspect is discussed based on current scientific evidence, aiming to clarify the mechanisms through which Nano-Se exerts its benefits and to identify its potential role in the development of more efficient and sustainable rabbit production systems.

Production Performance

Numerous studies have demonstrated that dietary supplementation with Nano-Se significantly enhances production performance in growing rabbits. One of the most consistently reported effects is the improvement in body weight (BW), body weight gain (BWG), and feed conversion ratio (FCR), largely attributable to

Table 1. Summary of Nano-Se supplementation effects on rabbits

Reference	Source	Dose	Form	Strain[1]	Main outcomes
Sheiha *et al.* (2020)	Feed	25, 50 mg/kg diet	Biological and chemical Nano-Se	Male weaners, 35–91 days	↑ Growth, improved liver and kidney function, ↑ antioxidant markers
Abdel-Wareth *et al.* (2019)	Feed	400 μg/kg diet	Chemical Nano-Se	CAL bucks, 120–180 days	↑ FCR, improved hepatic and renal biomarkers, ↓ oxidative stress
Abdel-Wareth *et al.* (2024)	Feed	0.6 mg/kg diet	Chemical Nano-Se	NZW weaners, both sexes, 30–90 days	↑ BW, improved FCR, ↓ lipid levels, ↑ carcass yield
Moustafa *et al.* (2024)	Feed	0.02, 0.05 mg/kg diet	Chemical Nano-Se	NZW weaners, males, 42–98 days	↑ Nutrient and fiber digestibility, ↑ BW, improved FCR, ↑ economic return
El-Shobokshy *et al.* (2022)	Intramuscular injection	0.2 mg/kg BW	Chemical Nano-Se	V-line does, 98–126 days	↑ Growth and reproductive performance, reversal of ivermectin-induced damage
El-Ratel *et al.* (2023)	Feed	25 mg/kg diet	Chemical Nano-Se	APRI bucks, 212–243 days	↑ Reproductive performance, improved biochemical and antioxidant status
Eid *et al.* (2019)	Intramuscular injection	4 ml/head	Chemical Nano-Se	NZW weaners, males, 35–91 days	↑ SOD, GPx, GSH, IgG, IgM, T3/T4; ↓ GSSG, NO, 8-OHdG, MDA (liver)
Emara (2019)	Intramuscular injection	4 ml/head	Chemical Nano-Se	NZW weaners, both sexes, 35–91 days	↑ FCR, ↑ liver and edible organ weights, no effect on carcass yield
Qin *et al.* (2016)	Feed	0.3 mg/kg diet	Chemical Nano-Se	NZW weaners, both sexes, 70–112 days	↑ BW, GPx, T-AOC, GPx-1 mRNA expression; ↔ Lipids, ALT, AST
Ali *et al.* (2021)	Drinking water	0.5, 1.0 mL/L in water	Chemical Nano-Se	NZW bucks, 152–236 days	↑ Seminal antioxidant status, ↑ sperm quality
Al-Sagheer *et al.* (2023)	Feed	0.3 mg/kg diet	Chemical Nano-Se	NZW weaners, males, 35–56 days	↑ Hemoglobin concentration, ↑ profitability

Note: [1]NZW: New Zealand White; CAL: Californian; BW: Body weight; FCR: feed conversion ratio.

better nutrient digestibility and metabolic efficiency. Abdel-Wareth *et al*. (2024) reported that the addition of Nano-Se, either alone or in combination with Nano-ZnO, improved BWG and feed efficiency, with the maximum being at a dietary level of 0.6 mg/kg. The improvements were associated with higher digestibility of crude protein and ether extract. Abd Allah *et al*. (2020) also documented similar findings, with 0.3 mg/kg Nano-Se treated rabbits exhibiting significantly greater BW, BWG, and improved FCR compared to the control. Emara (2019) also confirmed these findings, revealing that Nano-Se supplementation had a marked positive effect on daily gain (24.4 g/day), total gain (1465 g), and final BW (2092 g), with enhanced performance compared to other treatment groups ($p<0.0001$). Qin *et al*. (2016) also demonstrated that sodium selenite and Nano-Se (0.3 mg/kg diet) both promoted final BW, relative growth rate, daily gain, and feed intake, with greater effects in the Nano-Se group. Ali *et al*. (2021) once again proved these by reporting that Nano-Se supplementation via drinking water at 0.5 and 1.0 mL/L (100 mg/L solution) considerably improved BWG in breeding bucks, although feed intake was not significantly different from controls.

Similarly, El-Shobokshy *et al*. (2022) indicated that 0.2 mg/kg body weight of low-dose Nano-Se treatment considerably improved growth performance over inorganic selenium even in stressed animals under ivermectin stress. Sheiha *et al*. (2020) presented dose-dependent BW and BWG increases in Nano-Se-supplemented rabbits at 25 and 50 mg/kg diet. Bashar *et al*. (2024) also found that 50 mg/kg SeNPs improved FCR in the growth phase of 6-14 weeks, although no differences were reported in carcass attributes other than increased liver weight and edible giblets. Improvements in feed efficiency have been widely reported as well. Abdel-Wareth *et al*. (2022) found that 0.1 and 0.3 mg/kg Nano-Se and 30 or 60 mg/kg Nano-ZnO markedly increased feed intake and improved FCR. However, Ali *et al*. (2021) stated that although consumption of feed was not altered with drinking water supplying 0.5 and 1.0 mL/L Nano-Se, both doses greatly increased FCR, with no difference between the two levels. Similarly, Sheiha *et al*. (2020) exhibited dose-dependent responses on FCR by Nano-Se 25 and 50 mg/kg, and Abdel-Wareth *et al*. (2019) also observed that Nano-Se at 400 μg/kg as a single administration or in combination with 700 mg/kg garlic oil significantly enhanced FCR compared to controls. Carcass traits have also been reported to be enhanced by Nano-Se, but with variability depending on dosage and route of supplementation. Abdel-Wareth *et al*. (2024) showed that supplementing with 0.6 mg/kg Nano-Se and 40 mg/kg Nano-ZnO exhibited a significant improvement in dressing percentage and carcass yield, most likely because of improved nutrient utilization.

Moustafa *et al*. (2024) confirmed the same impacts for organic selenium and nano-selenium, attributing hot carcass weight and dressing percentage gains to live BW and average daily gain increments. Abd Allah *et al*. (2020) reported higher kidney and liver weights and greater muscle tissue mass in rabbits given 0.3 mg/kg of Nano-Se supplementation. The authors showed that such changes may be due to the antioxidant effects of selenium, which increase muscle growth and protect tissues against oxidative stress. Sheiha *et al*. (2020) also reported similar results with significant increases in liver, heart, lungs, kidneys, and spleen weights at higher concentrations of Nano-Se (25 and 50 mg/kg), indicating dose-dependent effect on organ growth. Bashar *et al*. (2024) also noted that 50 mg/kg dietary SeNPs significantly affected liver and edible giblet weights, but not other carcass traits.

While literature generally supports the beneficial role of Nano-Se in enhancing growth and carcass parameters, inconsistencies in experimental designs, selenium forms, and durations of supplementation highlight the need for standardization. Moreover, although increased organ weights may reflect enhanced metabolic function and protein synthesis, they also raise questions regarding physiological balance and consumer acceptability, especially when internal organ development becomes excessive.

Reproductive Performance and Fertility

Reproductive efficiency is a crucial determinant of profitability in rabbit production. Nano-Se has recently emerged as a promising additive to enhance fertility and reproductive outcomes in both male and female rabbits, especially under stressful conditions. El-Shobokshy *et al*. (2022) demonstrated that dietary supplementation of doe rabbits with Nano-Se (≥0.1 mg/kg), combined with Spirulina platensis, significantly improved litter size at birth and weaning, as well as neonatal survival. Notably, embryo yield increased significantly at Nano-Se levels over 0.2 mg/kg. Moreover, the encapsulation with Spirulina helped mitigate reproductive challenges during heat stress, likely via enhanced antioxidant capacity, immune function, and hormonal balance (e.g., elevated estradiol-17β, progesterone, prolactin). In another study, female rabbits receiving 0.2 mg/kg body weight of Nano-Se showed better reproductive outcomes - earlier puberty onset, higher conception rates, larger litter size, and increased birth weight, compared to those given 0.3 mg/kg dietary inorganic selenium, especially under ivermectin-induced reproductive stress (El-Shobokshy *et al*., 2022). This highlights Nano-Se's protective and performance-enhancing effects under pharmacological challenges. Equally compelling are the results in male rabbits. Ali *et al*. (2021) reported that supplementation with Nano-Se at concentrations equivalent to 0.05 and 0.10 mg per L of drinking water significantly improved semen quality. Higher doses (0.10 mg/L) enhanced sperm motility, concentration, and proportion of live and motile spermatozoa, while reducing abnormal forms ($p<0.01$). Semen volume and pH remained unchanged. Further, reproductive performance, assessed by kindling rate, number of kits born alive per litter, and litter weight at birth, was significantly improved with 0.05 and 0.10 mg/L Nano-Se, with stronger effects at the higher concentration ($p<0.01$). These findings collectively support the potential of Nano-Se to enhance reproductive traits by modulating oxidative stress, supporting hormonal regulation, and improving semen parameters. Its benefits hold for both female and male rabbits under normal and stressful conditions. Nevertheless, due to variability in dosage strategies and combinations with other nutrients, further research is needed to define optimal supplementation protocols. Future studies should investigate the molecular pathways by which Nano-Se regulates reproductive biology and establish safe and effective dosing guidelines for different production systems.

Hematological and Biochemical Parameters

Evaluation of hematological and biochemical markers provides superior data regarding rabbits' physiological and metabolic state to dietary supplementation. The majority of published research has examined the effect of nano-selenium (Nano-Se) on blood biochemistry and organ function, with results in the literature being comparatively inconsistent and, in some cases, contradictory. Several reports mentioned the beneficial effect of Nano-Se on liver and kidney functions, lipid metabolism, and levels of oxidative stress. Abdel-Wareth *et al*. (2024) have reported that 0.3 mg/kg supplementation with Nano-Se profoundly increased total plasma protein levels and improved hepatic and renal function. These modifications were also followed by lowering triglycerides and oxidative stress markers. Similarly, Sheiha *et al*. (2020) observed increased liver and kidney biomarkers, malondialdehyde and triglyceride reduction, and increased antioxidant enzyme activity in rabbits given Nano-Se. Abdel-Wareth *et al*. (2019) also revealed that diet supplementation with 400 μg/kg Nano-Se either alone or in combination with 700 mg/kg garlic oil significantly improved liver and kidney function compared to the control groups.

However, Qin *et al*. (2016) revealed no considerable effect of 0.3 mg/kg Nano-Se or sodium selenite on total protein, cholesterol, HDL, triglycerides, or liver enzyme activities (ALT, AST) in grown rabbits. In contrast, Tag-El Din (2019) revealed that combined supplementation with Nano-Se and Nano-ZnO caused an outstanding increase in certain biochemical parameters, including total protein, cholesterol, ALT, AST, albumin, globulin, creatinine, and urea. These findings indicate that synergistic effects with other trace minerals can improve the physiological response to Nano-Se. Further support for the hematological action of Nano-Se comes from Al-Sagheer *et al*. (2023), who discovered significantly higher hemoglobin concentrations in rabbits administered 0.3 mg/kg of Nano-Se, suggesting enhanced erythropoiesis and oxygen transport capacity. Also, El-Ratel *et al*. (2023) proved that co-treatment with Nano-Se and Spirulina platensis improved the red blood cell numbers and hemoglobin concentrations in doe rabbits and increased plasma levels of thyroid hormones [triiodothyronine (T3) and thyroxine (T4)], insulin, albumin, and total proteins. These enhancements are particularly relevant under stress conditions, where endocrine and metabolic stability are crucial. Additional data from Moustafa *et al.* (2024) demonstrated that although most blood plasma parameters were unaffected by dietary selenium supplementation, T4 concentrations increased significantly ($p \leq 0.05$) in rabbits receiving 0.05, 0.04, and 0.03 mg/kg of Nano-Se, in a dose-responsive pattern. The lowest levels were observed in the control group. Similarly, Eid *et al*. (2019) found that Nano-Se administration led to significant increases ($p<0.0001$) in both T3 and T4, with recorded means of 2.94 and 58.56 nmol/L, respectively. Interestingly, Nano-Se also increased AST (23.34 U/mL) while decreasing ALT activity compared to the control group ($p<0.0001$), suggesting a complex but favorable modulation of liver enzyme profiles. Collectively, these findings suggest that Nano-Se can positively influence hematological and biochemical markers by enhancing liver and kidney function, modulating lipid metabolism, boosting antioxidant defenses, and supporting endocrine regulation. However, the heterogeneity in findings, particularly concerning liver enzyme responses, highlights the importance of dose optimization and consideration of interactive effects with other dietary components.

Immunity and Antioxidant-Related Parameters

Both antioxidant defense and the immune system are interdependent on each other, existing to maintain physiological homeostasis as well as to protect rabbits from metabolic and environmental stresses. Selenium, particularly in its Nano-Se form, has been found to enhance such systems by allowing the synthesis of selenoproteins and maintaining redox balance. El-Ratel *et al*. (2023) quoted that Nano-Se supplementation of 25 mg/kg in rabbits' does greatly augmented the activity of superoxide dismutase (SOD), the most important enzyme involved in neutralization of reactive oxygen species (ROS). Concurrently, supplementation of 0.3, 0.4, and 0.5 mg/kg Nano-Se significantly reduced the levels of plasma malondialdehyde (MDA), a widely used marker of lipid peroxidation and oxidative damage. These processes are particularly significant in the context of physiological stress, such as reproduction and heat stress, when oxidative burdens rise. Similarly, Qin *et al*. (2016) demonstrated Nano-Se (0.3 mg/kg diet) significantly enhanced hepatic GPx activity and T-AOC in rabbits compared to control. GPx-1 mRNA expression was also enhanced by Nano-Se, suggesting direct activation of antioxidant defense mechanisms at the level of gene transcription. Interestingly, Nano-Se surpassed sodium selenite in these measures, reflecting its higher bioavailability and intra-cellular activity.

Eid *et al*. (2019) provided additional evidence for the antioxidant effectiveness of Nano-Se. Rabbits treated with Nano-Se showed notably elevated activities of SOD, GPx, GSH, TAC, and ATP in liver tissue, with maximum TAC at 527.52 U/g tissue versus 429.47 U/g in controls. On the other hand, Nano-Se lowered glutathione disulfide (GSSG), nitric oxide (NO), 8-hydroxy-2′-deoxyguanosine (8-oHdG), and MDA levels significantly. While MDA reductions in plasma were not notably different in some trials, liver tissue consistently showed antioxidant improvements. In addition, Nano-Se significantly improved serum immunoglobulin G (IgG) and immunoglobulin M (IgM), with IgM reaching a peak value of 35.30 ng/mL, showing a good immunostimulatory effect. Emara (2019) confirmed the antioxidant activity of Nano-Se by reporting a significant ($p<0.001$) increase in serum glutathione reductase (GR) and TAC and a remarkable reduction in MDA content, compared to controls. GR and TAC were elevated by 2.96 U/mL and 0.091 mM/L, respectively, with Nano-Se supplementation. These changes reflect improved endogenous defense systems and reduced oxidative stress. Antioxidant improvement was also noted in seminal plasma. Ali *et al*. (2021) also found that Nano-Se supplementation at 0.5 and 1.0 mL/L in drinking water resulted in a significant increase in the activity of total glutathione, GPx, SOD, and glutathione S-transferase (GST) ($p<0.01$) in reproductive bucks. These increases in seminal antioxidant enzymes may be responsible for improved sperm viability and fertility potential, as per the reproductive findings described in other sections. Taken as a whole, these findings point up the bivalent role of Nano-Se as a trace element and an antioxidant promoter. Through the induction of enzymatic antioxidants such as SOD, GPx, GR, and raising GSH and lowering oxidative markers like MDA, GSSG, and 8-oHdG, Nano-Se plays a part in cell protection, immune function enhancement, and increased physiological buffering. These effects are particularly relevant under conditions of stress, e.g., heat stress, inflammation, or reproductive stress, where there is heightened demand for antioxidant supplementation. These optimistic findings aside, variability in study designs, dosing regimens, and markers used makes it necessary to continue with further research to maximize supplementation regimens. Further research needs to explore the specific pathways by which Nano-Se affects inflammatory cytokines, immunoglobulin profiles, and immune cell function, to further illuminate its potential as an immunomodulator for application in rabbit production systems.

Economic Efficiency and Sustainability

In addition to its well-documented physiological and health contributions, supplementation with Nano-Se also holds great potential in augmenting the economic efficiency and sustainability of rabbit production operations. Improvement in growth performance, FCR, and nutrient utilization immediately translates into greater profitability because of reduced cost per unit of body weight gain. Al-Sagheer *et al*. (2023) reported that rabbits fed diets supplemented with 0.3 mg/kg of Nano-Se were found to have the highest profit margins among all the experimental groups. Surprisingly, gain in total body weight and return on gain increased by 12.95% and 27.7%, respectively, as compared to the control group. All these enhancements were essentially due to better feed efficiency and higher growth rate, thus reducing overall production costs. Concurrently, Moustafa *et al*. (2024) concluded that dietary supplementation with Nano-Se significantly improved net income and overall economic efficiency relative to control-diet-fed rabbits. Although organic selenium (e.g., 0.1 mg/kg selenium yeast) also led to positive economic impacts, the size of these benefits was smaller than with Nano-Se supplementation, confirming the greater cost–benefit ratio of the nanoparticulate product. Aside from economic returns, Nano-Se could also help make rabbit farming systems more environmentally sustainable. Enhanced nutrient digestibility and feed efficiency decrease overall feed input needs, which can minimize the carbon footprint and reduce nitrogen excretion in the environment. Moreover, the high bioavailability of Nano-Se allows for effective supplementation at lower doses compared to traditional inorganic selenium supplements and could minimize the risk of selenium tissue accumulation and decrease environmental contamination.

Sustainability advantages can be additionally magnified when Nano-Se is synthesized through green or biological pathways, such as microbial or plant-based reduction systems. Green synthesis pathways do not involve toxic solvents or harsh chemicals, which reduces the environmental impact while adhering to the tenets of sustainable nanotechnology. Biosynthesized Nano-Se, especially, can offer a safer and more ethically valid means of long-term trace mineral supplementation in agriculture. Taken together, the use of Nano-Se in rabbit feeding improves production performance and profitability, along with environmental sustainability. With its twin economic and environmental value, Nano-Se is put forward as a strategic feed supplement to promote sustainable intensification of rabbit production. Yet, more studies, including life cycle assessments and large-scale cost–benefit analysis, are required to assess its economic and environmental values in commercial production fully.

FUTURE RECOMMENDATIONS

The information presented herein highlights the Nano-Se's huge benefits in rabbit production, including increased growth rates, improved carcass quality, increased antioxidant activity, improved utilization of nutrients, and higher economic returns. Its high bioavailability and functional responsiveness make Nano-Se a very desirable choice to be added to sustainable and precision-based feeding regimens in rabbits. However, despite these encouraging findings, fears remain regarding the potential toxicity of selenium, most notably at high levels of addition or with long-term use. Even in nanoparticulate form, excessive selenium consumption has been shown to cause adverse effects such as weight loss, impairment of organs, and mortality risk enhancement in rabbits (Bano *et al*., 2022; Michalak *et al*., 2022). These findings emphasize the strong demand to define safe and efficient dose levels for Nano-Se under various manufacturing conditions. Further efforts should address dose–response studies to identify optimal inclusion rates between different breeds, physiological status, and environmental circumstances.

Particular emphasis needs to be placed on molecular mechanisms that control Nano-Se absorption, distribution among the tissues, and interaction with other nutrients, especially with vitamins and trace minerals. Also, studies of longer duration are required to evaluate the cumulative effect of Nano-Se on key health parameters, like immune response, oxidative state, organ integrity, and reproductive performance. At the same time, there is an urgent need to establish standardized methods for the efficient and safe use of Nano-Se in rabbit feed. These should include quality control methods for nanoparticle production, standard reporting of particle size and form, and consistent outcome measures across studies. Bridging these gaps will improve comparability among trials and accelerate the process of developing evidence-based recommendations. Lastly, the addition of Nano-Se to rabbit diets should be considered within the context of sustainable animal agriculture. Environmentally friendly synthesis routes, improved feed conversion ratio, and reduced nutrient excretion put Nano-Se at the forefront as an innovative approach toward both economic and ecological sustainability in rabbit production. Exploring its application in other animal species may further extend its use and help in more secure food production systems.

CONCLUSION

Nano-Se supplementation has emerged as a promising nutritional strategy for enhancing rabbit health, performance, and production efficiency. The optimal dietary selenium concentrations typically range from 0.05 to 0.3 mg/kg, depending on the diet composition. When Nano-Se is synthesized using biological or green methods, like microbial or plant-based reduction, its sustainability benefits can be significantly increased. These eco-friendly production techniques eliminate the need for toxic solvents and harsh chemicals, thereby lowering environmental impact and supporting the principles of sustainable nanotechnology. Further research is needed to establish accurate and safe guidelines for Nano-Se supplementation in sustainable rabbit production.

CONFLICTS OF INTEREST

K. El-Sabrout serves as editor of the Tropical Animal Science Journal but has no role in the decision to publish this article. The authors declare that there are no known conflicts of interest associated with this publication.

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DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the author(s), in some sentences, used Google Gemini v2.5, Grammarly v1.2, and QuillBot v28 in order to improve the readability and language of the manuscript. After using this tool/service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the publication.

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