



## Review Article

## New horizons for selenium in animal nutrition and functional foods

Xin Gu <sup>a, b</sup>, Chun-qi Gao <sup>a, \*</sup><sup>a</sup> Guangdong Provincial Key Laboratory of Animal Nutrition Control/Key Laboratory of Chicken Genetics, Breeding and Reproduction, Ministry of Agriculture, College of Animal Science, South China Agricultural University, Guangdong, China<sup>b</sup> College of Animal Sciences, Zhejiang University, Hangzhou, China

## ARTICLE INFO

## Article history:

Received 29 December 2021

Received in revised form

29 April 2022

Accepted 29 June 2022

Available online 5 July 2022

## Keywords:

Selenium

Antioxidant

Meat quality

Functional foods

## ABSTRACT

Selenium (Se), one of the indispensable nutrients for both human health and animal growth, participates in various physiological functions, such as antioxidant and immune responses and metabolism. The role of dietary Se, in its organic and inorganic forms, has been well documented in domestic animals. Furthermore, many feeding strategies for different animals have been developed to increase the Se concentration in animal products to address Se deficiency and even as a potential nutritional strategy to treat free radical-associated diseases. Nevertheless, studies on investigating the optimum addition of Se in feed, the long-term consequences of Se usage in food for animal nutrition, the mechanism of metallic Se nanoparticle (SeNP) transformation *in vivo*, and the nutritional effects of SeNPs on feed workers and the environment are urgently needed. Starting from the absorption and metabolism mechanism of Se, this review discusses the antioxidant role of Se in detail. Based on this characteristic, we further investigated the application of Se in animal health and described some unresolved issues and unanswered questions warranting further investigation. This review is expected to provide a theoretical reference for improving the quality of food animal meat as well as for the development of Se-based biological nutrition enhancement technology.

© 2022 The Authors. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co. Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Selenium (Se) has been reported to be one of the essential trace elements influencing the physiological function and growth performance of animals (Ferro et al., 2021). However, Se concentrations exceeding the biological requirements may lead to acute and chronic poisoning (Chantiratikul et al., 2018). Concerning livestock and poultry production, researchers have proposed that supplementation with appropriate Se doses not only plays a critical role in improving slaughter performance and the quality of livestock and poultry products but also promotes the enrichment of Se in animal tissues, thereby producing functional livestock products. Conversely, an overdose of Se generates oxygen radicals and

results in apoptosis by inducing oxidation and cross-linking of protein thiol groups essential for cell survival.

Based on the mechanisms of absorption and metabolism, this paper focuses on the roles of Se compounds, both organic and inorganic forms, in the defense against oxidants as well as their potential pro-oxidant properties. Based on these contrasting roles, we further discuss the effect of Se on the quality of livestock and poultry meat, providing a reference for research on biological Se enrichment technology and the development of Se-rich products.

## 1. Species of selenium

Se additives in animal feed are divided into 2 main forms: organic Se and inorganic Se. The general consensus is that organic Se, in the form of both selenoamino acids and Se-enriched yeast (SY), is more effective than inorganic Se at increasing growth performance, antioxidant status, and tissue Se concentration, as well as in improving the meat quality of livestock, mainly due to its higher bioavailability and tissue retention. Inorganic Se exists in the form of Se compounds with diverse valence states, including selenite (SeO<sub>3</sub><sup>2-</sup>), selenate (SeO<sub>4</sub><sup>2-</sup>), selenium (Se) and selenide (Se<sup>2-</sup>)

\* Corresponding author.

E-mail address: [cqgao@scau.edu.cn](mailto:cqgao@scau.edu.cn) (C.-q. Gao).

Peer review under responsibility of Chinese Association of Animal Science and Veterinary Medicine.



(Kieliszek, 2021). Se nanoparticles (SeNPs), inorganic Se molecules designed by regulating shape and size of the particle at the nanometer scale, have become an interesting topic of research in recent years. Compared with organic and traditional inorganic forms, SeNPs have been regarded as a promising feed additive to promote immune and antioxidant strength due to their novel properties, such as a large specific surface area, increased surface activity and reduced toxicity (Kumar and Prasad, 2021; Rana, 2021; Surai and Kochish, 2020). However, SeNPs are still at the beginning of their development, and in animal and poultry nutrition, they are still a minor source of Se and are not legal or regulated in Europe and the USA. Some concerns have also been raised about the toxicity of SeNPs and the optimal dosage of additives, which need to be further studied (Alian et al., 2020; Zheng et al., 2020).

## 2. Absorption and metabolism of selenium

The metabolic mechanism of Se in vivo is shown in Fig. 1. The uptake of Se from selenate and selenite is presumed to be realized through active transportation and passive diffusion in the small intestine, respectively. After absorption, selenate may undergo enzymatic activation with ATP to form adenosine-5'-selenophosphate, which is either catalyzed by thioredoxin or thioredoxin reductase (TrxR) or reduced to the intermediate selenodiglutathione by glutathione reductase, ultimately generating H<sub>2</sub>Se (Burk and Hill, 2015). Inorganically sourced Se recombines with other nutrients in the intestine, forming insoluble complexes that are excreted, which reduces the absorption of Se in the small intestine (Nemati et al., 2021).

In contrast to inorganic Se, the absorption of selenomethionine (SeMet) and selenocysteine is mediated by an amino acid uptake mechanism. SeMet is likely transformed into the intermediate product Sec through the transsulfuration pathway and then

subsequently decomposed into H<sub>2</sub>Se or undergoes transamination to demethylate into H<sub>2</sub>Se (Burk and Hill, 2015). Recently, a possible mechanism for the conversion of nano-Se to selenite has been proposed, suggesting that gut microbes convert nano-Se into selenite, Se-phosphate, or H<sub>2</sub>Se, leading to the synthesis of selenoproteins (Surai et al., 2017). As the branch point of 2 metabolic pathways, H<sub>2</sub>Se is ultimately converted into selenophosphate to supply Se in an active form for the synthesis of selenoproteins (Arnaut et al., 2021). On the other hand, some SeMet is incorporated into selenoenzymes or in place of Met to participate in the synthesis of selenoproteins, thereby increasing the total Se content in body tissues (Zhang et al., 2020a, 2020b). Thus, differences in the degrees of improvement of livestock products and human health with the use of different Se sources may be clarified by determining their probable metabolic pathways and absorption processes.

Unused Se is excreted as methyl selenide, dimethylselenide, and trimethylselenonium ion, among others, through feces, urine, and respiratory pathways (Cai et al., 2019).

## 3. Antioxidant mechanism of selenium

It is postulated that most of the antioxidant effects of Se are likely exerted by its presence in the form of catalytically active residues, SeMet, in reactive oxygen species (ROS)-detoxifying selenoenzymes (Schwarz et al., 2020). Se-containing proteins (selenoproteins), including glutathione peroxidase (GPx) (Chang et al., 2020; Sharma et al., 2021), TrxR (Jastrzab and Skrzydlewska, 2021; Jia et al., 2019; Mohammadi et al., 2019), and selenoprotein P (SeP) (Ha et al., 2019; Saito, 2020), are primarily implicated in maintaining redox homeostasis and reversing cell apoptosis induced by oxidative stress-related factors, suggesting that selenoproteins may protect against oxidant-induced toxicity in cells (Hariharan and Dharmaraj, 2020). The expression

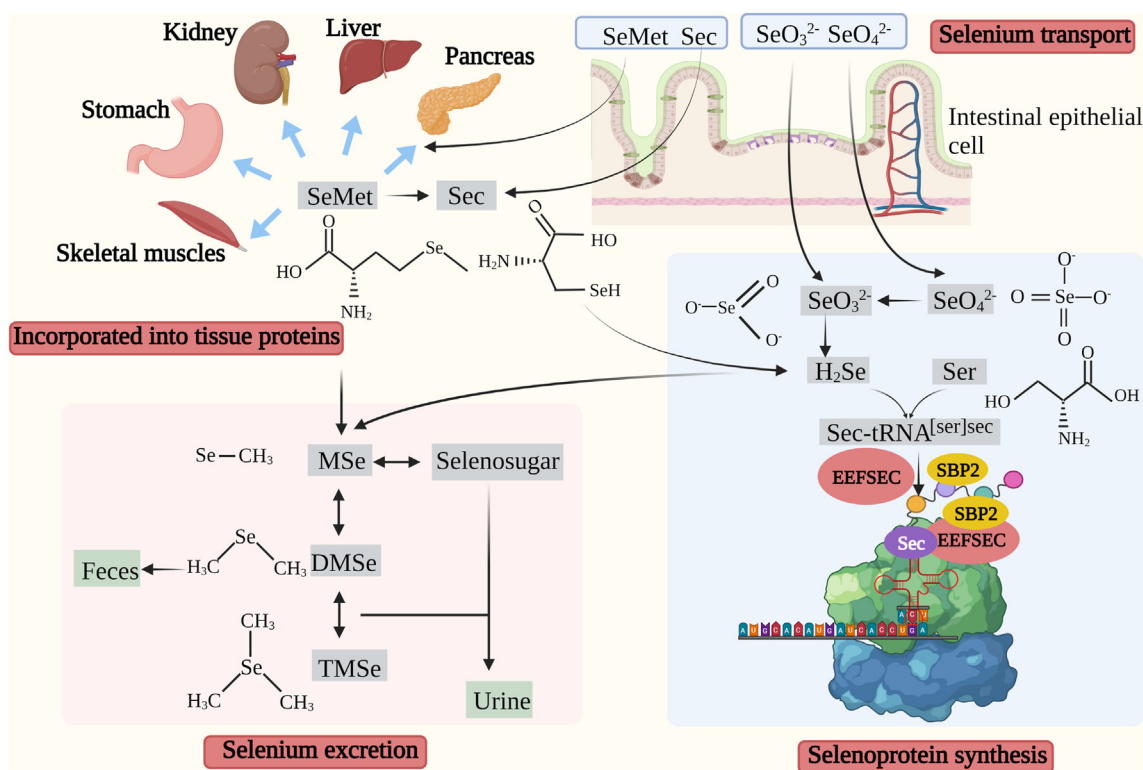


Fig. 1. The mechanism of selenium metabolism in vivo. DMSe = dimethylselenide; EEFSEC = selenocysteine elongation factor in eukaryotes; MSe = methylselenide; SBP2 = SECIS binding protein 2; Sec = selenocysteine; SeMet = selenomethionine; Ser = serine; TMSe = trimethylselenonium.

of selenoproteins is strictly controlled by the Se translation process, which is highly dependent on the full utilization of Se (Zoidis et al., 2014; Zwolak, 2020).

In addition to being present at the catalytic site of enzymes, Se compounds are implicated in direct redox reactions (Abdelnour et al., 2021; Dumore and Mukhopadhyay, 2020), with presumably higher rate constants for reactions with multiple oxidants than its sulfur analog (Rahmanto and Davies, 2012) due to the nucleophilic properties of ionized selenol and the ease of oxidation of Sec and SeMet (Kuras et al., 2018). Notably, accumulating evidence has emerged regarding the effects of a super physiological Se dose on generating oxygen radicals by inducing oxidation and cross-linking of protein thiol groups essential for cell survival (Lee and Jeong, 2012; Rehman et al., 2021) (Fig. 2). These contradictory roles pose new challenges to the development and application of Se in livestock production.

#### 4. Development of Se-based biological nutrition enhancement technology

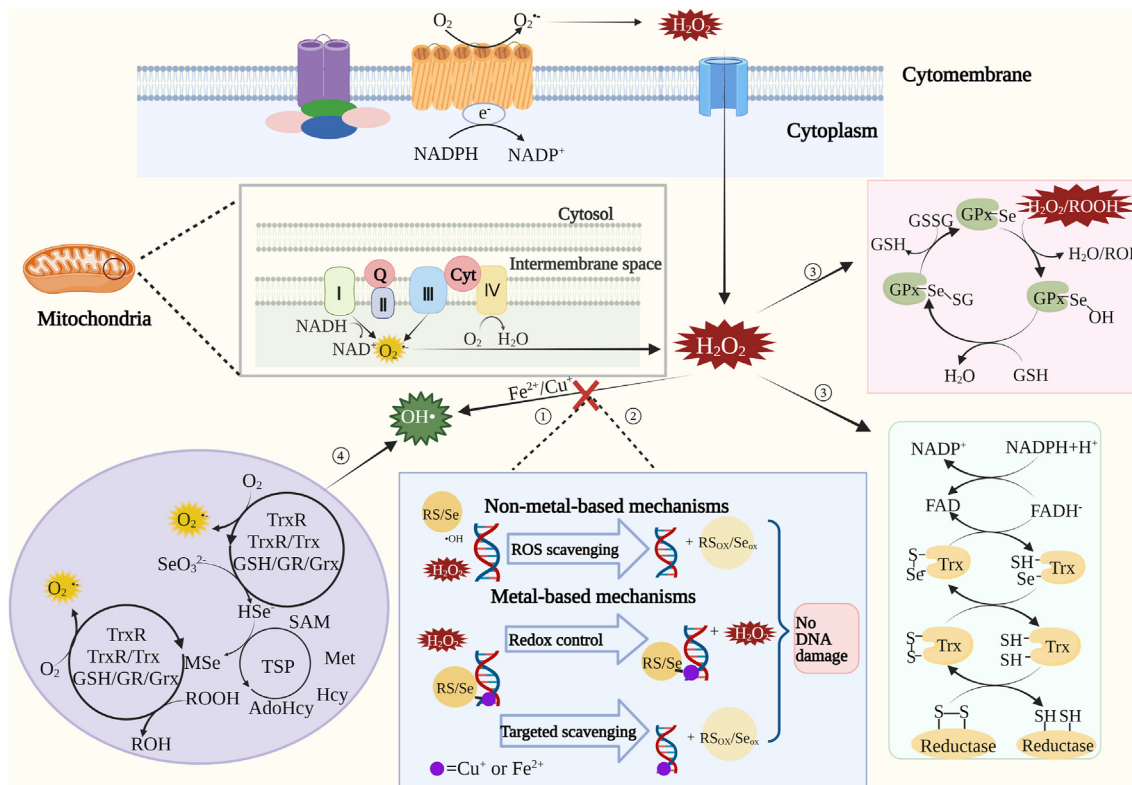
After slaughter, the collapse of the endogenous antioxidant system and the biochemical changes that occur during the conversion of muscle to meat are considered responsible for deteriorating meat quality. These alterations remarkably influence the physical and chemical properties of proteins, including solubility, water-holding capacity, and meat tenderness. In addition, protein oxidation decreases the bioavailability of amino acid residues, thus

negatively affecting the nutritional values of meat proteins. Lipid peroxidation is suggested to be responsible for the destruction of cell membrane integrity and pigment reduction systems, resulting in a reduced muscle water-holding capacity and meat discoloration along with an off-flavor (Zhang et al., 2013). Furthermore, increasing evidence indicates that the interactions between protein and lipid oxidation concomitantly lead to further oxidation.

Se, which is very important for the antioxidant defense system of cells, contributes to counteracting pro-oxidant factors and protecting against lipid and protein oxidation in meat (Carvalho et al., 2017). Se, particularly its organic form, helps to improve the overall total antioxidant capacity, avoiding changes in color and undesirable aroma formation (Grossi et al., 2021a,b), which may be the basis for improving the quality of livestock and poultry meat.

#### 4.1. Improving meat color

The biomolecular interactions between myoglobin and other factors, such as lipid oxidation, are widely accepted to jointly govern meat color, and the autoxidation of myoglobin is the main reason for deviations from bright cherry-red to brown (Ramanathan et al., 2020). Additionally, several studies have shown an underlying relationship between a change in meat color, lipid oxidation, and protein oxidation; the oxidation reactions occurring in the lipids and proteins are transferred to the myoglobin fraction, thereby affecting fresh meat color (Wang et al., 2021). In this case, strategies for supplementing Se to enhance the activity of



**Fig. 2.** Reactive oxygen species generation and bimodal actions of Se both as an antioxidant and pro-oxidant determined by intake concentrations. ① Direct scavenging of reactive oxygen species (ROS) by selenium compounds occurs through a nonmetal-based mechanism. ② Direct or indirect scavenging of ROS by selenium compounds occurs through a metal-based mechanism. ③ Se-containing amino acids exert biological and cellular effects as catalytically active residues in ROS-detoxifying selenoenzymes, thus protecting against oxidant-induced toxicity in cells and maintaining redox homeostasis. ④ An overdose of Se generates oxygen radicals and results in apoptosis by inducing oxidation. AdoHcy = S-adenosyl-homocysteine; Cyt = cytochrome; FAD = flavin adenine dinucleotide; GPx = glutathione peroxidase; GSH = glutathione; GR = glutathione reductase; Grx = glutaredoxin; GSH = glutathione; GSSG = glutathione disulfide; GPx = glutathione peroxidase; Hcy = homocysteine; MSe = methylselenide; Met = methionine; NADH = nicotinamide adenine dinucleotide; NADPH = nicotinamide adenine dinucleotide phosphate; RSe = redox selenide; RS = redox sulfide; RS = redox sulfide; RAC1 = ras-related C3 botulinum toxin substrate 1 protein; SAM = S-adenosylmethionine; TrxR = thioredoxin reductase; Trx = thioredoxin; TSP = transsulfuration pathway.

antioxidant selenoproteins such as GPx and thioredoxin would be useful in preserving the color of fresh meat by disrupting the co-oxidation reactions of myoglobin, lipids, and proteins (Carvalho et al., 2017) as well as promoting myoglobin synthesis (Chen et al., 2019; Li et al., 2018).

A study by Calvo et al. (2017) showed that dietary supplementation with organic Se improves the meat color of fattening pigs. Meanwhile, a significant increase in the redness ( $a^*$ ) and lightness ( $L^*$ ) of pork after slaughter and 7 days of cold storage was observed. This finding is consistent with other studies that have documented the unique role of hydroxy selenomethionine in inducing the early expression and enhancing the activity of GPx, thioredoxin, and SeP, thus maintaining an optimal meat color (Grossi et al., 2021a,b). Nevertheless, other authors reported an inverse relationship between excessive inorganic Se and meat color, and the paleness of tissue increased linearly with the addition of increasing levels of sodium selenite ( $\text{Na}_2\text{SeO}_3$ , SS) (Mahan et al., 1999). Researchers have speculated that the binding mode of inorganic Se with muscle tissue destroys the protein–water interaction structure, leading to a paler color (Jiang et al., 2017). As the most intuitive index of meat quality and an important index of meat product shelf-life management, the correlation between color changes and the quality of meat during storage has received increasing attention from consumers and researchers. Based on research examining the effect of Se on meat color and its internal mechanism, targeted measures to control the change in meat color and improve the stability of meat color may improve the sales of meat products.

#### 4.2. Increasing pH value

After slaughter, the relative increase in anaerobic respiration leads to the substantial accumulation of lactic acid, resulting in a decrease in the muscle pH value, which exerts an adverse effect on meat quality indexes such as tenderness, water-holding capacity, and color (Li et al., 2018). In terms of improving muscle pH, Se has been shown to increase the ability of muscle cells to scavenge the metabolite lactic acid. In addition, it seems to effectively enhance the elimination of  $\text{H}_2\text{O}_2$  by GPx, thus facilitating an increase in meat pH (Shin et al., 2021).

Calvo et al. (2017) detected a significant increase in the pH of meat 24 h after slaughter after treatment with Se-enriched yeast. Consistent with those observed results, other data have been reported on the opposite role of hydroxy selenomethionine in a postmortem low pH caused by chronic heat stress (Liu et al., 2021). Thus, a Se-enriched diet may be a good nutritional strategy for meat products with longer shelf lives due to the inhibition of microbial reproduction in meat by a low pH.

Nevertheless, Zhang et al. reported no significant effects on pH at 45 min and 24 h after slaughter among the Se treatment groups when using different sources of Se (Zhang et al., 2020a, 2020b), consistent with the findings of Zheng et al. (2020) and Silva et al. (2019a,b). The discrepancies among the results of these studies most likely result from the differences in the dosages and treatment times of Se, animal species, and feeding management.

#### 4.3. Reducing drip loss

The degradation of cytoskeletal proteins may lead to swelling of muscle cells to retain the water discharged from myofibrils. The activation of calcium-activated neutral proteases (calpains) produces a rapid fragmentation of intermediate protein filaments in meat, thereby preventing the shrinking of the whole muscle cell membrane (Hyatt and Powers, 2020). However, calpains are highly susceptible to oxidation and pH because of the histidine and SH-containing cysteine residues present in their active sites.

Meanwhile, a low pH inhibits the ability of muscle protein to bind water and reduces negative electrostatic repulsion between muscle filaments, resulting in the dehydration and contraction of myofibrils (Silva et al., 2019a,b). Moreover, lipid peroxidation induced by free radicals attacks polyunsaturated fatty acids in muscle, destroying the integrity of the muscle cell membrane, which is one of the leading causes of seepage of intracellular fluids (Chen et al., 2019). An increase in the meat antioxidant capacity caused by Se, namely, increased synthesis and activity of GPx, reduces calpain oxidation and membrane damage, thereby helping to modify drip loss (Grossi et al., 2021a,b; Zhang et al., 2020a, 2020b), whereas other evidence has highlighted the antioxidant capacity of activated calpains in enhancing muscle water-holding capacity by increasing pH and rapidly degrading intermuscular proteins (Pearce et al., 2011).

In a report by Zhang et al. (2020a, 2020b), a significant reduction in drip loss was observed after 24 and 48 h with the addition of organic Se (SeMet) or a combination of the organic form and inorganic form (SeMet + SS) to pig diets. Consistent with those observed results, a few studies have recorded a significantly lower drip loss in broilers in response to 0.3–0.6 mg/kg and 0.15 mg/kg SeNPs (Surai et al., 2018; Zhang et al., 2020a, 2020b). Interestingly, Li et al. (2011) found that a diet supplemented with SY at 3.0 mg of Se/kg increased the abundance of selenoprotein W1 mRNA and markedly improved the water retention of meat. Se-enriched probiotics, an effective feed additive that combines the beneficial qualities of organic Se and probiotics, prevent the induction of a low pH by increasing the expression of the GPx gene and down-regulating the expression of the heat shock protein 70 (HSP70) gene, thereby reducing the formation of lactic acid (Khan et al., 2018).

#### 4.4. Improving the muscle nutritional component

Accumulating evidence has described the insulin-mimetic effects of Se by activating Akt and other kinases responsible for triggering the insulin signaling cascade. Conversely, oxidative stress induced by Se deficiency enhances glycolysis and pentose phosphate pathways, accompanied by dysfunction of the tricarboxylic acid cycle, thereby regulating hepatic fat formation and lipolysis (Tang et al., 2020). The hypoglycemic effect of selenate might also be supported by other mechanisms, such as inhibition of intestinal glucose transport and accelerated renal glucose excretion (Mohamed et al., 2021).

The mechanisms described above may be at least partially responsible for the antioxidant effect of Se, which has been shown to persist in postmortem muscle tissue (Calvo et al., 2017; Ibrahim et al., 2019). Additionally, the mechanism underlying the effect of Se on muscle protein content appears to involve the change in iodine-thyronine deiodinase activity induced by selenoproteins, thereby regulating thyroid hormone secretion and muscle energy metabolism (Markovic et al., 2018). Presently, the effect of Se on muscle fat content and fatty acid composition remains a controversial issue.

According to the results obtained by Ibrahim et al., no significant effect on fat content in the breast, leg, liver, and abdomen of broilers was observed when using different Se sources (Ibrahim et al., 2019). In contrast to the effects described above, the percentage of intramuscular fat was reported to increase with increasing SY supplement levels (Markovic et al., 2018). This finding was similar to those obtained by Zhang et al., who reported a higher content of abdominal fat and backfat thickness in response to both dietary SY and the SeMet + SS combination compared with the control group supplemented with SS on the basal diet (Zhang et al., 2020a, 2020b). This finding might be explained by the fact

that Se provides some nutrients, such as vitamins, amino acids, and proteins, leading to subsequent increases in fat accumulation. Consistent with these findings, a study by Hassan revealed that Se supplementation increases lipid droplet accumulation in chicken embryonic fibroblasts (CEFs) in a dose-dependent manner, probably by enhancing the adipogenic determination and differentiation of CEFs. Furthermore, upregulation of an anti-lipolytic G0/G1 switch 2 and downregulation of a pro-lipolytic monoglyceride lipase resulted in the effect of Se restraining lipolysis, further supporting the pro-adipogenic role of Se (Hassan et al., 2014).

In contrast, Calvo et al. (2017) reported lower backfat thickness in pigs fed high doses of SY or Vitamin E (VE) + SS diets, indicating that Se compounds may have anti-adipogenic potential. These inconsistent conclusions may be attributed to the activation of GPx1 and SeP, which are responsible for reciprocal biomedical functions resulting in opposing directions: one mode is the enhancement of adipogenic differentiation in adipose tissue by accelerating the expansion of mitotic cloning and increasing key regulators of adipocyte differentiation, thus enhancing adipogenic differentiation, and the other is the activation of the protein kinase/heat shock protein pathway and stimulation of lipolysis (Wang et al., 2016).

Oxidative rancidity exerts negative effects on the sensory, nutritional, and shelf-life quality of animal products, especially meat with high polyunsaturated fatty acid (PUFA) contents, whose lipid oxidation products may greatly harm human health (Li et al., 2021). In this sense, several recent studies have obtained promising results for PUFA concentrations in response to organic Se (Shin et al., 2021), indirectly indicating the effect of Se on preventing meat from undergoing lipid oxidation and protecting PUFAs. The essential role of omega-3 (n-3) fatty acids in preventing cardiometabolic and inflammatory diseases is well known. PUFAs derived from animal foods, rather than purified dietary supplements, are combined with antioxidant nutrients such as Se and glutathione, further synergizing with long-chain n-3 fatty acids and inducing them to play an active role in protection (Gjerlaug-Enger et al., 2015). Accordingly, optimizing the Se content and the ratio of n-3 and n-6 fatty acids in livestock products has been considered a new target for increasing the intake of Se and long-chain n-3 fatty acids in humans. Concerning a healthier meat product for human consumption, Gjerlaug-Enger et al. (2015) found that diets rich in rapeseed products and organic Se efficiently increased n-3 fatty acid and Se contents in pork and backfat, indicating that the production of high-quality pork through ameliorative animal nutrition is a broad strategy for regulating the dietary fatty acid balance.

Nevertheless, differences in lipid composition may also lead to products with different sensory properties. The effect of Se on the contents of fat and fatty acids in livestock and poultry muscles, as well as its mechanism, requires further investigation.

#### 4.5. Increasing selenium deposition in muscle

When discussing Se enrichment in animal products, several studies using a Se-enriched diet showed a trend of greater effectiveness in the accumulation of organic than inorganic forms in muscle (Grossi et al., 2021a,b). The mechanism underlying these better effects appears to involve different metabolic pathways. SeMet is metabolized either directly to reactive forms that are incorporated in selenoproteins or in place of Met in proteins (Chen et al., 2019), indicating that organic Se can be efficiently used and participates in Se deposition in meat-producing livestock.

According to a study by Zhang et al., 2020a, 2020b, who compared the effects of different Se compounds (MeSeCys, SeMet, and SeNa) on the tissue Se content and selenoprotein gene expression in finishing pigs, SeMet was proven to increase Se

concentrations more effectively, while MeSeCys was the most efficient in increasing the mRNA expression of selenoproteins among the three forms. Similar results were observed in broiler tissues (Woods et al., 2020). Furthermore, Soliman et al. (2020) concluded that the increased retention of Se in tissues is accompanied by SeNP supplementation at a rate of 0.3 mg/kg of diet rather than inorganic Se. The current results confirmed that SeNP tissue residues disappeared earlier in the liver and muscles than inorganic Se, which may be attributed to the nanoparticle size. Based on these results, the organic form may be used as an effective source of Se supplements for animals and even humans. This promising evidence represents the beginning of organic Se application, which will ultimately lead to the complete replacement of inorganic Se as a feed additive. These conclusions support the potential to produce Se-enriched pork via supplementation of animal feed. Animal products that accumulate Se are anticipated to contribute to a new strategy for increasing the average daily Se intake and solving Se deficiency in human nutrition, which is a national and global issue.

## 5. Discussion

With the increasing demand for healthy food, increasing interest in safe and high-quality animal products with longer shelf lives has been observed. Se is an essential trace element for both human and livestock health that is necessary for numerous metabolic processes, such as antioxidant defense capacity, immune function, and reproductive function, thereby effectively reducing the risk of many diseases. The World Health Organization (WHO) recommends a daily Se dose of 55 µg for adults, and 400 µg is considered harmless. The Food and Nutrition Board (FNB) in the US has also acknowledged that the nutritional requirement for Se changes with age, ranging from 40 to 70 µg for men and 45 to 55 µg for women (Kieliszek, 2021). Unfortunately, insufficient sources of Se in human diets due to its low content in food products has become a global problem. Conversely, the results derived from clinical studies suggest that the enrichment of animal-derived foods with Se via supplementation of animal feed may be an effective method for addressing Se deficiencies and simultaneously providing some protection against cancer. Therefore, Se-enriched food, which provides organic forms of Se with the highest bioavailability in ready-to-use products to supplement micronutrient deficiencies and maintain the metabolic balance of organisms, has attracted extensive attention. In pork, the increased Se content without a reduction in production performance indicates its comparatively low toxicity and the commercial opportunities for using organic Se at high doses to produce Se-enriched pork. Similarly, beef is considered a potential major source of dietary Se with the inclusion of Se in cattle feed. Therefore, the addition of Se to cattle feed should be further investigated.

Importantly, Se has been shown to possess a dual-targeting modality with both pro-oxidant and antioxidant potential, depending on the duration, dose and oxidation state. At the physiological level, Se significantly reduces ROS levels and improves intracellular antioxidant activity, which leads to other important improvements in meat quality in addition to increased Se levels in meat, including better color, lower drip loss, extended shelf life, and improved nutritional composition. This antioxidant effect is the basis for the development of high-quality meat that optimizes the function of Se in preventing chronic diseases induced by pro-oxidant/inflammatory factors. Conversely, excessive Se intake is responsible for excess ROS generation, impaired antioxidant defenses, and reduced cell viability, which has been considered the major mechanism of Se-induced cytotoxicity and anticarcinogenic effects. These bimodal actions pose challenges to the effective use

of Se in livestock and poultry production. Therefore, the oxidation mechanisms of different Se sources and their effects on meat quality must be conclusively determined to drive research on biological Se-rich technology and the development of functional meat products as oxidative stress modulators and even potential strategies for cancer treatment. Moreover, it is essential to address the following questions related to the application of Se as a feed additive to avoid any adverse effects on livestock, the environment, and humans: 1) Does uncontrolled and enhanced SeNP penetration through cell barriers exert a negative effect on animal health? 2) Does the application of Se in animal nutrition exert a long-term negative effect? 3) Are the nanosized Se particles in feed harmful to the health of feed workers?

### Declaration of competing interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service or company that could be construed as influencing the content of this paper.

### Acknowledgments

This work was jointly supported by grants from the National Natural Science Foundation of China (31972585), the Guangdong Basic and Applied Basic Research Foundation (2019B1515210001), and the Technical System of Poultry Industry of Guangdong Province, China (2021KJ128).

### References

- Abdelnour SA, Alagawany M, Hashem NM, Farag MR, Alghamdi ES, Hassan FU, et al. Nanominerals: Fabrication methods, benefits and hazards, and their applications in ruminants with special reference to selenium and zinc nanoparticles. *Animals (Basel)* 2021;11:1916.
- Alian HA, Samy HM, Ibrahim MT, Mahmoud M. Nanoselenium effect on growth performance, carcass traits, antioxidant activity, and immune status of broilers. *Environ Sci Pollut Res Int* 2020;27:38607–16.
- Arnaut PR, Da SVG, Da FL, Alves WJ, Muniz J, Pettigrew JE, et al. Selenium source and level on performance, selenium retention and biochemical responses of young broiler chicks. *BMC Vet Res* 2021;17:151.
- Burk RF, Hill KE. Regulation of selenium metabolism and transport. *Annu Rev Nutr* 2015;35:109–34.
- Cai Z, Zhang J, Li H. Selenium, aging and aging-related diseases. *Aging Clin Exp Res* 2019;31:1035–47.
- Calvo L, Segura J, Toldra F, Flores M, Rodriguez AI, Lopez-Bote CJ, et al. Meat quality, free fatty acid concentration, and oxidative stability of pork from animals fed diets containing different sources of selenium. *Food Sci Technol Int* 2017;23:716–28.
- Carvalho RH, Ida EI, Madruga MS, Martinez SL, Shimokomaki M, Estevez M. Underlying connections between the redox system imbalance, protein oxidation and impaired quality traits in pale, soft and exudative (PSE) poultry meat. *Food Chem* 2017;215:129–37.
- Chang C, Worley BL, Phaëton R, Hempel N. Extracellular glutathione peroxidase GPx 3 and its role in cancer. *Cancers* 2020;12:2197.
- Chantiratikul A, Chinrasri O, Chantiratikul P. Effect of selenium from Selenium-Enriched kale sprout versus other selenium sources on productivity and selenium concentrations in egg and tissue of laying hens. *Biol Trace Elem Res* 2018;182:105–10.
- Chen J, Tian M, Guan W, Wen T, Yang F, Chen F, et al. Increasing selenium supplementation to a moderately-reduced energy and protein diet improves antioxidant status and meat quality without affecting growth performance in finishing pigs. *J Trace Elem Med Biol* 2019;56:38–45.
- Dumore NS, Mukhopadhyay M. Antioxidant properties of aqueous selenium nanoparticles (AsENPs) and its catalysts activity for 1, 1-diphenyl-2-picrylhydrazyl (DPPH) reduction. *J Mol Struct* 2020;1205:127637.
- Ferro C, Florindo HF, Santos HA. Selenium nanoparticles for biomedical applications: from development and characterization to therapeutics. *Adv Health Mater* 2021;10:e2100598.
- Gjerlaug-Enger E, Haug A, Gaarder M, Ljokjel K, Stenseth RS, Sigfridson K, et al. Pig feeds rich in rapeseed products and organic selenium increased omega-3 fatty acids and selenium in pork meat and backfat. *Food Sci Nutr* 2015;3:120–8.
- Grossi S, Rossi L, De Marco M, Sgoifo RC. The effect of different sources of selenium supplementation on the meat quality traits of young charolaise bulls during the finishing phase. *Antioxidants* 2021a;10:596.
- Grossi S, Rossi L, De Marco M, Sgoifo Rossi CA. The effect of different sources of selenium supplementation on the meat quality traits of young charolaise bulls during the finishing phase. *Antioxidants* 2021b;10:596.
- Ha HY, Alfulajij N, Berry MJ, Seale LA. From selenium absorption to selenoprotein degradation. *Biol Trace Elem Res* 2019;192:26–37.
- Hariharan S, Dharmaraj S. Selenium and selenoproteins: It's role in regulation of inflammation. *Inflammopharmacology* 2020;28:667–95.
- Hassan A, Ahn J, Suh Y, Choi YM, Chen P, Lee K. Selenium promotes adipogenic determination and differentiation of chicken embryonic fibroblasts with regulation of genes involved in fatty acid uptake, triacylglycerol synthesis and lipolysis. *J Nutr Biochem* 2014;25:858–67.
- Hyatt HW, Powers SK. The role of calpains in skeletal muscle remodeling with exercise and inactivity-induced atrophy. *Int J Sports Med* 2020;41:994–1008.
- Ibrahim D, Kishawy A, Khater SI, Hamed AA, Mohammed HA, Abdelaziz AS, et al. Effect of dietary modulation of selenium form and level on performance, tissue retention, quality of frozen stored meat and gene expression of antioxidant status in ross broiler chickens. *Animals (Basel)* 2019;vol. 9.
- Jastrzab A, Skrzydlewska E. Thioredoxin-dependent system. Application of inhibitors. *J Enzym Inhib Med Chem* 2021;36:362–71.
- Jia JJ, Geng WS, Wang ZQ, Chen L, Zeng XS. The role of thioredoxin system in cancer: strategy for cancer therapy. *Cancer Chemother Pharmacol* 2019;84:453–70.
- Jiang J, Tang X, Xue Y, Lin G, Xiong YL. Dietary linseed oil supplemented with organic selenium improved the fatty acid nutritional profile, muscular selenium deposition, water retention, and tenderness of fresh pork. *Meat Sci* 2017;131:99–106.
- Khan AZ, Kumbhar S, Liu Y, Hamid M, Pan C, Nido SA, et al. Dietary supplementation of selenium-enriched probiotics enhances meat quality of broiler chickens (*Gallus gallus domesticus*) raised under high ambient temperature. *Biol Trace Elem Res* 2018;182:328–38.
- Kieliszek M. Selenium. *Adv Food Nutr Res* 2021;96:417–29.
- Kumar A, Prasad KS. Role of nano-selenium in health and environment. *J Biotechnol* 2021;325:152–63.
- Kuras R, Janasik B, Stanislawski M, Wasowicz W. Revision of the reciprocal action of mercury and selenium. *Int J Occup Med Env* 2018;31(5):575–92.
- Lee KH, Jeong D. Bimodal actions of selenium essential for antioxidant and toxic oxidant activities: the selenium paradox (Review). *Mol Med Rep* 2012;5:299–304.
- Li JG, Zhou JC, Zhao H, Lei XG, Xia XJ, Gao G, et al. Enhanced water-holding capacity of meat was associated with increased Sepw1 gene expression in pigs fed selenium-enriched yeast. *Meat Sci* 2011;87:95–100.
- Li JL, Zhang L, Yang ZY, Zhang ZY, Jiang Y, Gao F, et al. Effects of different selenium sources on growth performance, antioxidant capacity and meat quality of local Chinese subei chickens. *Biol Trace Elem Res* 2018;181:340–6.
- Li N, Jia M, Deng Q, Wang Z, Huang F, Hou H, et al. Effect of low-ratio n-6/n-3 PUFA on blood lipid level: a meta-analysis. *Hormones (Basel)* 2021;20:697–706.
- Liu Y, Yin S, Tang J, Liu Y, Jia G, Liu G, et al. Hydroxy selenomethionine improves meat quality through optimal skeletal metabolism and functions of selenoproteins of pigs under chronic heat stress. *Antioxidants* 2021;10:1558.
- Mahan DC, Cline TR, Richert B. Effects of dietary levels of selenium-enriched yeast and sodium selenite as selenium sources fed to growing-finishing pigs on performance, tissue selenium, serum glutathione peroxidase activity, carcass characteristics, and loin quality. *J Anim Sci* 1999;77:2172–9.
- Markovic R, Ciric J, Drljacic A, Sefer D, Jovanovic I, Jovanovic D, et al. The effects of dietary Selenium-yeast level on glutathione peroxidase activity, tissue Selenium content, growth performance, and carcass and meat quality of broilers. *Poultry Sci* 2018;97:2861–70.
- Mohamed AA, Khater SI, Hamed AA, Metwally M, Mostafa-Hedeab G, El-Shetry ES. Chitosan-stabilized selenium nanoparticles alleviate cardio-hepatic damage in type 2 diabetes mellitus model via regulation of caspase, Bax/Bcl-2, and Fas/FasL-pathway. *Gene* 2021;768:145288.
- Mohammadi F, Soltani A, Ghahremanloo A, Javid H, Hashemy SI. The thioredoxin system and cancer therapy: a review. *Cancer Chemother Pharmacol* 2019;84:925–35.
- Nemati Z, Alirezalu K, Besharati M, Holman B, Hajipour M, Bohrer BM. The effect of dietary supplementation with inorganic or organic selenium on the nutritional quality and shelf life of goose meat and liver. *Animals (Basel)* 2021;11:261.
- Pearce KL, Rosenvold K, Andersen HJ, Hopkins DL. Water distribution and mobility in meat during the conversion of muscle to meat and ageing and the impacts on fresh meat quality attributes—a review. *Meat Sci* 2011;89:111–24.
- Rahmanto AS, Davies MJ. Selenium-containing amino acids as direct and indirect antioxidants. *IUBMB Life* 2012;64:863–71.
- Ramanathan R, Suman SP, Faustman C. Biomolecular interactions governing fresh meat color in post-mortem skeletal muscle: a review. *J Agric Food Chem* 2020;68:12779–87.
- Rana T. Nano-selenium on reproduction and immunocompetence: an emerging progress and prospect in the productivity of poultry research. *Trop Anim Health Prod* 2021;53:324.
- Rehman A, John P, Bhatti A. Biogenic selenium nanoparticles: potential solution to oxidative stress mediated inflammation in rheumatoid arthritis and associated complications. *Nanomaterials* 2021:11.
- Saito Y. Selenoprotein P as an in vivo redox regulator: Disorders related to its deficiency and excess. *J Clin Biochem Nutr* 2020;1:1–7.
- Schwarz M, Lossow K, Schirl K, Hackler J, Renko K, Kopp JF, et al. Copper interferes with selenoprotein synthesis and activity. *Redox Biol* 2020;37:101746.

- Sharma G, Shin EJ, Sharma N, Nah SY, Mai HN, Nguyen BT, et al. Glutathione peroxidase-1 and neuromodulation: novel potentials of an old enzyme. *Food Chem Toxicol* 2021;148:111945.
- Shin YG, Rathnayake D, Mun HS, Dilawar MA, Pov S, Yang CJ. Sensory attributes, microbial activity, fatty acid composition and meat quality traits of hanwoo cattle fed a diet supplemented with stevioside and organic selenium. *Foods* 2021;10.
- Silva VA, Bertechini AG, Clemente A, de Freitas L, Nogueira B, de Oliveira BL, et al. Different levels of selenomethionine on the meat quality and selenium deposition in tissue of finishing pigs. *J Anim Physiol Anim Nutr* 2019a;103:1866–74.
- Silva VA, Clemente A, Nogueira B, de Carvalho AC, de Freitas L, Ramos A, et al. Supplementation of selenomethionine at different ages and levels on meat quality, tissue deposition, and selenium retention in broiler chickens. *Poultry Sci* 2019b;98:2150–9.
- Soliman ES, Mahmoud FF, Fadel MA, Hamad RT. Prophylactic impact of nano-selenium on performance, carcasses quality, and tissues' selenium concentration using reversed-phase high-performance liquid chromatography during microbial challenge in broiler chickens. *Vet World* 2020;13:1780–97.
- Surai PF, Kochish II. Food for thought: nano-selenium in poultry nutrition and health. *Anim Health Res Rev* 2020;21:103–7.
- Surai PF, Kochish II, Fisinin VI, Velichko OA. Selenium in poultry nutrition: from sodium selenite to organic selenium sources. *J Poultry Sci* 2018;55:79–93.
- Surai PF, Kochish II, Velichko OA. Nano-Se assimilation and action in poultry and other monogastric animals: is gut microbiota an answer? *Nanoscale Res Lett* 2017;12:612.
- Tang C, Li S, Zhang K, Li J, Han Y, Zhan T, et al. Selenium deficiency-induced redox imbalance leads to metabolic reprogramming and inflammation in the liver. *Redox Biol* 2020;36:101519.
- Wang X, Wu H, Long Z, Sun Q, Liu J, Liu Y, et al. Differential effect of Se on insulin resistance: regulation of adipogenesis and lipolysis. *Mol Cell Biochem* 2016;415:89–102.
- Wang Z, Tu J, Zhou H, Lu A, Xu B. A comprehensive insight into the effects of microbial spoilage, myoglobin autoxidation, lipid oxidation, and protein oxidation on the discoloration of rabbit meat during retail display. *Meat Sci* 2021;172:108359.
- Woods SL, Sobolewska S, Rose SP, Whiting IM, Blanchard A, Ionescu C, et al. Effect of feeding different sources of selenium on growth performance and antioxidant status of broilers. *Br Poultry Sci* 2020;61:274–80.
- Zhang K, Zhao Q, Zhan T, Han Y, Tang C, Zhang J. Effect of different selenium sources on growth performance, tissue selenium content, meat quality, and seleno-protein gene expression in finishing pigs. *Biol Trace Elem Res* 2020a;196:463–71.
- Zhang S, Xie Y, Li M, Yang H, Li S, Li J, et al. Effects of different selenium sources on meat quality and shelf life of fattening pigs. *Animals (Basel)* 2020b;10:615.
- Zhang W, Xiao S, Ahn DU. Protein oxidation: Basic principles and implications for meat quality. *Crit Rev Food Sci Nutr* 2013;53:1191–201.
- Zheng Y, Dai W, Hu X, Hong Z. Effects of dietary glycine selenium nanoparticles on loin quality, tissue selenium retention, and serum antioxidation in finishing pigs. *Anim Feed Sci Technol* 2020;260:114345.
- Zoidis E, Demiris N, Kominakis A, Pappas AC. Meta-analysis of selenium accumulation and expression of antioxidant enzymes in chicken tissues. *Animal* 2014;8:542–54.
- Zwolak I. The role of selenium in arsenic and cadmium toxicity: an updated review of scientific literature. *Biol Trace Elem Res* 2020;193:44–63.