

## Effects of Selenium on Sow Reproductive Performance and Its Mechanism of Action: Postprint

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### Abstract

Selenium is one of the essential trace elements in animal organisms. Supplementation of selenium in sow diets can effectively improve their reproductive performance. Research indicates that selenium enhances the antioxidant capacity of sows through selenoproteins and synergistic action with vitamin E, and regulates sow reproductive performance through metabolic modulation of deiodinases and pancreatic digestive enzymes. This paper reviews the effects of selenium on sow reproductive performance and its potential mechanisms of action, aiming to provide a reference for related in-depth research and rational application of selenium in sows.

### Full Text

## Effects of Selenium on Reproductive Performance of Sows and Its Mechanism

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### Abstract

Selenium is one of the essential trace elements for animals, and dietary selenium supplementation can effectively improve the reproductive performance of sows. Studies have shown that selenium enhances sow antioxidant capacity through selenoproteins and synergistic action with vitamin E, and regulates reproductive performance through metabolic modulation of deiodinases and pancreatic digestive enzymes. This paper reviews the effects of selenium on sow reproductive performance and its potential mechanisms, aiming to provide references for related research and rational application of selenium in sows.

**Keywords:** selenium; sows; reproductive performance; effects; mechanism

Since 1957, selenium has been identified as an essential trace element for animals, and subsequent research has gradually deepened our understanding of this nutrient. Studies have demonstrated that selenium plays important roles in promoting growth, resisting oxidative stress, enhancing immune function and reproductive performance, anti-aging, anti-tumor effects, and alleviating metal toxicity. Sow reproductive performance is crucial for pig production, yet oxidative stress can adversely affect the reproductive performance and welfare of modern high-yielding sows, causing issues such as poor ovulation quality. Dietary supplementation of antioxidants like selenium in sow feed can effectively improve reproductive performance and consequently enhance the direct economic benefits of farming operations. Therefore, this paper reviews the effects of selenium on sow reproductive performance and its potential mechanisms to provide references for further research and rational selenium application in sows.

## 1 Distribution and Utilization Forms of Selenium

Selenium content and distribution in soil vary across different countries and regions [1]. Soil selenium content typically ranges from 0.1 to 2.0 mg/kg, existing as elemental selenium, inorganic selenides, and organic selenides [2]. The mid-western United States [3-4] and China's Enshi in Hubei Province and Ziyang in Shaanxi Province have been reported as typical high-selenium regions. The Great Lakes region, northeastern United States, and parts of the West Coast are low-selenium areas. In China, selenium-deficient regions form a northeast-to-southwest belt, including parts of Heilongjiang, Sichuan, and Chongqing [4-5].

In practical production, the inorganic selenium added to livestock feed is mostly sodium selenite ( $\text{Na SeO}_3$ ), while organic selenium is primarily selenium yeast [6]. Sodium selenite contains 98.0% of the compound and 44.7% selenium. Selenium yeast is produced through fermentation, where yeast converts inorganic selenium into various organic forms, mainly selenomethionine, which accounts for 60%-70% of total selenium content [6-8].

## 2 Absorption and Metabolism of Selenium

Selenium is primarily absorbed in the small intestine, with most forms being effectively absorbed, though subsequent metabolism differs depending on the source and form of selenium [9-11]. Selenite is passively absorbed through simple diffusion across the intestinal wall, while selenate is absorbed through co-transport with sodium ions, similar to sulfate [9-10]. Selenomethionine and selenocysteine are actively absorbed via amino acid transport mechanisms [4,12]. Groce et al. [13] reported that the apparent digestibility of sodium selenite and organic selenium from corn in pigs was 71.8% and 64.2%, respectively. Mahan et al. [14] demonstrated through balance trials that the apparent digestibility of sodium selenite in growing pigs ranged from 73.9% to 80.5%, while that of selenium-enriched yeast ranged from 70.8% to 75.2%.

Mammalian cells cannot distinguish between methionine and selenomethionine, allowing selenomethionine to enter the methionine pool and directly (non-specifically) incorporate into body proteins or be catabolized [9,11]. The metabolic mechanism of exogenous selenium in cells under genetic control involves: (1) selenomethionine conversion to selenocysteine and then to hydrogen selenide; (2) selenate reduction to selenite, then to oxidized glutathione, selenopersulfide, and hydrogen selenide; and (3) hydrogen selenide metabolism to methylselenol, dimethylselenide, and trimethylselenonium ion, or conversion to selenophosphate for selenoprotein synthesis [15-17]. Synthesized selenoproteins are widely distributed throughout animal tissues and organs, performing corresponding biological functions.

### 3 Effects of Selenium on Sow Reproductive Performance

Selenium deficiency adversely affects animal growth, reproduction, and antioxidant stress resistance, while excess selenium can cause toxicity [1-3,7,18]. The NRC (2012) [19] recommends dietary selenium requirements of 0.15-0.30 mg/kg for pigs, with 0.15 mg/kg for gestating and lactating sows. China's "Feeding Standard of Swine" (NY/T 65-2004) recommends 0.14 mg/kg selenium for lean-type gestating sows and 0.15 mg/kg for lactating sows, while meat-fat type sows require 0.15 mg/kg for both stages. The "Safety Specification for Feed Additives" (Ministry of Agriculture Announcement No. 1224) stipulates a maximum limit of 0.50 mg/kg (as elemental selenium) for sodium selenite or selenium yeast in complete feed or total mixed rations, which should first be prepared as a premix.

#### 3.1 Effects of Selenium on Reproductive Performance of Gilts

Dalto et al. [20] suggested that dietary selenium at 0.3 mg/kg helps improve basal ovulation rate in sows, as selenium participates in cell proliferation of small follicles and responds to gonadotropin stimulation. From first estrus, adding 0.3 mg/kg organic or inorganic selenium to diets containing 0.2 mg/kg selenium had no significant effect on conception rate. However, compared with inorganic selenium, organic selenium increased average embryo length, weight, and protein and DNA content by 5.5%, 11.5%, 11.6%, and 9.0%, respectively, likely due to enhanced embryonic cell proliferation [21].

When gilts were fed diets supplemented with 0.3, 3.0, 7.0, or 10.0 mg/kg inorganic or organic selenium starting at 25 kg body weight, litter size at birth, number of weaned piglets, and litter weight gain decreased with increasing selenium levels. Compared with inorganic selenium, organic selenium resulted in lower litter size at birth, number of weaned piglets, and litter weight gain. At supplementation levels of 7 and 10 mg/kg organic selenium, piglet birth litter weight and individual birth weight were 11.39 and 10.38 kg, and 1.32 and 1.25 kg, respectively, with 7.00 and 6.67 weaned piglets [22]. Feeding diets containing 0.3 mg/kg organic or inorganic selenium starting 60 days before mating had no

significant effect on litter size [23]. Studies on growing-finishing pigs indicated that dietary selenium levels exceeding 5 mg/kg reached toxic doses [24].

These studies demonstrate that appropriate selenium levels benefit gilt reproductive performance, while excessive selenium (>5 mg/kg) causes toxicity and reduces reproductive performance. Due to higher bioavailability of organic selenium compared to inorganic selenium, equivalent high doses of organic selenium cause greater harm.

### **3.2 Effects of Selenium on Reproductive Performance of Gestating and Lactating Sows**

Studies showed that compared with sodium selenite, dietary selenomethionine at 0.3 mg/kg for gestating and lactating sows significantly increased average daily gain of piglets from birth to weaning by 12.20% [8]. Hu et al. [25] added 0.3 mg/kg inorganic or organic selenium to gestating and lactating sow diets, finding that organic selenium significantly improved piglet average daily gain, 28-day body weight, and 28-day litter weight compared with inorganic selenium.

Other reports indicated that when dietary selenium was 0.085 mg/kg for gestating sows, adding 0.3 mg/kg organic or inorganic selenium had no significant effect on total litter size, live-born litter size, stillbirth number, or piglet birth weight. When dietary selenium was 0.057 mg/kg for lactating sows, adding 0.38 mg/kg organic or inorganic selenium had no significant effect on piglet 14-day body weight [26]. Adding 0.3 mg/kg organic or inorganic selenium to gestating sow diets had no significant effect on litter size, litter weight, or piglet 21-day growth performance (body weight, average daily gain, liver weight) [27].

These studies suggest that selenium supplementation in gestating or lactating sow diets benefits reproductive performance, though inconsistent results may relate to selenium dosage, form, sow breed, parity, and management practices. In summary, dietary selenium content in sow diets should not exceed 0.5 mg/kg.

## **4.1 Antioxidant Effects**

### **4.1.1 Hazards of Oxidative Stress**

Reactive oxygen species (ROS) play both physiological and pathological roles in the female reproductive tract, being present in the ovary, oviduct, and embryos. ROS are involved in regulating multiple physiological processes from oocyte maturation and fertilization to pregnancy and embryonic development [28-29]. In healthy animals, ROS and antioxidant substances maintain balance. Oxidative stress occurs when excessive ROS disrupt this balance, creating an imbalance between free radical production and elimination [29].

Oxidative stress can cause decreased oocyte and embryo quality. Increased ROS or reduced antioxidant capacity in follicular fluid leads to lower fertilization rates [30]. Excessive free radicals may cause lipid and protein oxidation,

impair endothelial cell function, and affect fetal skeletal formation. Disruption of the antioxidant system can cause pregnancy complications such as fetal growth restriction, preeclampsia, miscarriage, or preterm birth [31].

During proestrus, enhanced ovarian metabolism generates excessive ROS that may cause ovulatory dysfunction [20]. During gestation, increased energy and oxygen demands lead to excessive superoxide and hydrogen peroxide production from maternal metabolism and the placenta, causing oxidative stress. In late gestation and lactation, increased metabolic burden and reduced antioxidant availability further elevate oxidative stress [32]. Endogenous free radicals, particularly superoxide from the mitochondrial respiratory chain, cause DNA damage. Berchierironchi et al. [32] reported that in high-producing sows, lymphocyte DNA oxidative damage was relatively low in early gestation (21.3%) but increased significantly in mid-to-late gestation (38%–47%), remaining high through weaning.

These findings demonstrate that oxidative stress from excessive ROS seriously harms sow reproductive physiology and reduces reproductive performance.

#### 4.1.2 Antioxidant Selenoproteins

Selenium regulates antioxidant function by participating in selenoprotein synthesis. Selenium is known to be a component of 25 selenoproteins, at least 16 of which have antioxidant functions [28], as detailed in Table 1 [7,11,33-34].

Selenoproteins primarily involved in intracellular redox regulation belong to the glutathione peroxidase family (GPXs), including GPX1, GPX2, GPX3, GPX4, GPX5, and GPX6, all using selenocysteine as the active site [6,33,35]. GPXs are the strongest antioxidant enzymes in the body, reducing hydrogen peroxide and lipid peroxides (such as malondialdehyde) to harmless water and alcohols, inhibiting ROS production [17] and maintaining cell membrane integrity while protecting lipids, lipoproteins, and DNA from oxidative damage [36]. Pre-ovulatory follicles have strong antioxidant defenses because GPXs maintain low hydrogen peroxide levels, facilitating fertilization and gamete formation [29].

Fortier et al. [21] investigated dietary organic and inorganic selenium effects on sow antioxidant capacity and reproductive performance, finding that from first estrus to gestation day 30, blood GPXs activity decreased by 3.2% in control sows but increased by 19.6% and 13.7% in inorganic and organic selenium groups, respectively. Zhan et al. [8] reported that at equal supplementation levels (0.3 mg/kg), organic selenium significantly increased selenium content in sow serum, colostrum, and milk compared with inorganic selenium; enhanced total antioxidant capacity and significantly reduced malondialdehyde content in serum; and significantly improved total antioxidant capacity while reducing malondialdehyde content in offspring tissues.

These studies indicate that dietary selenium supplementation improves antioxidant capacity in both sows and their offspring, protecting against oxidative

stress.

#### 4.1.3 Selenium and Vitamin E

Selenium and vitamin E have synergistic antioxidant effects, though vitamin E cannot completely replace selenium. From gestation day 30 to weaning at day 28 postpartum, sows fed diets supplemented with 30 mg/kg vitamin E and injected with 30 mg sodium selenite on gestation days 30, 60, and 90 showed increased litter size and number of weaned piglets, with higher piglet birth and weaning weights compared with control, vitamin E alone, or selenium alone groups [37]. Chen et al. [38] studied simultaneous supplementation of selenium (0.3 mg/kg organic or inorganic) and vitamin E (30, 90 IU/kg) in gestating and lactating sow diets, finding that combined supplementation of 0.3 mg/kg organic selenium and 90 IU/kg vitamin E increased serum glutathione content in nursery piglets and showed a trend toward increased liver glutathione content and total antioxidant capacity in newborn piglets.

Studies have shown that selenium deficiency in sow diets depletes tissue selenium and vitamin E reserves, leading to increased embryonic atrophy and death and reduced litter size [39]. Therefore, simultaneous supplementation of appropriate selenium and vitamin E in sow diets helps maintain or improve reproductive performance.

## 4.2 Regulating Offspring Metabolism Through Maternal Deposition and Transfer

Studies indicate that during early gestation, higher metabolic selenium requirements are needed not only for active redox reactions during placental formation but also for embryonic selenium deposition [20,40]. Supplementing 0.3 mg/kg organic selenium to sow diets containing 0.3 mg/kg selenium increased average selenium transfer from mother to embryo [20]. Adding 0.3 mg/kg organic or inorganic selenium to sow diets containing 0.2 mg/kg selenium increased average embryonic selenium content and total litter selenium content by 52% and 63%, respectively, in the organic selenium group compared with inorganic selenium [21].

Starting 60 days before mating, first-parity gilts fed diets supplemented with 0.1 or 0.3 mg/kg inorganic or organic selenium showed higher liver selenium content in newborn and weaned piglets in the 0.3 mg/kg selenium groups, with the highest levels in the 0.3 mg/kg organic selenium group [41]. Mahan [42] found that organic selenium increased tissue selenium content in newborn piglets compared with inorganic selenium, and that 0.3 mg/kg selenium increased tissue selenium content compared with 0.15 mg/kg. Zhan et al. [8] reported that at 0.3 mg/kg supplementation, organic selenium significantly increased selenium content in sow serum, colostrum, and milk, as well as in offspring serum, liver, kidney, pancreas, muscle, thymus, and thyroid compared with inorganic selenium.

Sow dietary supplementation with 0.3 mg/kg selenium increases selenium content in embryos and offspring tissues, with organic selenium being more effective than inorganic selenium. Selenium deposited in embryos and tissues can influence offspring metabolism and regulate their growth and development, thereby affecting sow reproductive performance.

#### 4.2.1 Selenium and Thyroid/Liver

Selenium is an essential component of the active center of deiodinases (DIOs), including DIO1, DIO2, and DIO3, which are distributed in important organs such as the thyroid and liver [43-44]. DIO1 and DIO2 convert thyroxine (T4) to triiodothyronine (T3) and reverse T3 (rT3) to diiodothyronine (T2), while DIO1 and DIO3 convert T4 to rT3 and T3 to T2 [15,44]. Thus, selenium participates in thyroid hormone metabolism regulation through deiodinases. Studies show that DIO1 knockout mice have abnormal thyroid hormone levels, DIO2-deficient mice exhibit impaired hearing, temperature maintenance, and brain development, and DIO3 knockout mice show developmental impairment, growth retardation, and reproductive disorders with reduced T3 to T4 conversion [45].

Compared with inorganic selenium, organic selenium intake by sows significantly increased serum T3 content and decreased T4 content and T4/T3 ratio in 28-day-old piglets [8]. Jianhua et al. [46] found that selenium deficiency in broiler chickens reduced growth rate by inhibiting liver deiodinase activity, causing significantly decreased plasma T3 and increased T4 levels.

#### 4.2.2 Selenium and Pancreas

Campbell et al. [47] cultured mouse pancreatic  $\alpha$ -cell Min6 in vitro and found that selenium upregulated insulin promoter factor 1 (Ipf1) mRNA expression, increased insulin mRNA expression, and consequently increased insulin secretion and content, indicating that selenium can enhance pancreatic islet cell function and thus potentially improve metabolism.

Zhan et al. [8] reported that maternal organic selenium intake significantly increased pancreatic digestive enzyme activity in 28-day-old piglets, with pancreatic amylase, trypsin, and lipase activities increasing by 50.81%, 17.61%, and 14.87%, respectively. Therefore, selenium may regulate digestion, metabolism, and growth by affecting pancreatic digestive enzyme activity.

These studies demonstrate that maternal selenium intake affects selenium deposition in offspring organs, and selenium deposited in offspring tissues regulates digestion, metabolism, and growth through deiodinase and pancreatic digestive enzyme activities, thereby reflecting selenium's effects on sow reproductive performance.

### 4.3 Other Considerations

Low-selenium diets in boars reduce sperm metabolic activity, decrease sperm motility, increase abnormal sperm numbers, and impair semen quality, consequently reducing fertilization rates. Boars fed diets supplemented with 0.5 mg/kg sodium selenite showed 54 mL increased semen volume, with sperm motility, normal sperm proportion, and fertilization rates increasing by 28%, 38%, and 25%, respectively, compared with controls [48]. Thus, selenium can indirectly affect sow reproductive performance by influencing boar sperm quality.

## 5 Summary

In summary, dietary selenium supplementation improves sow reproductive performance, but pigs have low selenium tolerance, and dietary selenium content should not exceed 0.5 mg/kg. Sodium selenite was traditionally used in pig production, but due to its strong toxicity and narrow safety margin, organic selenium (selenium yeast) has gradually replaced sodium selenite as the selenium source in pig diets, with numerous studies demonstrating superior efficacy of organic selenium compared with inorganic selenium.

Selenium exerts antioxidant effects through selenoproteins such as GPXs and synergistic action with vitamin E. Selenium transferred and deposited from mother to offspring in organs such as the thyroid affects metabolism and regulates offspring growth and development, thereby influencing sow reproductive performance. Additionally, selenium deficiency affects boar semen quality, reducing fertilization rates and indirectly impacting sow reproductive performance. However, the mechanisms by which selenium participates in small follicle and embryonic cell proliferation and regulates female gonadotropins remain unclear. Research on selenium's effects on the entire follicular development process in female animals is lacking, and the specific mechanisms by which selenium improves basal ovulation rate in sows require further investigation.

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