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RESEARCH

A Meta-analysis of Optimum Level of Dietary Nanoselenium on Performances, Blood Constituents, Antioxidant Activity, Carcass, and Giblet Weight of Broiler Chickens

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Abstract
Contradictory reports regarding the effects of nanoselenium (NanoSe) on the performance of broiler chickens may occur. Therefore, the optimum supplementation of NanoSe doses needs to be determined. The current meta-analysis study was aimed at evaluating the effectiveness and the optimum doses of NanoSe supplementation in broiler diets on performance, blood constituents, carcass, and giblet weight by considering breed and sex. The database was obtained from online scientific publications by searching through search engines such as Scopus, Web of Science, Google Scholar, and PubMed by entering the keywords nanoselenium, performance, antioxidants, and broiler. A total of 25 articles were included in the meta-analysis database. The study group was treated as a random effect while NanoSe dose, breed, and sex were treated as fixed effects. Daily body weight gain, carcass weight, and breast weight increased quadratically ($P < 0.05$), and FCR decreased quadratically ($P < 0.05$) in the starter and cumulative periods with increasing NanoSe supplementation. NanoSe supplementation tended to decrease cumulative feed intake linearly ($P < 0.1$) and decreased ($P < 0.05$) abdominal fat, albumin, red blood cells, ALT, and MDA levels. In contrast, levels of total protein, globulin, glucose, AST, white blood cells, cholesterol, triglyceride, and the weight of the liver, heart, gizzard, bursa of Fabricius, thymus, and spleen were not affected by NanoSe supplementation. Increasing the dose of NanoSe increased ($P < 0.05$) the GSHPx enzyme and Se concentration in breast muscle and liver and tended to enhance ($P < 0.01$) the CAT enzyme. It is concluded that a proper dose of NanoSe supplementation in a broiler diet improves body weight gain, feed efficiency, carcass, and breast weight without adverse effects on giblets. Dietary NanoSe elevates Se concentration in the breast muscle and liver and antioxidant activity. The current meta-analysis shows that the optimum dose for body weight gain and FCR is 1 to 1.5 mg/kg.

Keywords Antioxidant · Breed · Body weight · Internal organ · Meta-analysis · Selenium

Introduction

Broiler chickens are currently programmed to be able to grow fastly with high feed efficiency, which induces high metabolic processes that lead to oxidative stress. Unfavorable environmental conditions such as high density, poor circulation, poor quality of drinking water, and high ambient temperatures exacerbate these conditions. Also, it has been proven that the inhibition of protein synthesis by cells exposed to high temperatures caused broiler chickens' final weight loss and mortality

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[1]. To overcome this condition, providing mineral antioxidants such as nanoselenium (NanoSe) is very important. Nanotechnology refers to technologies aimed at synthesizing materials with dimensions smaller than 100 nm through different methods to produce various material characteristics, including organic, inorganic, dispersion, emulsion, and nanoclay [2]. Nanoparticle synthesis can be carried out using top-down and bottom-up approaches. The top-down approach creates nanoparticles by processing macromaterials into nanosized particles, while the bottom-up approach assembles nanoparticles from atoms or molecules [3]. Further, the synthesis methods of nanoparticles can be classified into biological (extraction of plants, microbes, fungi, algae), chemical (sol–gel, colloidal formation), and physical (mechanical grinding, sputtering, laser pyrolysis) methods, in which its development has attracted the poultry industry's attention since nanoparticles have many advantages, such as high catalytic properties, large surface area, and readily adsorbed [2]. NanoSe has a crucial role in reducing oxidative stress in poultry, which is associated with their ability to promote antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, and catalase [4]. Selenium (Se) is crucial due to its involvement in thyroid hormone activity, energy metabolism, immunity [5, 6], and heat stress gene expression [7].

Previous studies showed that dietary NanoSe enhanced antioxidant activity and immunity [8, 9], growth and live body weight [6, 10], feed efficiency and intestinal surface area [11], intestinal microflora, villus height, and crypt depth of broiler chicken [12]. However, according to Prasoon et al. [13], the addition of NanoSe did not significantly increase body weight. Likewise, Cai et al. [14] found that Se supplementation had no impact on either body weight or feed conversion. Instead, it reduced antioxidant enzyme activity at high doses. The different response rates to NanoSe supplementation may be affected by various factors such as dose, breed, sex, ambient temperature, and other environmental conditions. As a result, several narrative review studies have mediated the debate over this NanoSe supplementation effect [3, 15, 16]. However, to our knowledge, no meta-analysis studies that integrate data from various studies of dietary NanoSe in the performances of broiler chicken to provide quantitative information have been carried out. Therefore, our meta-analysis was aimed at evaluating the effectiveness and the optimum doses of NanoSe supplementation in diet on broiler performance, blood constituent, carcass, and giblet weight by considering breed and sex.

Materials and Method

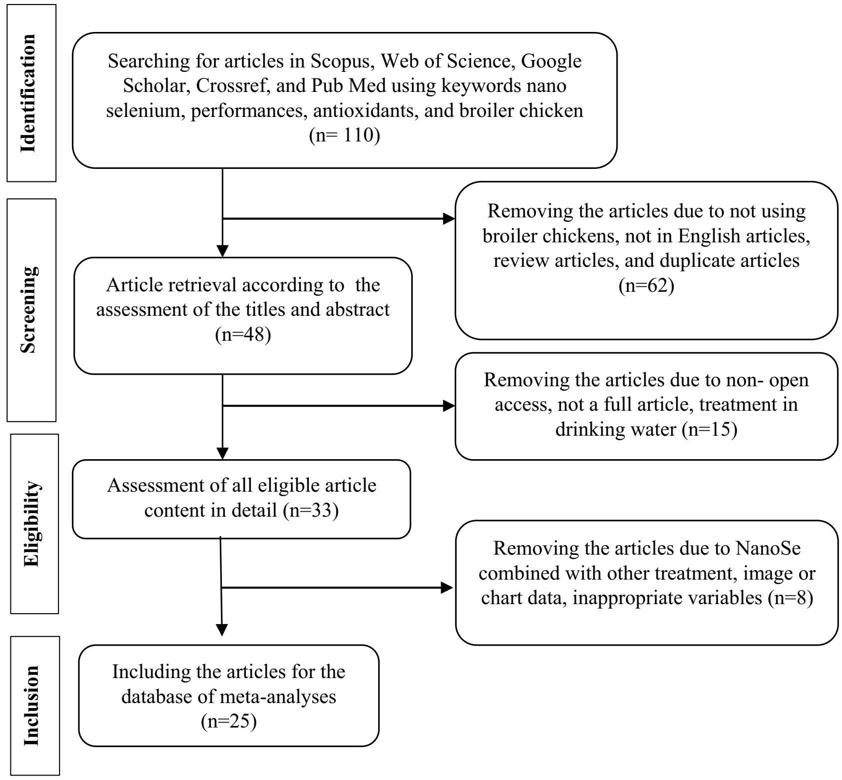
Constructing the Database

The database was compiled from online scientific publications obtained by searching through search engines such as Scopus, Web of Science, Google Scholar, and PubMed by entering the keywords nanoselenium, performance, antioxidants, and broiler. We also typed the name of the journal during the browsing process to eliminate the appearance of unrelated journals to our topic. The title of the article was used as the initial selection and a total of 110 articles was obtained. All articles were evaluated and assessed for abstract, material, and method as well as all data based on the following criteria: (i) in vivo trial of NanoSe supplementation in the treatment group, (ii) articles reporting the dose of NanoSe clearly, (iii) NanoSe unmixed with other treatments, (iv) studies using broiler chickens, (v) articles reporting at least one of parameters observed during the field trial period, and (vi) open access articles. A total of 62 articles were excluded due to not being in accordance with the objectives of the current meta-analysis such as not using broiler chickens, treatment in drinking water, review, and duplicate articles. Then, an assessment of the entire method, observed variables, and presentation of data was carried out. We excluded articles that combined NanoSe supplementation with other treatments and presented data as graphs or charts. Additionally, we excluded articles that did not use Se in the form of nanoparticles including selenium yeast (SY), selenomethionine (SM), and sodium selenite (SS). Finally, 25 articles were included in the meta-analysis database. Prior to further data analysis, NanoSe dose units were changed in the same unit (mg/kg), as well as the observed variable units. The detailed step of article selection is presented in Fig 1.

Data Description

A summary of the 25 articles in the database and the distribution of data (mean, standard deviation, minimum, maximum) are summarized in Tables 1 and 2, respectively. Table 1 contained the author's name, publication year, NanoSe dose, breed, sex, number of chickens, and length of rearing. Articles were published from 2012 to 2022. Chicken breeds consisted of Ross (54.17%), Cobb (25%), Arbor Acres (16.67%), and Vencobb (4.17%), with the proportion of 50% male and 50% unsexed. A total of 6.589 birds (min 100 birds; max 810 birds) were reared for a minimum of 27 days and a maximum of 49 days. NanoSe dose ranged from 0 to 3-mg/kg diet. Meanwhile, the variables observed were broiler performances (body weight gain, feed intake, feed conversion ratio (FCR)), breast muscle and liver Se concentration, carcass weight, breast weight, giblets weight (liver, heart, gizzard, bursa of Fabricius, spleen, thymus, abdominal fat), blood constituents (total protein, albumin, glucose, globulin, aspartate aminotransferase (AST), alanine transaminase enzyme (ALT), red and white blood cells, triglycerides, cholesterol), antioxidant parameters (superoxide dismutase enzyme (SOD), glutathione peroxidase (GSH-Px) enzyme, catalase enzyme (CAT), and malondialdehyde (MDA). Intestinal morphological variables (villus height and surface area, crypt depth), immunity, and intestinal microbial population were not included due to the limited articles reporting these variables.

Fig. 1 Step of article selection for meta-analysis database



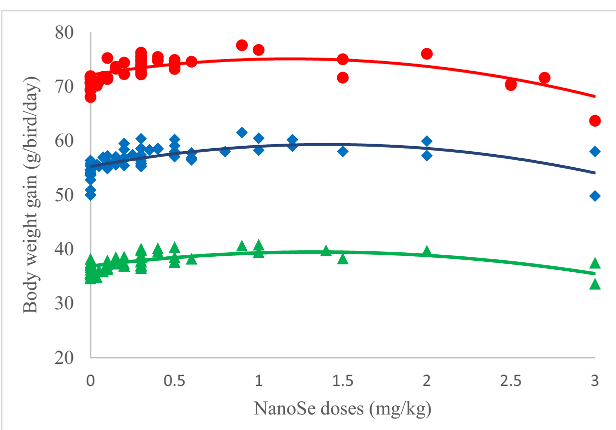


Fig. 2 Effect of NanoSe supplementation in broiler diet on body weight gain in starter phase (green triangle) with the equation of $Y = -1.451X^2 + 3.890X + 36.867$ ($n = 53$, $P < 0.05$, RMSE = 16.035), finisher phase (red dot) with the equation of $Y = -2.110X^2 + 5.006X + 72.107$ ($n = 53$, $P < 0.05$, RMSE = 22.176), and cumulative body weight gain (blue diamond) with the equation of $Y = -2.066X.^2 + 5.810X + 55.205$ ($n = 79$, $P < 0.05$, RMSE = 14.549)

Statistical Analysis

The data were analyzed according to the mixed model methodology [17]. The study group was treated as a random effect while NanoSe dose, breed, and sex were treated as fixed effects. SAS® OnDemand for Academics was applied to analyze all data, where RMSE, AIC, and significance value of $P < 0.05$ were used to determine the appropriate statistical model, while the value of $P < 0.1$ tended to be significant. The linear regression model was selected when the quadratic regression model was identified as insignificant. The slope and intercept were employed to determine the relationship trend between variables. The following statistical model was used:

$$Yij = \beta 0 + \beta 1Xij + \beta 2X2ij + si + biXij + eij$$

where Yij is dependent variable; $\beta 0$ intercept; $\beta 1$ linear regression coefficient; $\beta 2$ quadratic regression coefficient; si random effect (study group); Xij predictor of the continuous variable value; bi random effect of study i on the regression coefficient Y on X; and eij unexplained residual error.

Results

Broiler Performances

The correlation regression between NanoSe supplementation in diet and broiler performance is presented in Tables 3 and 4. Daily body weight gain increased quadratically ($P < 0.05$) in all phases with increasing NanoSe supplementation. Conversely, an increased NanoSe level quadratically decreased ($P < 0.05$) the

Table 1 Summary of the study in meta-analysis database

Author	Dose (mg/kg)	Breed	Sex	Total (birds)	Duration (day)
[4]	0–0.3	Ross 308	Unsexed	156	1–42
[6]	0–0.5	Ross 308	Male	160	1–42
[8]	0–0.3	Arbor Acres	Unsexed	210	1–35
[9]	0–0.0375	Cobb 500	Unsexed	180	1–42
[10]	0–0.5	Ross 308	Unsexed	315	1–35
[11]	0–0.5	Ross 308	Male	180	1–42
[12]	0–0.3	Ross 308	Male	360	1–42
[14]	0–2	Arbor Acres	Unsexed	500	1–42
[18]	0–0.225	Cobb 500	Unsexed	150	1–35
[19]	0–0.3	Cobb 500	Unsexed	336	1–42
[22]	0–0.3	Cobb 500	Male	150	1–35
[30]	0–1.2	Ross 308	Male	180	1–42
[32]	0–1.5	Ross 308	Unsexed	300	1–42
[33]	0–0.3	Cobb 500	Male	320	1–42
[40]	0–0.3	Arbor Acres	Unsexed	400	1–40
[41]	0–0.5	Cobb 500	Male	100	1–27
[42]	0–1.2	Arbor Acres	Male	810	1–49
[57]	0–0.3	Ross 308	Male	100	1–30
[58]	0–1.2	Ross 308	Male	500	1–42
[59]	0–3	Ross 308	Male	360	1–35
[60]	0–0.5	Ross 308	Male	180	1–42
[61]	0–0.6	Vencobb 400	Unsex	180	1–42
[62]	0–0.35	Ross 308	Unsexed	234	1–35
[63]	0.01	Arbor Acres	Male	108	1–35
[64]	0–0.6	Ross 308	Unsexed	120	1–42

cumulative and the starter FCR. NanoSe supplementation did not affect the feed intake in the starter and finisher phases. However, NanoSe supplementation tended to decrease cumulative feed intake linearly ($P < 0.1$). Increasing NanoSe levels increased daily body weight gain and feed efficiency with curvilinear patterns ($P < 0.05$; Figs. 2 and 3). Using the quadratic equations, the optimum dosage of dietary NanoSe for broiler body weight gain and feed conversion ratio is approximately 1 to 1.5 mg/kg. In addition, cumulative daily body weight gain and FCR were significantly affected by the interaction between NanoSe doses and broiler breeds (Table 3). NanoSe supplementation yielded a higher cumulative daily weight gain efficacy in Cobb 500 than in Ross 308 and Arbor Acres (Fig. 4).

Carcass Weight, Giblet Weight, and Se Deposition

The regression correlation between NanoSe supplementation in the boiler diet and the carcass weight, breast weight, giblets weight, and Se deposition in breast muscle and liver is demonstrated in Table 5. The carcass and breast weight increased quadratically ($P < 0.05$), whereas abdominal fat weight decreased quadratically ($P < 0.05$). Meanwhile, the increasing dose of NanoSe did not affect the weight of the heart, liver, gizzard, bursa of Fabricius, thymus, and spleen. Increasing doses of NanoSe in the diet produced a linear increase ($P < 0.05$) in the Se concentration of breast muscle and liver.

Blood Constituent and Antioxidant Activity

The regression correlation between NanoSe supplementation in the broiler diet and blood constituents and antioxidant variables is presented in Tables 6 and 7, respectively. Increasing doses of NanoSe in the diet produced a quadratic decrease ($P < 0.05$) in albumin and red blood cells. Meanwhile, there was a decrease ($P < 0.05$) in ALT enzyme with increasing doses of NanoSe. In contrast, levels of total protein, globulin, glucose, AST, white blood cells, cholesterol, and triglyceride were not affected by the increase in NanoSe levels. Regarding antioxidant parameters, improving the dose of NanoSe linearly increased ($P < 0.05$) the GSHPx enzyme and tended to increase ($P < 0.1$) the CAT enzyme. An increase in antioxidant activity was also demonstrated by a linear decrease

Table 2 The statistical description of each variable observed

Variables	Unit	Mean ± Std	Minimum	Maximum
Broiler performances				
Starter				
Body weight gain	g/bird/day	38.75 ± 7.50	25.43	54.62
Feed intake	g/bird/day	50.12 ± 7.98	29.98	67.56
FCR		1.40 ± 0.17	1.12	2.02
Finisher				
Body weight gain	g/bird/day	73.18 ± 11.92	51.83	96.86
Feed intake	g/bird/day	88.61 ± 10.65	72.97	119.50
FCR		1.74 ± 0.24	1.31	2.18
Cumulative				
Body weight gain	g/bird/day	61.00 ± 7.35	38.79	71.78
Feed intake	g/bird/day	102.80 ± 12.27	59.19	115.87
FCR		1.99 ± 0.22	1.30	2.18
Carcass, breast, and giblet weight				
Carcass	%	72.22 ± 4.59	65.35	79.25
Breast	%	23.26 ± 5.97	12.30	33.89
Liver	%	2.32 ± 0.41	1.67	2.83
Hearth	%	0.53 ± 0.08	0.37	0.70
Gizzard	%	1.74 ± 0.61	1.01	2.82
Spleen	%	0.19 ± 0.16	0.05	0.52
Bursa of Fabricius	%	0.19 ± 0.27	0.06	1.31
Thymus	%	0.37 ± 0.21	0.17	1.08
Abdominal fat	%	1.12 ± 0.44	0.38	1.91
Se concentration				
Breast muscle	mg/g	3.94 ± 2.20	1.09	8.00
Liver	mg/kg	0.67 ± 0.50	0.16	2.16
Blood constituents				
Total protein	g/dl	3.40 ± 0.71	1.80	4.43
Albumin	g/dl	1.45 ± 0.77	0.07	2.74
Globulin	g/dl	1.90 ± 0.46	1.27	2.53
Glucose	g/dl	148.75 ± 72.85	52.93	240.50
AST	U/l	186.87 ± 40.80	120.00	268.00
ALP	U/l	20.96 ± 5.21	10.65	26.81
Red blood cell	$10^6/mm^3$	15.05 ± 3.44	10.23	20.87
White blood cell	$10^3/mm^3$	15.05 ± 3.44	10.23	20.87
Triglyceride	mg/dl	31.88 ± 25.95	6.18	91.33
Cholesterol	mg/dl	141.30 ± 37.26	69.33	248.80
Antioxidant parameters				
SOD	U/ml	31.61 ± 10.77	17.45	48.11
GSH	U/ml	63.58 ± 51.31	0.94	141.00
MDA	U/ml	5.00 ± 2.40	2.31	10.50
CAT	nmol/ml	19.28 ± 10.24	8.41	37.70

FCR feed conversion ratio, *AST* aspartate transaminase enzyme, *ALT* alanine transaminase enzyme, *SOD* superoxide dismutase enzyme, *GSH-Px* glutathione peroxidase enzyme, *CAT* catalase enzyme, *MDA* malondialdehyde

($P < 0.05$) in the MDA with increasing NanoSe supplementation. The SOD enzyme's activity was unaffected by the elevated level of NanoSe in the diet.

Discussion

The current meta-analysis results confirmed that NanoSe supplementation in the broiler diet generated a quadratic equation on body weight gain and FCR with a positive trend in the starter, finisher, and cumulative periods. It demonstrated that the higher level of NanoSe supplementation in the diet positively affected chicken body weight gain and FCR at the appropriate dose. Thus, this finding may mediate discrepancies among previous studies that reported contradictory results.

The ability of NanoSe to improve the activity of antioxidant enzymes, thyroid hormone production, intestinal membrane integrity, and beneficial intestinal population and protect essential organs, including immunity organs (Fig. 5), may explain why NanoSe increased broiler weight gain and feed efficiency. The current meta-analysis also confirmed the improvement in antioxidant enzyme activity, in which the GSHPx enzyme increased with NanoSe supplementation. It was also evidenced by the decreasing MDA value (Tabel 5), which was a product of fatty acid peroxidation and oxidative stress marker [9]. Se is a component of the GSHPx enzyme, which functions as an antioxidant defense by detoxifying organic hydroperoxide and $H_2 0_2$ [14]. Similarly, previous studies reported that NanoSe at a dose of 0.1 to 0.2 mg/kg [18] and 0.3 mg/kg [19] decreased MDA and improved the activity of the GSHPx enzyme, which correlated with the increase in oxidation resistance and change in free radical into the stable product, thus increasing growth and body weight. Supplementation of various sources of Se in chickens was disclosed by Prasoon et al. [13] that SY, SS, and NanoSe at 0.3 mg/kg improved liver antioxidant enzymes. However, it did not affect the broiler's final body weight, feed consumption, or FCR. Also, contrary to Li et al.'s [20] results, there was no significant impact on chicken performances, SOD, and CAT enzyme activity between the NanoSe treatment and the control groups. Positive effects on blood biochemical parameters indicated Se's capacity to suppress oxidative stress. For instance, ALT enzyme and blood albumin were confirmed to decrease with increasing dietary Se (Table 5). Previously, environmental stress increased ALT, glucose, and albumin [21] and negatively affected the broiler chickens' performance [7]. However, reductions in ALP and ALT enzyme levels were also reported in Se supplementation [22].

The favorable effect of NanoSe supplementation on body weight and FCR could be due to higher absorption or utilization of NanoSe form and also associated with Se as a component of 5′ deiodinase, which converted thyroxine (T4) to triiodothyronine (T3). This hormone affects protein synthesis and bone metabolism, further increasing

Table 3 Interaction effect of NanoSe dose, breed, and sex on performance, blood constituent, breast muscle and liver Se concentration, carcass weight, breast weight, and giblet weight

Variables	*D*	*B*	*S*	*D*B*	*D*S*	*B**i	*D*B*S*
Broiler performances							
Starter							
Body weight gain	0.002	ns	0.023	ns	ns	ns	ns
Feed intake	ns	ns	ns	ns	ns	ns	ns
FCR	0.002	ns	0.005	ns	ns	0.003	0.061
Finisher							
Body weight gain	0.001	ns	ns	ns	ns	ns	ns
Feed intake	ns	ns	ns	ns	ns	ns	ns
FCR	ns	ns	ns	ns	ns	ns	ns
Cumulative							
Body weight gain	0.002	ns	ns	0.007	ns	ns	< 0.0001
Feed intake	0.068	ns	ns	ns	ns	ns	ns
FCR	0.047	ns	ns	0.001	ns	ns	0.001
Carcass, breast, and giblet weight							
Carcass	ns	ns	ns	ns	ns	ns	ns
Breast	0.022	ns	0.003	ns	ns	ns	ns
Liver	ns	ns	ns	ns	ns	ns	ns
Hearth	ns	ns	ns	ns	ns	ns	ns
Gizzard	ns	ns	ns	ns	ns	ns	ns
Spleen	0.013	ns	ns	0.028	ns	ns	ns
Bursa of Fabricius	0.010	ns	ns	ns	ns	ns	ns
Thymus	ns	0.003	0.003	ns	ns	ns	ns
Abdominal fat	0.017	ns	ns	ns	ns	un	ns
Se concentration							
Breast muscle	0.001	ns	un	ns	un	un	ns
Liver	0.004	un	ns	un	0.004	un	0.004
Blood constituents							
Total protein	ns	ns	ns	0.049	0.024	< 0.0001	0.024
Albumin	0.042	ns	ns	0.011	ns	ns	0.011
Globulin	0.005	ns	ns	ns	0.038	ns	ns
Glucose	ns	ns	ns	ns	ns	ns	ns
AST	ns	ns	ns	ns	ns	ns	ns
ALT	ns	< 0.0001	ns	ns	ns	ns	ns
Red blood cell	ns	0.014	ns	0.057	ns	ns	ns
White blood cell	ns	ns	0.074	ns	ns	ns	ns
Triglyceride	ns	ns	ns	ns	ns	ns	ns
Cholesterol	ns	ns	ns	ns	ns	ns	ns
Antioxidant parameters							
SOD	0.041	0.011	ns	ns	ns	ns	ns
GSHPx	0.006	0.008	ns	ns	ns	ns	ns
CAT	0.072	ns	ns	ns	ns	un	ns
MDA	0.010	0.013	un	ns	un	un	ns

D dose, *B* breed, *S* sex, *ns* non-significant, *un* unavailable, *FCR* feed conversion ratio, *AST* aspartate transaminase enzyme, *ALT* alanine transaminase enzyme, *SOD* superoxide dismutase enzyme, *GSH-Px* glutathione peroxidase enzyme, *CAT* catalase enzyme, *MDA* malondialdehyde

the growth of chickens [23]. Furthermore, Hu et al. [24] emphasized that Se regulated energy, fatty acid metabolism, and purine and pyrimidine bases. Unfortunately, the increase in T3 and T4 concentrations could not be confirmed by the current study due to limited data reported. However, previous studies revealed an increase in the hormone thyroxine T3, a decrease in T4 with dietary SS at 0.44 mg/kg [25], and a linear increase in T3 with increasing doses of SY [5]. It was further explained that a linear increase in the ratio of T3 to T4 had a positive correlation

Table 4 Effect of NanoSe supplementation in diet on broiler performances

Variables	Unit	N	Parameter estimates				Model statistics				
			Intercept	SE intercept	Slope	SE slope	P-value	RMSE	AIC	Tend	Model
Starter											
Body weight gain	g/bird/day	60	36.86	1.99	3.890 −1.451	1.086 0.438	0.002	16.035	258.7	+	quadratic
Feed intake	g/bird/day	60	50.99	2.10	0.313	0.801	0.698	13.826	268.7	+	linear
FCR		60	1.43	0.05	−0.146 0.055	0.055 0.022	0.016	0.322	−67.1	-	quadratic
Finisher											
Body weight gain	g/bird/day	54	72.10	3.11	5.006 −2.110	1.443 0.593	0.001	22.176	236.3	+	quadratic
Feed intake	g/bird/day	50	88.67	3.44	−2.965	3.197	0.361	20.693	261.8	-	linear
FCR		50	1.71	0.06	−0.068	0.052	0.195	0.434	−40.1	-	linear
Cumulative											
Body weight gain	g/bird/day	81	55.20	1.48	5.810 −2.066	1.480 0.651	0.003	14.549	436.7	+	quadratic
Feed intake	g/bird/day	80	95.77	2.69	−1.655	0.888	0.068	23.150	418.1	-	linear
FCR		80	1.72	0.04	−0.183 0.054	0.064 0.027	0.047	0.396	−59.7	-	quadratic

n treatment number, *RMSE* root mean square error, *AIC* Akaike information criterion, *SE* standard error, *FCR* feed conversion ratio

with broiler growth performance. Meanwhile, it was reported that there was a decrease in T3 plasma concentrations when broilers were exposed to high temperatures, and Se has a role in preventing a reduction in T3 through its ability to increase antioxidant enzyme activity [26].

The ability of Se supplementation to improve intestinal health may be related to its beneficial effect on chicken performance. This statement was supported by Bami et al. [12], who discovered that dietary 0.3 mg/kg NanoSe increased the density of goblet cells, villus height, and surface area of ileum and jejunum, which increased nutrient absorption, while dietary 0.1 mg/kg NanoSe increased mRNA expression from mucin jejunum. Furthermore, intestinal goblet cells secrete mucin (especially Mucin2), which contains glycoproteins to lubricate the intestinal epithelium that protects against intestinal damage due to diet movement, harmful substances, and microorganisms [27]. Moreover, the benefit of Se on the intestinal structure was also stated by Moghaddam et al. [27] and He et al. [28] that dietary 0.30 mg /kg NanoSe and 0.15 mg/kg SS improved villus density and surface area. Also, dietary 0.3 mg/kg SY enhanced beneficial bacteria (*Lactobacilli* spp) in laying hens' cecum [29]. The favorable effect of Se on intestinal histology is associated with its ability to regulate the activity of inflammatory cytokines and improve antioxidant activity [30]. Bami et al. [12] further explained that the mechanism of NanoSe in enhancing intestinal morphology might be due to a decrease in pathogenic intestinal microbial growth thereby reducing the inflammation of intestinal mucosa.

Se supplementation was able to induce lymphocytes to secrete cytokinins and trigger humoral immunity and immunoglobulins, and it was able to reduce toxic effects including aflatoxins [31], both of which could be reasons for improving broiler performance. Previously, it was reported that dietary 0.3 mg/kg NanoSe enhanced antibody responses to broiler IgG and SRBC. Similarly, Mohammadi et al. [32] and Boostani et al. [33] found that dietary NanoSe produced significantly higher serum IgM and IgG levels than inorganic Se. However, according to the current meta-analysis, supplementation of NanoSe has no effect on the weight of broiler immune organs (Table 6). These results are in line with those reported by Abou-Ashour and El-Naga [8] and Korzeniowska et al. [34], which confirmed that the weight of the spleen, thymus, bursa, and liver was not affected by the provision of Se in the diet. Therefore, this indicates that increasing broiler immunity with NanoSe supplementation may be through the hormonal system rather than affecting the immune organs' weight. On the other hand, the weight of abdominal fat decreased significantly with increasing Se dose. Previously, it was explained that SM, SS, and NanoSe can inhibit abdominal fat accumulation by modulating the inhibition of mRNA expression levels of liver lipogenesis genes [35], differentially regulating the expression of β-oxidation fatty acid genes in the liver [36], and reducing the activity of the cytosolic malic enzyme that produces NADPH for lipogenesis in adipose tissue [37, 38]. Therefore, dietary 0.4 mg/kg SY [39], 0.3

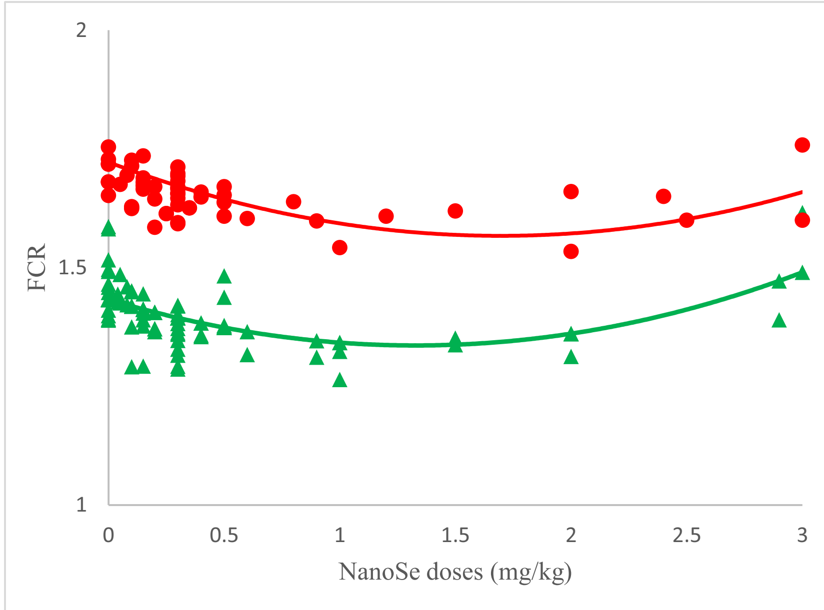


Fig. 3 Effect of NanoSe supplementation in broiler diet on FCR in starter phase (green triangle) with the equation of $Y=0.055X^2-0.146X+1.433$ ($n=55$, $P<0.05$, RMSE = 0.322) and cumulative FCR (red dot) with the equation of $Y=0.054X.^2-0.183X+1.722$ ($n=55$, $P<0.05$, RMSE = 0.396)

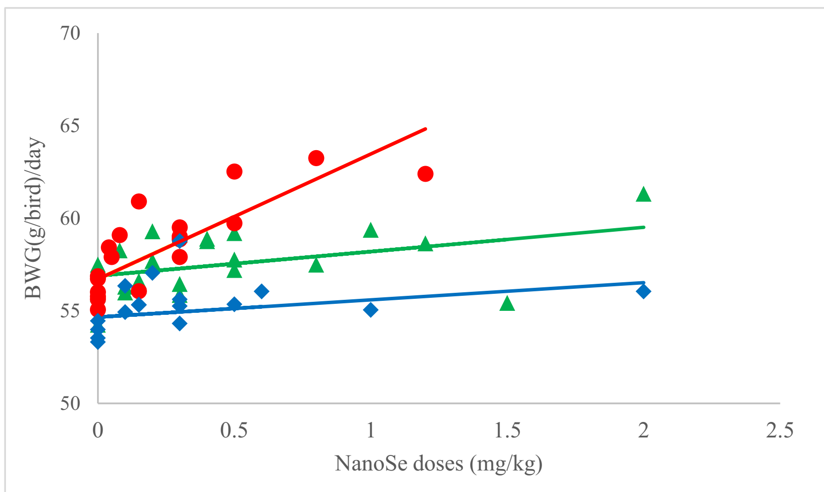


Fig. 4 Effect of NanoSe supplementation in broiler diet on cumulative body weight gain (BWG) of Cobb 500 (red dot) with the equation of $Y=6.76X+56.71$ ($n=19$, $P<0.05$), Ross 308 (green triangle) with the equation of $Y=1.31X+56.89$ ($n=42$, $P<0.05$), and Arbor Acres (blue diamond) with the equation of $Y=0.93X+54.66$ ($n=18$, $P<0.05$)

mg/kg NanoSe [40], and 1 mg /kg SS [41] were revealed to reduce abdominal fat weight significantly. However, at high doses, Se may encourage hyperlipidemia in tissues, which is consistent with the opinion of Zhou et al. [35] that Se can induce hyperlipidemia, hyperinsulinemia, hyperglycemia, and glucose intolerance. These results further emphasized our meta-analysis result that increasing dietary NanoSe quadratically reduced abdominal fat.

The Se concentration of broiler breast muscle and liver was linearly increased by increasing the NanoSe supplementation. Our data is in line with that of Abou-Ashour et al. [8] and Hu et al. [42], in which NanoSe can be stored in muscles more effectively than SY and SS. Likewise, the increase in Se breast muscle was linear with increasing dietary NanoSe [32]. Different absorption rates and metabolic pathways may be associated with different retention rates of different forms of Se. Smaller particles with a higher surface area can be highly absorbed by the villus epithelium, directly enter the bloodstream, and then be partly stored in the liver and the muscles as the main organ [43]. Also, nanoparticles are efficiently deposited through Peyer patches into lymphatic system organs, including the spleen and mesenteric lymph nodes [42]. The liver is responsible for the biosynthesis and activity of liver antioxidant enzymes [13]; thus, an increase in the liver Se level has a beneficial effect on antioxidant defense, as confirmed by the current meta-analysis with an enhancement in the GSHPx enzyme and a decrease in MDA levels. According to Cai et al. [14], dietary NanoSe can easily saturate selenoenzymes, consequently markedly elevating Se deposition in tissues. Moreover, another possible reason

Table 5 Effect of NanoSe supplementation in broiler diet on the weight of carcass, breast, giblet, and Se concentration in the breast muscle and liver

Variables	Unit	*N*	Parameter estimates				Model statistics				
			Intercept	SE intercept	Slope	SE slope	*P*-value	RMSE	AIC	Tend	Model
Carcass, breast, and giblet weight											
Carcass	%	35	71.57	2.21	6.641 −3.340	2.198 1.381	0.042	8.935	56.1	+	Quadratic
Breast	%	36	21.69	3.43	6.373 −3.332	1.391 0.909	0.005	112.102	57.9	+	Quadratic
Liver	%	33	2.27	0.15	0.0026	0.137	0.985	0.754	15.0	+	Linear
Hearth	%	30	0.50	0.03	0.044	0.037	0.250	0.141	−37.5	+	Linear
Gizzard	%	30	1.60	0.26	−0.060	0.083	0.482	1.189	3.8	-	Linear
Spleen	%	33	0.17	0.05	−0.014	0.029	0.629	0.304	−36.3	-	Linear
Bursa of Fabricius	%	33	0.17	0.09	0.062	0.136	0.654	0.553	11.4	+	Linear
Thymus	%	35	0.36	0.05	−0.022	0.094	0.811	0.376	−0.6	-	Linear
Abdominal fat	%	35	1.26	0.16	−1.215 0.734	0.413 0.273	0.017	0.760	18.4	-	Quadratic
Se concentration											
Breast muscle	mg/g	23	2.70	0.91	7.564	1.538	0.001	3.565	53.1	+	Linear
Liver	mg/kg	20	0.25	0.05	1.594	0.081	<0.001	0.230	−9.6	+	Linear

n treatment number, *RMSE* root mean square error, *AIC* Akaike information criterion, *SE* standard error

Table 6 Effect of NanoSe supplementation in broiler diet on blood constituents

Variables	Unit	*n*	Parameter estimates				Model statistics				
			Intercept	SE intercept	Slope	SE slope	*P*-value	RMSE	AIC	Tend	Model
Total protein	g/dl	33	3.23	0.29	− 0.663	0.640	0.316	1.242	40.6	-	Linear
Albumin	g/dl	29	1.72	0.29	− 3.435 8.047	1.310	0.022	1.313	27.1	-	Quadratic
Globulin	g/dl	21	1.78	0.19	0.215	1.067	0.844	0.861	23.2	+	Linear
Glucose	g/dl	20	167.00	47.16	76.082	64.05	0.279	42.71	89.3	+	Linear
AST	U/l	26	194.24	19.42	− 18.379	34.582	0.608	73.35	119.2	-	Linear
ALT	U/l	22	20.46	2.72	− 10.741	3.298	0.013	8.528	48.1	-	Linear
Red blood cell	10^6/mm^3	23	2.42	0.12	− 2.027 7.227	0.959 1.962	0.010	0.533	4.5	-	Quadratic
White blood cell	10^3/mm^3	21	14.99	1.87	− 3.03	3.874	0.463	6.682	51.3	-	Linear
Triglyceride	mg/dl	21	38.83	12.87	− 2.114	18.8	0.913	45.948	98.3	-	Linear
Cholesterol	mg/dl	39	132.79	11.06	4.495	28.210	0.875	64.904	263.2	+	Linear

n treatment number, *RMSE* root mean square error, *AIC* Akaike information criterion, *SE* standard error, *AST* aspartate transaminase enzyme, *ALT* alanine transaminase enzyme

is explained by Surai et al. [44] that NanoSe is converted into SeCys (SC) and active selenoproteins before it is absorbed in the intestine. NanoSe can be converted to selenite, H_2Se, Se-phosphate, SC, and selenoprotein by intestinal bacteria, especially the genus *Veillonella*. Indeed, Se is characterized in muscle mainly as SM and SC [45].

The current meta-analysis also confirmed that NanoSe supplementation resulted in a higher cumulative daily weight gain efficacy in Cobb 500 than in Ross 308 and Arbor Acres (Fig. 5). However, differences in breed response to NanoSe supplementation on growth performance and FCR cannot be fully explained due to the lack of reported studies. Similarly, supplementation of other minerals, such as chromium, had been confirmed to enhance body weight and feed efficiency at Cobb 500 compared to Ross 308 for unexplained reasons [46]. According to studies on the comparative performance of broiler breeds, Cobb 500 had a greater body weight and lower FCR than other broiler breeds [47]. However, different results reported that Ross 308 yielded better body weight and carcass than Cobb 500 [48, 49]. It was explained that differences in feed quality, rearing management strategies, and breeding conditions in various countries could cause variations in the performance of each broiler breed. Likewise, with the current meta-analysis, where literature sources greatly influence the results. All the studies selected were written in English and open access. Articles published in other languages and not open access may have impacted this meta-analysis.

Although many previous studies have described the beneficial effects of Se, excessive Se intake can also have adverse effects. This was confirmed by the findings of a meta-analysis, which discovered that increasing NanoSe intake produced a quadratic increase in daily body weight gain (Fig. 3), carcass weight, and breast weight and a quadratic decrease in FCR (Fig. 4). According to Cai et al. [14], although Se is an essential mineral, it is harmful at levels slightly higher than the requirement. Indeed, Se lowered glutathione levels, inhibited the ability to scavenge free radicals, and produced high levels of malondialdehyde at a dose of 2 mg/kg. This is conclusive evidence of NanoSe's adverse effects at higher concentrations. Therefore, to avoid negative effects, the results of the current meta-analysis can be considered the applied dose of NanoSe (around 1 to 1.5 mg/kg). However, these doses may differ due to environmental factors,

Table 7 Effect of NanoSe supplementation in broiler diet on antioxidant activity

Variables	Unit	*n*	Parameter estimates				Model statistics				
			Intercept	SE intercept	Slope	SE slope	*P*-value	RMSE	AIC	Tend	Model
SOD	U/ml	32	31.11	5.10	5.170	6.107	0.425	21.018	64.2	+	Linear
GSHPx	U/ml	36	85.26	27.20	24.279	12.107	0.041	122.18	209.3	+	Linear
CAT	U/ml	34	15.28	5.16	38.325	18.870	0.072	18.953	87.1	+	Linear
MDA	nmol/ml	32	6.05	1.04	− 5.965	1.868	0.010	4.661	81.0	-	Linear

n treatment number, *RMSE* root mean square error, *AIC* Akaike information criterion, *SE* standard error, *SOD* superoxide dismutase enzyme, *GSH-Px* glutathione peroxidase enzyme, *CAT* catalase enzyme, *MDA* malondialdehyde

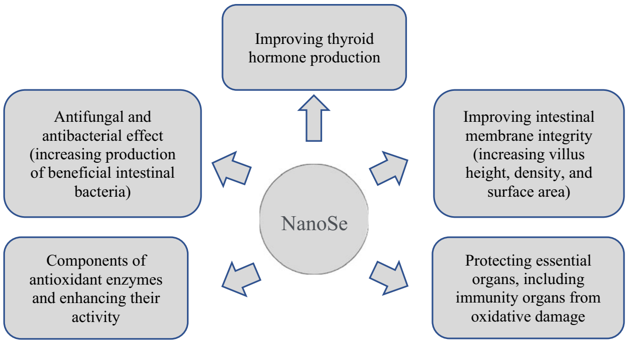


Fig. 5 The potential role of NanoSe in improving chicken performances

including breed and sex, which were confirmed in the current meta-analysis. Indeed, Se toxicity dramatically depends on its form, dose, and exposure time. For instance, dietary SS levels exceeding 1.2 mg/kg reduced broiler performance [42], but not in the nanotreatment at the same dose. The results confirmed that the range between optimal and toxic doses of NanoSe is broader than that of SS. The current meta-analysis also emphasized these results, in which decreased body weight gain and feed efficiency occurred at doses above 1.5 mg/kg. However, Se is generally toxic to poultry when applied at more than 5 mg/kg of feed, which selenite and selenate are the most toxic [50]. With a smaller particle and larger surface area, NanoSe enhances mucosal permeability, gastrointestinal absorption, and retention in the muscle, which may effectively reduce available Se to induce selenosis [51]. Hence, it may be one reason for the lower toxicity level of NanoSe compared to the SS form. Chronic toxicity from long-term exposure to high doses of Se leads to reduced feed intake, slowed growth, cirrhosis of the liver, and anemia [52]. The mechanism of toxicity of high doses of Se, both NanoSe and SS, includes its prooxidative properties, which lead to redox imbalance and overproduction of reactive oxygen species. Besides damaging lipids and proteins, excess reactive oxygen species can damage mitochondrial membranes [53]. In addition, Se can interact with glutathione to form Se^0, glutathiolseleol, selenodiglutathione, hydrogen selenide, and selenotrisulfide. Furthermore, selenotrisulfide compounds can react with thiol compounds to produce toxic compounds such as hydrogen peroxide and superoxide [54, 55]. Se is capable of interacting with metallothionein to release Zn, affecting DNA binding capacity and genome stability [56].

Based on the current meta-analysis study, supplementing NanoSe in the broiler diet at the proper dose improves body weight gain, feed efficiency, carcass weight, and breast weight without adverse effects on giblets. Likewise, dietary NanoSe increases the GSHPx enzyme, and Se concentration in the breast muscle and liver and decreases the blood's ALT and MDA concentration. However, it is necessary to pay attention to the dose of NanoSe since the higher dose of NanoSe supplementation is proven to reduce broiler performances. The current meta-analysis shows that the optimum dose for body weight gain and feed conversion ratio is approximately 1 to 1.5 mg/kg.

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Author Contribution Conceptualization, methodology, analysis, and data curation: AD, MR, HF, and AJ. Writing draft: AD, EO, and RKR. Reviewing and editing: EO, AD, and RKR. All authors have approved the final manuscript to be submitted.

Data Availability The datasets created in this study are available from the corresponding author upon reasonable request.

Declarations

Competing interests The authors declare no competing interests.

Conflict of Interest The authors declare no conflict of interest.

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