Research Article

The Effect of Selenium as a Feed Additive on Blood Parameters Antioxidant Activity in Dairy Goat: Meta-Analysis

Dwi Putri Nurmala[1], Tri Eko Susilorini[1], Osfar Sjofjan[2*], Danung Nur Adli[2]

[1]Department of Animal Production, Faculty of Animal Science, Universitas Brawijaya, Malang, East Java, Indonesia; [2]Department of Animal Nutrition and Feed Science, Faculty of Animal Science, Universitas Brawijaya, Malang, East Java, Indonesia.

Abstract | This study aimed to provide more precise conclusions about the effect of selenium as a feed additive on the blood parameters and antioxidant activity in dairy goats using a meta-analysis method. A comprehensive literature search was conducted, selecting studies published from 2005 to 2023 that examined selenium supplementation in dairy goats. Using R software 4.3.3 (2024-02-29 ucrt), data from 16 studies were analyzed using meta-regression analyses. Selenium supplementation in dairy goats significantly enhanced GSH-Px activity ($P<0.01$), but had no significant effect on blood parameters (RBC, WBC, hemoglobin, hematocrit, cholesterol, glucose, and total selenium). Organic selenium, such as selenium yeast, selenium-enriched yeast, selenomethionine, selenium proteinate, and lactate protein complex, was found to be more effective than inorganic selenium after a post hoc analysis between selenium sources and parameters. In conclusion, supplementing with selenium, especially from organic sources, can improve some of the antioxidant status in dairy goats.

Keywords | Blood profiles, Dairy goat, Glutathione peroxidase, Meta-analysis, Selenium

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***Correspondence** | Osfar Sjofjan, Department of Animal Nutrition and Feed Science, Faculty of Animal Science, Universitas Brawijaya, Malang, East Java, Indonesia; **Email:** osfar@ub.ac.id
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INTRODUCTION

Feed is very important to support livestock growth and productivity. Feed holds the largest financing, between 60-70% of the total livestock production costs (Suroso *et al*., 2023). Yadav *et al*. (2018) stated that livestock requires five categories of nutrients, namely carbohydrates, proteins, lipids, minerals, and vitamins. Ruminants can experience poor growth if fed feeds with low protein, low energy, and unbalanced minerals. Twenty-one minerals are considered essential for animals. These minerals are classified into macro and micro mineral.

Selenium (Se) is one of the important minerals (trace minerals) in livestock production because of its diverse physiological roles (Arshad *et al*., 2020). Some of the benefits of selenium in the animal body include playing a role in thyroid gland synthesis and thyroid hormone function, reducing oxidative stress, ant mutagenic, ant carcinogenic, antimicrobial and ant parasitic, increasing immune function and providing protection against oxidative brain lipid damage (Hosnedlova *et al*., 2017).

Selenium is a mineral that is only a small part of feed, but is very important for livestock. The optimal amount of selenium in feed must be considered to maintain normal animal physiology, however, excess or deficiency can cause toxicity and deficiency. Schone *et al*. (2013) reported that Se toxicity is not considered a life threat to animals or humans. Selenium deficiency can affect reproductive efficiencies such as placental retention, abortion, premature embryo death and infertility, besides it can interfere with growth performance (white muscle disease) and skeletal muscle necrosis (Mehdi and Dufrasne, 2016). Blood profiles have been extensively utilized to assess animal stress and welfare levels, as well as to track nutritional status, metabolism, and health status (Astuti *et al*., 2021). Blood parameters in ruminants are correlated with the season, the herd management techniques, and the physiological state (Mekroud *et al*., 2021). However, the studies reported regarding the blood profiles are critical because they provide information regarding the animal's health status (Gao *et al*., 2022).

Meta-analysis is a systematic review of a specific topic in the literature that provides quantitative estimates of the impact of a treatment (Russo, 2007). Meta-analysis is the analysis of statistical studies by analyzing data from primary studies. The results of the primary study analysis are used as a basis for correction factors, accepting and supporting existing research (Adli *et al*., 2024). Meta-analysis overcomes the limitations of small sample sizes of individual studies, detecting effects of interest and reducing the risk of false-negative results. Combining data from separate studies can statistically provide more precise estimates than single studies (Lee, 2019). Therefore, this research aims to provide more precise conclusions about the effect of selenium as a feed additive on blood parameters and antioxidant activity in dairy goats through meta-analysis methods.

MATERIALS AND METHODS

Eligibility criteria, search strategy, and data extraction

A dataset comprising literature on the use of selenium as a feed additive in dairy goats was compiled, covering publications from 2005 to 2023. Literature searches were conducted on Scopus (https://www.sciencedirect.com/), PubMed (https://pubmed.ncbi.nlm.nih.gov/), and Google Scholar (https://scholar.google.com/). The keywords used included selenium, dairy goat, feed additive, red blood cell, white blood cell, haemoglobin, haematocrit, cholesterol, glucose, total protein, GSH-Px, selenium concentration, and blood.

The criteria for including articles in the database were: (1) the article was published between 2005 and 2023, (2) the treatment included the dose of selenium used, (3) the article reported on the use of selenium in dairy goats, excluding other animals, (4) the dairy goats were adult females, and (5) selenium was administered by mixing it into feed. Data from articles meeting these criteria were tabulated in Excel, including details such as author, year of publication, type of goat used, lactation phase of the goat, type of selenium used, amount of selenium used, and the values of each parameter. All data were converted into consistent units of measurement to facilitate direct analysis within specific parameters. The final database included 16 articles with a total of 129 data units. Figure 1 details the selection process of the studies used in this meta-analysis, while Table 1 provides a summary of the completed dataset, adhering to PRISMA-P guidelines (Adli *et al*., 2024).

Table 1: Studies selected to be included in the meta-analysis.

No	Reference	Source of selenium	Period	Level (mg/day)	Strain dairy goat
1	Zhang *et al*. (2017)	Se-enriched yeast and sodium selenite	L	0-1,12	Guanzhong
2	Rashnoo *et al*. (2020)	N/A	D	0-0,25	N/A
3	Petrera *et al*. (2009)	Sodium selenite and se yeast	L	0-0,26	Saanen
4	Kachuee *et al*. (2019)	Sodium selenite and selenomethionine	L	0-0,6	Khalkhali
5	Silveira *et al*. (2019)	Se yeast	L	0-0,4	Saanen
6	Shi *et al*. (2018)	Se enriched yeast	D	0-4,63	Taihang black
7	Barcelos *et al*. (2022)	Se yeast	L	0-11,2	Saanen X Pardo Alpine
8	Vasconcelos *et al*. (2023)	Se yeast	L	0-40	Saanen X Toggenburg
9	Ziaei *et al*. (2015)	-	D	0-0,86	Rainei
10	Shareef *et al*. (2019)	Se yeast	L	0,0,03	Local Iraqi does
11	Tozzi *et al*. (2016)	Sodium selenite and se yeast	L	0-0,2	Alpine chamois
12	Misurova *et al*. (2009)	Sodium selenite and lactate protein complex	D	0-0,28	White shorthair
13	Antuvonic *et al*. (2013)	Se yeast	L	0-0,03	Alpine
14	Pavlata *et al*. (2011)	Sodium selenite and lactate protein complex	D	0-0,3	White shorthair
15	Pavlata *et al*. (2012)	Sodium selenite, se-enriched yeast, selenium proteinate and lactate protein complex	D	0-0,24	Shite shorthair
16	Tsiplakou *et al*. (2021)	Se yeast	L	0-0,12	Alpine X local breed

Note: L= Lactation; D= Days open; N/A= Not available.

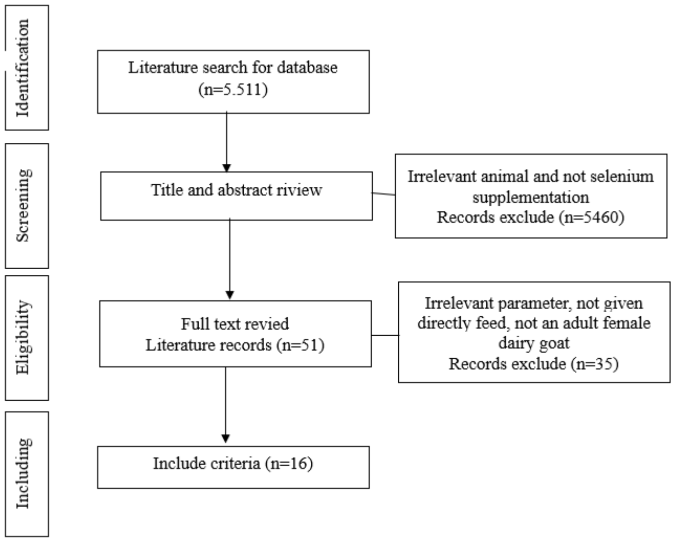

Figure 1: Diagram flow for study selection in meta-analysis study.

Coding and statistical analysis

The meta-analysis equation follows the following formula (St-Pierre, 2001; Sauvant *et al.*, 2008).

$$Y_{ijk} = \mu + S_i + \tau_j + S\tau_{ij} + \beta_1 X_{ij} + b_i X_{ij} + \beta_2 X^2_{ij} + b_i X^2_{ij} + e_{ijk} \quad ...(1)$$

Y_{ijk} represents the dependent variable, μ stands for the overall mean value (intercept value), S_i denotes the random effect of the i^{th} study, assumed to be ~ N_{iid} (0, σ_S^2), τ_j represents the fixed effect of the j^{th} of τ factor, and $S\tau_{ij}$ represents the random interaction effect between the i^{th} and j^{th} dosage of the τ factor, also assumed to follow a normal distribution with mean 0 and variance $\sigma_{S\tau}^2$. β1 represents the overall value of the linear regression coefficient for Y in relation to X, serving as a fixed effect or slope, β_2 denotes the general coefficient of the quadratic regression for Y concerning X, functioning as a fixed effect or slope, X_{ij} dan X^2_{ij} represent the continuous values of the predictor variable in both linear and quadratic forms, respectively. The b_i stands for the random effect specific to each study on the regression coefficient of Y with respect to X, assumed to be ~ N_{iid} (0, σ_S^2). Finally, e_{ijk} represents the residual value arising from unpredictable error. In case, the quadratic form presented insignificant different, the models changes into linear form.

The validation test was carried out utilizing the root mean square error (RMSE) and coefficient of determination (R^2) as metrics. The following equation represents RMSE and R^2.

$$RMSE = \sqrt{\frac{\Sigma(O-P)^2}{NDP}} \quad ...(2)$$

$$R^2 = \frac{(\sigma^2_f + \Sigma(\sigma^2_l))}{(\sigma^2_f + \Sigma(\sigma^2_l) + \sigma^2_e + \sigma^2_d)} \quad (3)$$

In this scenario, where *O* represents the actual value, *P* stand for the estimated value, *NDP* denotes the number of data point, σ^2_f represents the variant of a fixed factor, $\Sigma(\sigma^2_1)$ is the sum of component variances, σ^2_e signifies the variance attributed to predictor dispersion, and σ^2_d characterizes the specific distribution of the variance. All meta-regression analyses were carried out using R software 4.3.3 (2024-02-29 ucrt).

Table 2: Descriptive statistics of the effect selenium as feed additive on the blood profile of dairy goat.

No	Response	Unit	N	Mean	SD	Min	Max
1	RBC	x 10^{12}/L	12	11,02	1,07	9	12,46
2	WBC	x 10^9/L	12	13,34	3,59	9,24	21,73
3	Hemoglobin	g/dL	12	7,96	0,84	6,82	9,79
4	Hematocrit	%	15	33,20	18,58	20,25	72
5	Cholesterol	mg/dL	8	12,85	18,65	29,19	77,02
6	Glucose	mg/dL	9	57,59	4,51	48,29	61
7	Total protein	g/L	11	59,23	23,49	20,4	80,3
8	Selenium	µg/L	32	185,73	111,94	36,18	463,33
9	GSH-Px	µkat/L	18	329,44	385,89	45,5	1154,6

Note: RBC= Red Blood Cell; WBC= White Blood Cell.

RESULT AND DISCUSSION

The results of the meta-analysis on the relationship between selenium sources and blood profiles are presented in Table 2. The meta-analysis indicates that different selenium sources have significantly varied effects on white blood cells (WBC), glucose, and glutathione peroxidase (GSH-Px) activity in the blood (P<0.05), with selenium concentration showing a highly significant effect (P<0.01). Conversely, there was no significant effect on red blood cells (RBC), haemoglobin, haematocrit, cholesterol, or total protein (P>0.05). In dairy goats, the white blood cell (WBC) count ranges from 9.24 x 10^9/L to 21.73 x 10^9/L. Their glucose levels vary between 48.29 and 61 mg/dL, and the activity of glutathione peroxidase (GSH-Px) ranges from 45.5 to 1154.6 µkat/L. Post hoc analysis indicated that Se-enriched yeast was the most effective selenium source for improving WBC and glucose levels. Both Se-enriched yeast and selenomethionine were effective in increasing total se, whereas sodium selenite and lactate protein complex were most effective for enhancing GSH-Px activity. The study found that organic sources of selenium, such as Se-enriched yeast (782.2 µkat/L), Selenium proteinate (904.2 µkat/L), and lactate protein complex (926.47 µkat/L), were the most effective. The data supporting these findings is presented in Table 3.

According to Sevcikova *et al.* (2006), organic selenium is utilised more efficiently than inorganic selenium sources. Organic selenium is actively absorbed via amino acid

Table 3: Regression linear model of effect source of selenium on blood profile of dairy goat.

No	Response	Unit	Average							F value	Pr > F
			Control	Sodium selenite	Se yeast	Se-enriched yeast	Seleme thionine	Selenium proteinate	Lactate protein complex		
1	RBC	x 10^{12}/L	10.69	N/A	11.38	11.93	N/A	N/A	N/A	5.48	0.05
2	WBC*	x 10^9/L	12.94^a	N/A	11.64^a	18.59^b	N/A	N/A	N/A	7.97	0.01
3	Hemoglobin	g/dL	7.72	N/A	8.31	8.12	N/A	N/A	N/A	1.74	0.25
4	Hematocrit	%	32.16	N/A	24.98	34.63	N/A	N/A	N/A	4.33	0.08
5	Cholesterol	g/dL	48.83	N/A	59.74	34.84	N/A	N/A	N/A	1.29	0.39
6	Glucose*	mg/dL	54.81^a	N/A	49.75^a	58.79^b	N/A	N/A	N/A	26.54	0.03
7	Total protein	g/L	58.37	N/A	71.70	70.75	N/A	N/A	N/A	1.01	0.46
8	Selenium**	µg/L	128.36^a	238.6^{ab}	168.09^{ab}	340.97^b	435.86^b	167.2^{ab}	154.2^{ab}	5.98	0.001
9	GSH-Px*	µkat/L	325.77^a	972.72^b	170.29^{ab}	782.2^{ab}	N/A	904.2^{ab}	926.47^b	6.23	0.025

RBC= Red Blood Cell; WBC= White Blood Cell; N/A= Not available. *= significant different (P<0,05); **=significantly (P<0,01).

transport mechanisms, whereas inorganic selenium is absorbed passively through simple diffusion (Korzeniowska *et al*., 2018). Khalili *et al*. (2019) reported that organic selenium in the form of selenium yeast is more effective than inorganic selenium in the form of sodium selenite at increasing mean corpuscular hemoglobin (MCH), reproductive parameters, and health parameters. Additionally, Huang *et al*. (2023) found that organic selenium supplements, such as selenomethionine and selenium yeast, are more effective at enhancing the immune and antioxidant capacities of Chinese Xiangzhong Black beef cattle.

The bioavailability and toxicity of selenium are linked to its chemical form, with organic selenium being reported as more bioavailable and less toxic than inorganic selenium (Jin *et al*., 2018). Organic selenium compounds, such as selenomethionine and selenocysteine, are actively absorbed through amino acid transport mechanisms. On the other hand, inorganic selenium, like selenate and selenite, is passively absorbed through simple diffusion processes (Pavlata *et al*., 2011). The bioavailability of selenium in dairy goats is essential for their health and productivity. Studies have shown that organic selenium sources have higher oral bioavailability due to greater rumen microorganism incorporation and reduced formation of elemental selenium by rumen microorganisms (McDermott *et al*., 2024). Additionally, organic selenium supplementation has been linked to improved milk production in dairy goats (Dara *et al*., 2018). Conversely, inorganic selenium is quickly transformed into metabolically available selenide in the organism, which is then converted into functional selenoproteins containing selenocysteine (Mehdi and Dufrasne, 2016). The rapid metabolism of inorganic selenium and its difficulty in absorption contribute to its potential toxicity, emphasizing the importance of considering the chemical form of selenium to mitigate adverse effects (Zhang *et al*., 2023).

The key differences in study design, animal species, and dosage of supplementation between the two studies likely account for these contrasting results. The theoretical implications of our findings suggest that selenium plays a more critical role in glucose metabolism in dairy goats than previously understood. This aligns with theories proposing selenium's involvement in antioxidant defense and metabolic regulation. Our study's significant findings support the hypothesis that adequate selenium levels can enhance metabolic health and glucose homeostasis in dairy goats.

Long-term, these findings suggest that selenium supplementation could be a valuable strategy in managing metabolic health in dairy goats, potentially improving productivity and overall health. Future research should further explore the optimal selenium dosage and its effects on various metabolic parameters, considering different breeds and environmental conditions to generalize these findings.

The meta-analysis results regarding selenium levels and blood profiles are shown in Table 4. The illustration regression line between the level of selenium and blood profile is shown in Figures 2, 3, and 4. Different selenium levels had a highly significant effect on GSH-Px (µkat/L) in the blood (P<0.01), with the regression function y=329.44+1223.944x, Figure 5. Meanwhile, RBC, WBC, hemoglobin, hematocrit, cholesterol, glucose, total protein, and selenium concentration showed no significant effect (P>0.05). Each regression function, where RBC (x 10^{12}/L): y= 11.02 + 0.022x, WBC (x 10^9/L): y= 13.34 - 0.002x, hemoglobin (g/dL): y= 7.96 + 0.007x, hematrocit (%): y= 33.2 + 7.745x, cholesterol (mg/dL): y=49.47 + 12.854x; glucose (mg/dL): y= 57.59 +1.759x, total protein (g/L): y= 59.23 + 12.855x and selenium (µg/L): y= 185.73 + 0.104x.

Even though the research results are like that, feeding dairy cows a supra-nutritional selenium-yeast supplement during late gestation resulted in improved antioxidant status

Table 4: Regression linear model of effect level selenium on blood profile of dairy goat.

No	Response	Unit	Model	N	Intercept	SE intercept	Slope	SE slope	P value	RMSE	AIC
1	RBC	x 10^{12}/L	L	12	11.02	0.53	0.022	0.02	0.28	0.85	43.33
2	WBC	x 10^{9}/L	L	12	13.34	1.46	-0.002	0.08	0.98	0.99	69.72
3	Hemoglobin	g/dL	L	12	7.96	0.39	0.007	0.02	0.68	0.91	41.33
4	Hematocrit	%	L	15	33.20	7.74	7.745	0.06	0.48	0.95	96.43
5	Cholesterol	g/dL	L	8	49.47	12.85	12.854	0.11	0.31	0.78	57.16
6	Glucose	mg/dL	L	9	57.59	1.75	-0,479	0.43	0.31	1.07	55.62
7	Total protein	g/L	L	11	59.23	12.85	-0,043	0.06	0.48	0.87	71.19
8	Selenium	μg/L	L	32	185.73	30,03	0.104	2.49	0.97	1.52	379.32
9	GSH-Px**	μkat/L	L	18	329.44	133,83	1223.944	230,98	<0.001	0.86	219.59

Note: RBC= Red Blood Cell; WBC= White Blood Cell; N= amount of data; SE= standart error; RMSE= root mean squares error. AIC= akaike information criteria. **= significantly (P<0.01).

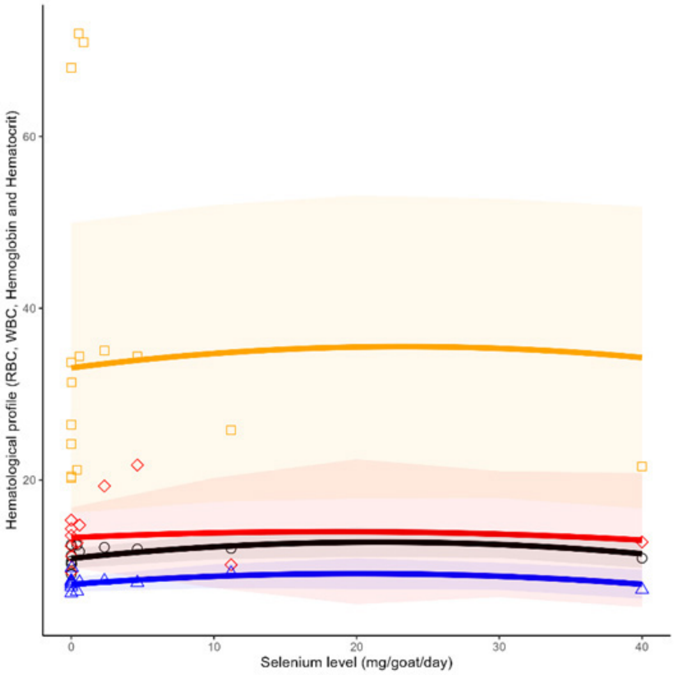

Figure 2: Linear regression of correlation between selenium level and RBC, WBC, hemoglobin and hematrocit (Black= RBC; red= WBC; blue= Hemoglobin, orange= Hematocrit).

postpartum, indicating a potentially positive impact on red blood cell, hemoglobin, and hematocrit (Żarczyńska *et al*., 2018). In addition, increasing RBC count, hemoglobin, and hematocrit by selenium supplementation was also reported in lactating donkeys (Tong *et al*., 2024).

The lack of a significant impact of selenium as a feed additive on glucose levels in dairy goats aligns with the findings of Żarczyńska *et al*. (2021), their study indicated that selenium supplementation, particularly in organic forms like selenite-triglycerides, did not significantly affect glucose levels in dairy cows. Despite the analytical results of this study, theoretically, there is a hypothesized influence of selenium on glucose metabolism; studies in rats and humans revealed that selenium might stimulate glucose intake and regulation of metabolic processes such as glycolysis, gluconeogenesis, fatty acid synthesis, or pentose phosphate pathway (Fontenelle *et al*., 2018). Total protein levels are a good indicator to describe the osmotic state, and nutrient transportation through extracellular fluid (blood plasma). In addition, total protein is also a good indication of the physiologic and biochemical function of liver tissue. Good liver function can fulfil the availability of nutrient precursors, both amino acids, glucose, and fatty acids for the biosynthesis of milk in the mammary gland (Januardani *et al*., 2023). However, in the research of Reczyńska *et al*. (2019) reported that selenium can increase the concentration of total blood protein in goats, but the effect was observed during a longer study, namely after 160 days of oral selenium supplementation.

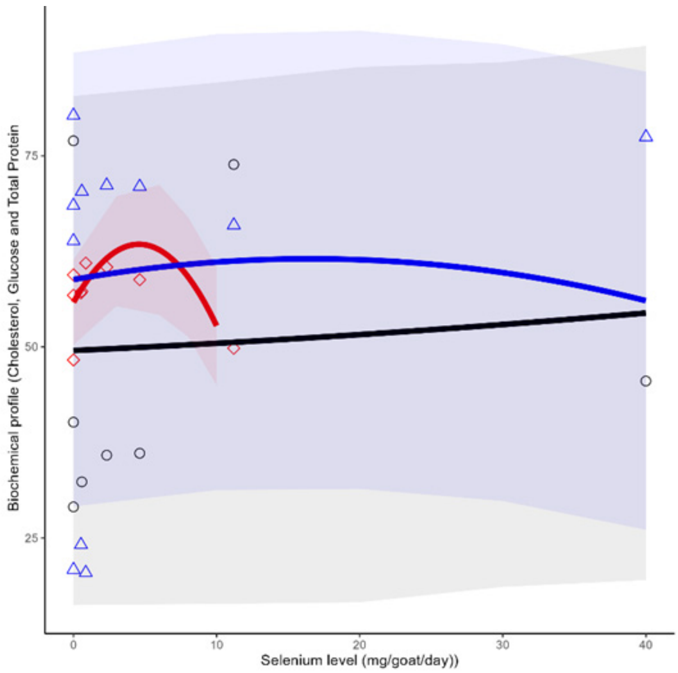

Figure 3: Linear regression of correlation between selenium level and cholesterol, glucose and total protein (Black= Cholesterol; red= Glucose; blue= Total Protein).

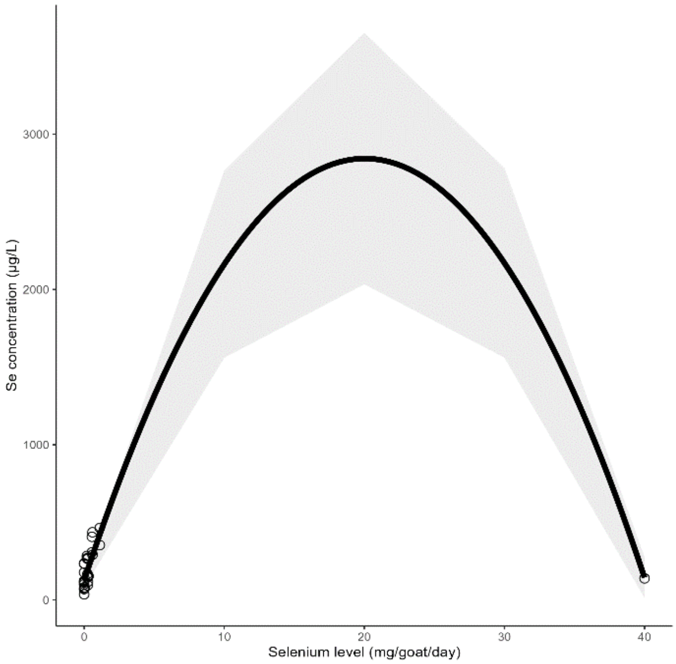

Figure 4: Linear regression of correlation between selenium level and se concentration.

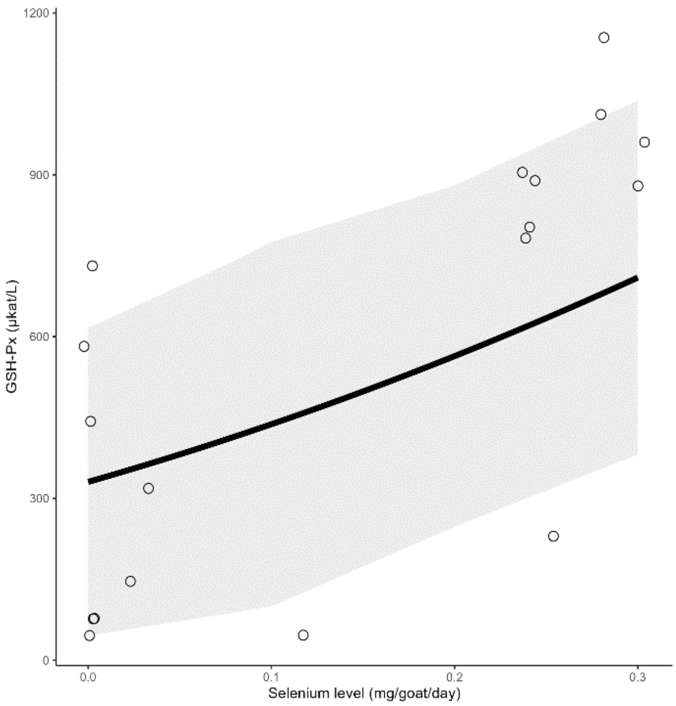

Figure 5: Linear regression of correlation between selenium level and GSH-Px.

There was an increase in the amount of Glutathione Peroxidase in the blood of dairy goats supplemented with selenium, the same as in cows in the study by Salman *et al.* (2013) has shown that dietary supplementation with selenium enhances the activity of GSH-Px in the blood. Arshad *et al.* (2020) the significant effects of selenium (Se) in dairy animals are largely due to the various functions performed by selenoproteins. The cellular redox system and the body's antioxidant defense depend on selenoenzymes (such as Glutathione Peroxidase) and selenoprotein. Therefore, an adequate dietary intake of Se is essential to provide sufficient Se-Cys and Se-Met for selenoprotein synthesis. Supplementing dairy animals' diets with Se is considered a potential strategy to enhance immune response and reduce metabolic and oxidative stress. Enzyme Glutathione peroxidase contains selenium as an integral structural component and plays an important role in animal physiology and health (Qazi *et al.*, 2019).

CONCLUSIONS AND RECOMMENDATIONS

Results from the meta-analysis showed that feeding dairy goats with selenium as a feed additive significantly increase the activity of glutathione peroxidase (GSH-Px) in their blood. The regression function y = 329.44 + 1223.944x indicates that giving 1 mg of selenium per goat per day will raise the glutathione peroxidase activity in the blood by 1223.944 µkat/L. GSH-Px is a selenoenzyme that plays a role in protecting cells from oxidative damage by catalyzing the breakdown of hydrogen peroxide and lipid peroxide, thus acting as a major antioxidant defense mechanism. An increase in glutathione peroxidase activity in the blood means improved antioxidant status in dairy goats.

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NOVELTY STATEMENT

The novelty of this research is by using meta-analysis to evaluate the impact of selenium as a feed additive on the blood profile of dairy goats.

AUTHOR'S CONTRIBUTION

Dwi Putri Nurmala contributed to data collection, data analysis and manuscript preparation. Tri Eko Susilorini, Osfar Sjofjan and Danung Nur Adli contributed to the research design, supervision and revision of the manuscript. All authors read and approved the final version of the manuscript in the journal at this time.

Conflict of interest

The authors have declared no conflict of interest.

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