symmetry

Article

Effects of Hydroxyselenomethionine with Symmetrical and Chelated Chemical Structure on Lactation Performances, Anti-Oxidative Status and Immunities, Selenium Transfer Efficiencies for Early-Lactating Dairy Cows

Yong Li [1,†], Weixian Zhang [2,*], Hualin Zhou [3,†], Jinfeng Zhu [1] and Chunmei Pan [2,*]

[1] College of Animal Husbandry Engineering, Henan Vocational College of Agriculture, Zhengzhou 451450, China; liyong7630427@126.com (Y.L.); zhujf6699@163.com (J.Z.)
[2] College of Animal Science and Technology, Henan University of Animal Husbandry and Economy, Zhengzhou 450046, China
[3] Agricultural College, Xiangyang Polytechnic, Xiangyang 441050, China; zhouhualin7804@126.com
* Correspondence: 80812@hnuahe.edu.cn (W.Z.); 80525@hnuahe.edu.cn (C.P.)
† These authors contributed equally to this work.

Abstract: The current study was conducted to investigate effects of hydroxyselenomethionine (HMBSe) with symmetrical and chelated chemical structure, a novel organic selenium (Se) source, on lactation performance, anti-oxidative status and immunities, and transfer efficiencies for early lactation dairy cows compared with that of sodium selenite (SS). Forty-five multiparous early-lactating dairy cows with similar days in milk, 56.0 d and milk yield 36.1 kg/d, were fed with same basal diet containing 0.04 mg of Se/kg of dry matter (DM) basis. They were assigned to 1 of 3 treatments according to one-way ANOVA design: control (basal diet, without Se supplementation), SS (0.30 mg of Se/kg of DM), or HMBSe (0.30 mg of Se/kg of DM). The experiment lasted for 9 weeks, with the first week as adaptation. Results showed that the organic HMBSe cows increased the milk yield, 4% fat-corrected milk yield, the numbers of red blood cells in whole blood, Se concentrations in milk and serum, ratio of milk to serum significantly ($P < 0.01$); feed efficiency, energy-corrected milk yield, contents of superoxide dismutase in serum, hemoglobin, and the numbers of white blood cells in whole blood significantly ($P < 0.05$) compared to control and SS. Moreover, HMBSe cows had trends to increase glutathione peroxidase activities ($P = 0.09$), total antioxidant capacity ($P = 0.06$), and had trends to decrease the contents of malonaldehyde ($P = 0.07$) in serum compared to control and SS. In conclusion, HMBSe was more effective on the lactation performances, anti-oxidative status, and immunities and Se transfer efficiencies for early-lactating dairy cows compared to control and SS, which was very meaningful to develop the enriched Se milk products.

Keywords: lactation performances; selenium; HMBSE; anti-oxidative status; immunities; Se transfer efficiencies; dairy cows

Citation: Li, Y.; Zhang, W.; Zhou, H.; Zhu, J.; Pan, C. Effects of Hydroxyselenomethionine with Symmetrical and Chelated Chemical Structure on Lactation Performances, Anti-Oxidative Status and Immunities, Selenium Transfer Efficiencies for Early-Lactating Dairy Cows. *Symmetry* **2022**, *14*, 916. https://doi.org/10.3390/sym14050916

Academic Editor: Francisco Ceacero

Received: 7 April 2022
Accepted: 27 April 2022
Published: 30 April 2022

1. Introduction

Selenium (Se) is an essential trace element for human and animals. It is known that feeding Se increased milk production, feed digestibility, anti-oxidative capacities, and immune function of dairy cows in different physiological stages [1]. The Se deficiency can lead to reduced performances and health status of the animals. In feeding management of dairy cows, Se feeding was frequently applied in inorganic and organic forms. However, inorganic Se, such as sodium selenite (SS), is more prone to dietary and environmental antagonisms [2]. Thus, compared with organic Se, inorganic Se has lots of disadvantages, such as potential toxic at high dietary level, low bio-availability, and potential pro-oxidation to the animals. Contrarily, organic Se species, such as yeast selenium and selenomethionine, are considered to be better on milk productivity, health status, absorption rates, and biological activities in lactating dairy cows, relative to those of inorganic Se [3].

Additionally, with the improvement of people's living standards, the demand for high-quality milk has increased. Exogenous nutrients such as Se are a potential candidate for milk products. Interest has increased to improve milk quality by increasing the Se composition in milk. It is found that the enrichment of milk Se was mainly conducted by feeding organic or inorganic Se sources. Organic Se is more beneficial to milk Se accumulation [4], which improves its utilization in the dairy industry.

Compared with yeast-Se, a widely used organic Se source in dairy feed industry, Se chelated to 2-hydroxy-4-methylthiobutanoic acid (HMBSe), which two hydroxymethionines with a Se in common, sulfur is replaced by Se, and formed a 1:2 symmetrical and chelated chemical structure [5,6], is a new kind of feed additive [7]. Notably, 2-hydroxy-4-(methylthio) butanoic acid is a source of supplemental Met whose chelated organic trace minerals (zinc, copper, manganese, or iron) had been used and studied extensively in dairy cows [6,8]. In mid-lactating dairy cows, a feeding diet including HMBSe could improve the lactation performance and antioxidant status of dairy cows compared to basal (without Se supplementation) and SS diet [9]. However, fewer trials about the benefits of HMBSe have been conducted on early-lactating cows. After all, compared with mid-lactating dairy cows, animals in the early-lactating period tend to suffer more from oxidative stress [9], which implied that the addition of organic HMBSe in the early-lactating period was more valuable. Therefore, the objectives of the present study were to determine the effects of HMBSe on milk production and quality, anti-oxidative status and immunities, and Se transfer efficiencies so as to evaluate its potential application during the early-lactating dairy cow industry.

2. Materials and Methods

This study was conducted on a local dairy farm (Zhengzhou, China). All procedures were conducted using protocols approved by the Henan Vocational College of Agriculture (Zhengzhou, China). All animals used in the current study were raised according to standards established by the Henan Vocational College of Agriculture (Zhengzhou, China). All cows were housed in individual tie-stalls and milked daily at 06:30, 14:30, and 20:30. Before the commencement of the feeding trial and throughout the experimental period, the health condition of the cows was monitored and recorded.

2.1. Animal, Diets, and Experimental Design

The experiment lasted for 9 weeks, with the first week for adaptation. Forty-five multiparous early-lactating dairy cows with days in milk of 56.0, milk production 36.1 kg/d, and average body weight (BW) 591.2 kg were divided into 15 blocks based on dry matter intake (DMI), milk production, and BW. They were assigned to 1 of 3 treatments according to one-way ANOVA design: control (basal diet, without Se supplementation); SS, 0.30 mg Se/kg feed (dry matter (DM) basis); HMBSe, 0.30 mg Se/kg (DM basis). The SS and HMBSe (white particles; Se, 2000 mg/kg) were provided by Shanghai Yanhua Bio-tech Co., Ltd. (Shanghai, China) and Novus International, Inc. (Shanghai, China), respectively. All cows received the same diet (total mixed ration, TMR) without Se supplementation. The background Se concentration in the TMR was 0.04 mg/kg on a DM basis. Composition of nutrient and contents of feed ingredients were presented in Table 1. All ingredients were mixed in a TMR and offered to individual cows 3 times per day. The SS and HMBSe preparation was top-dressed on the TMR based on diet assignment. All cows had free access to water throughout the entire experiment.

Table 1. Ingredients and chemical composition of basal diet (%, as-fed DM, unless noted).

Items	%
Ingredients	
Ground corn	21.10
Soybean meal, 44% CP	9.10
Barley	3.40
Wheat bran	2.10
Dried distillers grains with solubles	13.00
Cottonseed meal	4.40
Corn silage	12.10
Alfalfa hay	14.40
Grass hay	7.90
Beet pulp	8.00
Premix [1]	4.50
Nutrient Composition [2] (DM basis)	
Dry matter	44.90
Crude protein	16.60
Ether extract	2.62
Neutral detergent fiber	36.30
Acid detergent fiber	23.40
Selenium	0.04
Calcium	0.71
Phosphorous	0.37
Ash	8.56
Net energy for lactation [3], Mcal/kg	1.66

[1] Provided per kilogram of premix: 80,000 mg of vitamin A; 20,000 mg of vitamin D; ≥700 IU of vitamin E; 180 mg of Cu; 190 mg of Fe; 950 mg of Zn; 350 mg of Mn; ≥ 7% Ca; ≥1.30% P; ≥ 1.00% Co. [2] Calculated from the analyzed value of the dietary ingredients. [3] Calculated value based on MOA (2004) [10].

2.2. Sampling, Measurement, and Analyses

The offered and refused feeds were recorded for 2 consecutive days, and samples from fed TMR and the orts were collected on the same day and time every other week throughout the experimental period to calculate the dry matter intake, as was described previously [11]. The sample preparation and analysis were performed using methods described previously [12]. After all samples were dried in a forced air oven at 60 °C for 48 h, they were ground to pass a 2 mm Wileymill screen (Arthur H. Thomas, Philadelphia, PA, USA) and then through a 1 mm screen in a Cyclotec mill (Tecator 1093, Tecator, Sweden). They were placed in sealed containers until they were analyzed for DM, ash (#942.05; AOAC, Rockville, MD, USA, 1990), crude protein (CP, #988.05; AOAC, Rockville, MD, USA, 1990), ether extract (#920.39; AOAC, Rockville, MD, USA, 1990), calcium (#985.35; AOAC, Rockville, MD, USA, 1990), phosphorus (#986.24; AOAC, Rockville, MD, USA, 1990) [13], neutral detergent fiber (NDF), and acid detergent fiber (ADF), as described previously [14].

Milk yield was measured on the third and fourth day of every experimental week, and milk samples were collected from each milking using Waikato Milking System Meters (Waikato Milking Systems NZ Ltd., Hamilton, New Zealand). Milk samples were composited proportionally (4:3:3, composite) for analysis of contents [15]. A 50 mL subsample was treated with Bronopol (milk preservative; D&F Control Systems, San Ramon, CA, USA) and stored at 4 °C for later determination of fat, true protein, and lactose by infrared analysis (Milk-O-Scan, Foss Electric, Hillerød, Denmark) [16]; urea nitrogen (MUN) using the diacetylmonoxime-binding assay as described in a previous study [17]. Another milk subsample, which was obtained at week 1, 2, 4, and 8 of the experiment, was frozen and stored at −20 °C for the determination of Se concentration by a SpectorAA-30 atomic absorption spectrophotometer (Varian Techtron. Pty. Ltd., Mulgrave, Victoria, Australia).

Blood samples (10 mL) were collected from the coccygeal vein of cows 3 h after morning feeding on the third day of the fourth and eighth week [15], respectively, and then they were centrifuged at 4000 rpm for 10 min at 4 °C to collect serum, which was frozen at −20 °C until later thawed and analyzed for quantification of albumin, alkaline phosphatase, γ-glutamyl transferase, aspartate amino transferase, blood urea nitrogen, cholesterol, globulin, glucose, total protein, β- hydroxybutyric acid, non-esterified fatty acids (NEFA), and glutathione peroxidase (GSH-px), according to methods described in other studies [18]; the concentrations of superoxide dismutase (SOD), total antioxidant capacity (T-AOC), and malonaldehyde (MDA) reported methods previously [19]. The determination of Se concentration in serum was the same as in milk.

Another blood was sampled from cows with same method at the same time and week as above, and immediately placed into a 10-mL tube for whole blood variable determination, including red blood cells (RBC), hemoglobin concentration (HGB), mean corpuscular hemoglobin, and white blood cells (WBC) according to method [20]; neutrophil count, lymphocytes count, monocytes count, and eosinophil count according to a method previously reported [21].

2.3. Calculations and Statistical Analysis

ECM is the standard parameter calculated for feed efficiency (FE) because the fat and protein yield are corrected. Hence, ECM can be used to compare the differences of milk yield more accurately among dairy cows. 4% FCM is the milk yield with different milk fat content corrected to standard milk yield with 4% milk fat content, which has an important reference value in the ways of comparing the dairy cows' performances. FE was defined as the ratio of milk yield and dry matter intake. The equations were the following:

$$\text{ECM (energy-corrected milk, kg/d)} = 0.3246 \times \text{milk yield (kg/d)} + 12.86 \times \text{fat yield (kg/d)} + 7.04 \times \text{protein yield (kg/d)}$$

$$4\%\ \text{FCM (fat-corrected milk, kg/d)} = \text{milk yield (kg/d)} \times (0.4 + 15 \times \text{fat content}/100)$$

$$\text{FE (feed efficiency)} = \text{milk yield (kg/d)}/\text{dry matter intake (kg/d)}$$

All the data were analyzed using the MIXED procedure with repeated measurement using the covariance type AR (1) of the SAS software system (SAS Institute, Cary, NC, USA, 2000). A one-way ANOVA design with repeated measurements was used for treatment. The effect of cow was included as a repeated measure. LSD and Duncun's multiple range test were used for the evaluation of differences among groups. The results are reported as means and standard errors (SE). Probability values of $P < 0.05$ were used to define statistical significance and values $P < 0.10$ and $P > 0.05$ were accepted as statistical trends.

3. Results

3.1. Feed Intake and Lactation Performances

The results of feed intake and lactation performances were shown in Table 2. Briefly, the organic HMBSe did not affect the DMI and milk composition (fat, protein, and lactose, $P > 0.05$), but it increased the milk yield and 4% FCM yield ($P < 0.01$), ECM yield, and feed efficiency ($P < 0.05$) for early-lactating dairy cows significantly compared to control and SS.

3.2. Serum Parameters and Anti-Oxidative Status

Effects of HMBSe on serum parameters and anti-oxidative status are summarized in Table 3. HMBSe cows increased the SOD contents significantly ($P < 0.05$), had trends to increase the contents of GSH-px activities ($P = 0.09$) and T-AOC ($P = 0.06$), and had trends to decrease the contents of MDA ($P = 0.07$) in serum compared to control and SS.

Table 2. Effects of dietary sodium selenite (SS) and hydroxyselenomethionine (HMBSe) on feed intake and lactation performances for early-lactating dairy cows (15 cows/treatment).

Item	Treatment			SEM	*P*-Value
	Control	SS	HMBSe		
Dry matter intake, kg/d	21.24	21.09	21.00	0.07	0.38
Yield, kg/d					
Milk	34.33 ^{b}	33.44 ^{b}	36.84 ^{a}	0.35	<0.01
4% Fat-corrected milk	33.18 ^{b}	32.37 ^{b}	35.25 ^{a}	0.31	<0.01
Energy-corrected milk	35.35 ^{b}	35.14 ^{b}	36.97 ^{a}	0.32	0.03
Protein	1.08	1.09	1.13	0.01	0.10
Fat	1.29	1.29	1.32	0.02	0.60
Lactose	1.73	1.74	1.79	0.02	0.24
Total solid	4.49	4.54	4.60	0.04	0.39
Milk content, g/100 g					
Protein	3.11	3.19	3.14	0.02	0.28
Fat	3.75	3.84	3.75	0.03	0.28
Lactose	4.99	5.02	5.04	0.01	0.32
Total solid	13.06	13.13	12.96	0.06	0.48
Milk urea nitrogen, mg/dL	13.81	14.04	13.94	0.11	0.69
Feed efficiency	1.63 ^{b}	1.60 ^{b}	1.72 ^{a}	0.02	0.01

^{a,b} Mean values within treatment with different superscripts are significantly different ($P < 0.05$).

Table 3. Effects of dietary sodium selenite (SS) and hydroxyselenomethionine (HMBSe) on serum parameters and anti-oxidative status for early-lactating dairy cows (15 cows/treatment).

Item	Treatment			SEM	*P*-Value
	Control	SS	HMBSe		
Albumin (g/L)	42.49	40.96	42.18	0.50	0.43
Alkaline phosphatase (U/L)	52.37	49.03	46.77	1.75	0.43
γ-glutamyltransferase (U/L)	36.50	33.37	31.40	1.08	0.15
Aspartate Aminotransferase (U/L)	91.27	97.83	92.57	3.13	0.67
Blood urea nitrogen (mmol/L)	7.12	7.49	7.22	0.13	0.59
Cholesterol (mg/Dl)	6.34	5.80	6.06	0.15	0.35
Globulin (g/L)	37.97	42.59	40.66	1.05	0.20
Glucose (mmol/L)	3.22	3.34	3.17	0.05	0.37
β- hydroxybutyric acid (µg/mL)	43.25	38.04	39.89	1.34	0.28
Nonesterified fatty acids (µmol/L)	245.66	230.42	274.67	9.31	0.15
Glutathione peroxidase (U/mL)	112.71	109.53	122.04	2.44	0.09
Superoxide dismutase (U/mL)	103.32 ^{b}	105.74 ^{b}	116.04 ^{a}	2.04	0.02
Total antioxidant capacity (U/mL)	2.27	2.35	2.57	0.05	0.06
Malondialdehyde (nmol/L)	5.86	5.91	5.61	0.06	0.07

^{a,b} Mean values within treatment with different superscripts are significantly different ($P < 0.05$).

3.3. Whole Blood Parameters and Immunities

Effects of HMBSe on whole blood parameters and immunities were presented in Table 4. HMBSe only increased the numbers of RBC ($P < 0.01$), the numbers of WBC, and the contents of HGB ($P < 0.05$), but it did not affect the other whole blood parameters significantly ($P > 0.05$) compared to control and SS.

Table 4. Effects of dietary sodium selenite (SS) and hydroxyselenomethionine (HMBSe) on blood parameters and immunities for early-lactating dairy cows (15 cows/treatment).

Item	Treatment			SEM	*P*-Value
	Control	SS	HMBSe		
Red blood cells (10^6/µL)	6.60 ^{b}	6.84 ^{b}	7.70 ^{a}	0.14	<0.01
Hemoglobin (g/dL)	10.91 ^{b}	11.20 ^{b}	12.81 ^{a}	0.27	0.01
Mean corpuscular hemoglobin (pg)	16.61	16.40	16.75	0.15	0.65
White blood cells (10^3/uL)	13.66 ^{b}	14.07 ^{b}	19.57 ^{a}	0.89	0.01
Neutrophil (10^3/uL)	5.24	4.58	5.16	0.64	0.90
Lymphocytes (10^3/uL)	6.59	8.74	7.62	0.93	0.64
Monocytes (10^3/uL)	1.10	1.08	0.98	0.10	0.87
Eosinophil (10^3/uL)	0.69	0.51	0.67	0.05	0.35

^{a,b} Mean values within treatment with different superscripts are significantly different ($P < 0.05$).

3.4. Milk and Serum Se Status

The effects of HMBSe on Se distribution in biofluids of dairy cows were presented in Table 5. The Se concentrations in milk and serum, ratio of milk to serum all increased significantly in HMBSe cows compared to control and SS ($P < 0.01$).

Table 5. Effects of dietary sodium selenite (SS) and hydroxyselenomethionine (HMBSe) on selenium transfer efficiencies for early-lactating dairy cows (15 cows/treatment).

Item	Treatment			SEM	*P*-Value
	Control	SS	HMBSe		
Total Se					
Milk, µg/kg	25.18 ^{b}	26.49 ^{b}	42.06 ^{a}	1.78	<0.01
Serum, µg/kg	77.09 ^{b}	83.76 ^{b}	94.56 ^{a}	2.03	<0.01
Milk/serum, %	32.57 ^{b}	32.06 ^{b}	44.77 ^{a}	1.71	<0.01

^{a,b} Mean values within treatment with different superscripts are significantly different ($P < 0.05$).

4. Discussion

Se is a basic trace element which is essential for lactating dairy cows. One of the reasons for the importance of dietary Se of dairy cows is its contribution to glutathione peroxidase synthesis, which is an enzyme that catalyzes the reduction of hydrogen peroxide and lipid hydroperoxides and protects cell membranes against peroxidation [22]. Thus, Se additives in inorganic form (SS) and organic forms (such as DL-methionine and yeast chelated Se) has received more attention and been widely used for a long time in dairy cows. Moreover, due to the relatively higher bioavailability in dairy cows in comparison with inorganic Se (such as SS), the organic Se is considered to be more efficient and environmentally friendly [23]. The HMBSe with symmetrical and chelated chemical structure, a newly developed organic Se, has been studied in mid-lactating cows [9]. However, it is known that compared with mid-lactating dairy cows, animals in the early-lactating period tend to suffer more from oxidative stress, which might be attributed to the imbalance between energy consumption and excretion. Hence, it was more valuable to add organic HMBSe in the early-lactating period [24,25] so as to alleviate oxidative stress and increase immunities.

Some previous studies showed that oral administration of various amounts of Se, no matter organic or inorganic Se, did not affect milk yield and milk composition [26–28]. Sun et al. (2017) [9] also suggested that SS and HMBSe did not affect the DMI, milk yield, and milk characteristics for mid-lactating dairy cows. However, our studies results were the same as Batistel et al. (2017) [29] and (2018) [30], who reported that methionine supplementation could promote milk production changes, as well as mitigate early lactation oxidative stress. Since milk yields are affected by dietary HMBSe addition, the similar change of feed efficiency with increased HMBSe addition can be expected. The disagreement may be due to the physiological period of dairy cows being initially different, but the more important reasons may be the effects of organic HMBSe. To our knowledge, relative to mid-lactating dairy cows, early-lactating cows are more sensitive to oxidative stress [31]. Organic Se had advantages over SS in ways of alleviating oxidative stress. Hence, HMBSe is more efficiency for alleviating oxidative stress and increasing immunities of early-lactating dairy cows compared to mid-lactating dairy cows. On the other hand, it is found that cows fed organic Se had greater respiratory burst of neutrophils than those of cows fed inorganic Se additive, indicating that different Se sources led to difference immune status in transition dairy cows in early-lactating dairy cows [32]. Thus, the possibility of the different response on inorganic/organic effect between Sun et al. (2017) [9] and our studies may be also due to that the DIM of animals used in the current study is sensitive to Se source used, although the blood neutrophils count did not differ, but the GSH-Px, HGB, REC, WBC, SOD, and T-AOC of HMBSe can all be affected compared to the control and SS among cows. Accorrdingly, organic HMBSe increased the antioxidant functions and immunities for early-lactating dairy cows, which contributed to improved lactating performances of dairy cows compared to control and SS. Thus, our study suggested that relative to mid-lactating dairy cows, HMBSe is more efficiency for improving milk performances of early-lactating dairy cows compared to that of control and SS.

GSH-Px was an important Se-containing enzyme in the blood and tissues of animals, wherein it functions as an antioxidant by reducing hydrogen peroxides to water and lipid hydroperoxides to alcohols. Se status is usually evaluated directly by determining the concentration of Se, or indirectly by measuring the activities of GSH-Px in blood and tissues, whereas blood Se concentration is a good indicator of blood GSH-Px activities [33]. Moreover, increased plasma Se concentrations could lead to the improvement of antioxidant capacities (indicated by increasing activities of GSH-px, SOD, and T-AOC, as well as reducing MDA concentration) of dairy cows [34]. A previous study also found higher GSH-px, SOD, and T-AOC, as well as lower MDA in plasma, resulted from cows fed HMBSe compared to SS [9]. These results were partly consistent with the current study, which showed increased antioxidant capacities (plasma SOD and T-AOC) and reduced peroxidation product (plasma MDA) with dietary HMBSe addition [35]. On the other hand, the effects of Se supplementation on GSH-px depended on many factors, such as DIM, dietary Se contents, and the Se status of the animals [36,37]. In the current study, although DIM among three treatments, dietary Se between SS and HMBSe were similar, Se status of the dairy cows seemed to be better in HMBSe (94.56 ug/kg Se in serum) than of control (77.09 ug/kg Se in serum) and SS (83.76 ug/kg Se in serum), which resulted from higher bioavailability of organic HMBSe in early-lactating dairy cows. Maybe these were reasons for greater antioxidant capacity in HMBSe cows. Thus, HMBSe supplementation could improve the antioxidant capacities and health status for early-lactating dairy cows in current experimental conditions.

The previous research showed that high numbers of RBC and concentration of HGB could promote the swallowing function of WBC, improve the blood's ability to transport oxygen gas, and strengthen the metabolism and immunity functions of body [38]. The WBC, neutrophil count, and lymphocytes were important indexes which reflected the immunity functions of body. Their changes of quantities could reflect the functions of cells. RBC also had immunity and adhesion functions and could promote the swallowing function of white cells. It was a part of defensive functions of the host. It had been proved that RBC could catch antigen by immunity and adhesion functions, and clear away the oxide and metabolic products which were produced the swallowing functions of resisting during the course of swallowing by strong antioxidant effects of catalases and superoxide dismutases of high concentration in cells and took effects on swallowing functions. At same time, RBC took part in the production of γ-interferon, IL-1, and IL-2, which was one of the subsystems in the whole system of immunity [38]. In the present study, dietary supplementation with HMBSe had no effect on serum cell status among treatments except for RBC, WBC, and HGB concentration. They showed that dietary supplementation with HMBSe was more helpful for strengthening the immunity functions of body compared to control and SS for early-lactating dairy cows in current experimental conditions.

Selenium status was an important indicator of animal health, and this was commonly assessed by measuring Se concentration in whole blood or serum. The most previous studies concluded that the Se serum status was adequate if its serum concentration in dairy cows ranged from 70 to 79 µg/L [39]. However, the other survey found that cows have different requirements for Se in different periods [40], for example, 90 µg/L (the dry period), 130 µg/L (transition), and 100 µg/L (early lactation). It seems that early-lactating cows fed the basal diet had sufficient serum Se concentrations (77.09 µg/L) in the current study. In fact, it only implied that cows fed the basal diet in current study had achieved the required minimum level for Se. After all, the milk yield, Se concentration of serum, and milk increased significantly with HMBSe's addition compared to that of control and SS, which were consistent with the general view that the organic Se was more efficient than SS. Despite the Se concentration of HMBSe in serum and milk being approximately 1.23 and 1.13, 1.67 and 1.59 of control and SS, respectively, this was lower than results (1.43 and 1.23, 2.91 and 2.32) reported by Sun et al. (2017) [9], but the results of the two studies were similar. These results proved that the HMBSe, a novel organic Se, was an efficient Se source to increase the milk Se concentration for early-lactating dairy cows compared to control and SS. At same time, we know that milk/serum of total Se concentration in cows supplemented with HMBSe was also higher than that of control and SS, which showed a greater transfer of Se from blood to milk after HMBSe supplementation. The greater transfer might be due to there being different metabolic pathways between organic and inorganic Se [41]. On the other hand, this might be due to the symmetrical and chelated structure of HMBSe according to 1:2 ratio, which ensured that trace Se could be protected duplicatedly during the course of passing the gastrointestinal tract. At same time, it avoided antagonism of metal ion, resulting in lower absorption and utilization. Therefore, its stability promoted more trace elements to be absorbed by animals [6].

5. Conclusions

The present study showed that, compared to control and inorganic selenium, the addition of hydroxyselenomethionine with symmetrical and chelated chemical structure, a novel organic selenium source in diets, increased selenium concentration of milk and serum, improved milk production and quality, and enhanced antioxidant status and immunities for early-lactating dairy cows. Compared with that of control and sodium selenite, cows fed hydroxyselenomethionine had greater transfer efficiency into the blood circulation and milk, indicating that hydroxyselenomethionine could be a good source to produce high-selenium milk products. This implied that hydroxyselenomethionine was an effective inorganic selenium replacer in terms of performance, health status, and food qualities of dairy cows.

Author Contributions: Y.L.: Conceptualization, Methodology, Validation, Sample collection and preservation, Sample analysis, Data curation, Writing—original draft. W.Z.: Conceptualization, Methodology, Validation, Writing—review & editing, Project administration. H.Z.: Sample analysis, Data curation, Manuscript proofreading. J.Z.: Project administration, Funding acquisition. C.P.: Manuscript proofreading, Project administration. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Research on Teaching Innovative Team of National Vocational Education Teachers of the Second Group in Ministry of Education (ZI2021100105) and the Key Scientific and Research Projects of Colleges and Universities of Henan Province (22A230019).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of the College's guidelines for animal research.

Informed Consent Statement: All the experimental protocols performed in this study were approved by the Animal Care Committee of Henan Vocational College of Agriculture.

Data Availability Statement: Not applicable.

Acknowledgments: We are also grateful to the students of the Henan Vocational College of Agriculture (Zhengzhou, China) for their help with sample preparation and analysis.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Ceballos, A.; Sánchez, J.; Stryhn, H.; Montgomery, J.B.; Barkema, H.W.; Wichtel, J.J. Meta-analysis of the effect of oral selenium supplementation on milk selenium concentration in cattle. *J. Dairy Sci.* **2009**, *92*, 324–342. [CrossRef] [PubMed]
2. Suksombat, W.; Nanon, A.; Klangnork, P.; Homkhao, J. Effects of Met Hydroxy Analog plus MINTREX® Dairy Supplementation on Performance of Lactating Dairy Cows. *J. Anim. Vet. Adv.* **2011**, *10*, 2814–2818.
3. Phipps, R.H.; Grandison, A.S.; Jones, A.K.; Juniper, D.T.; Ramos Morales, E.; Bertin, G. Selenium supplementation of lactating dairy cows: Effects on milk production and total selenium content and speciation in blood, milk and cheese. *Animal* **2008**, *2*, 1610–1618. [CrossRef] [PubMed]
4. Martin, B.; Fedele, V.; Ferlay, A.; Grolier, P.; Rock, E.; Gruffat, D.; Chilliard, Y. Effects of grass-based diets on the content of micronutrients and fatty acids in bovine and caprine dairy products. *Grassl. Sci. Eur.* **2004**, *9*, 876–886.
5. Yang, Z.W.; Aygul, N.; Liu, X.R.; Zhao, S.S.; Zhao, W.Q.; Yang, S. Structure of copper chelate of 2-Hydroxy-4-methylthiobutanoic acid as trace mineral additive in animal feeding. *Chinese J. Struct. Chem.* **2015**, *34*, 147–153.
6. Conti, G.; Castillo, G.; Gallardo, M.; Toffano, S.; Vazquez-Anon, M. Supplementation of methionine hydroxy analog, trace mineral chelates and dietary antioxidants in the diet of dairy cows for milk production, milk composition, and hoof status. *J. Dairy Sci.* **2010**, *93*, 718.
7. Katya, K.; Lee, S.; Bharadwaj, A.S.; Browdy, C.L.; Vazquez-Anon, M.; Bai, S.C. Effects of inorganic and chelated trace mineral (Cu, Zn, Mn and Fe) premixes in marine rockfish, Sebastes schlegeli (Hilgendorf), fed diets containing phytic acid. *Aquac. Res.* **2017**, *48*, 4165–4173. [CrossRef]
8. St-Pierre, N.R.; Sylvester, J.T. Effects of 2-hydroxy-4-(methylthio) butanoic acid (HMB) and its isopropyl ester on milk production and composition by Holstein cows. *J. Dairy Sci.* **2005**, *88*, 2487–2497. [CrossRef]
9. Sun, P.; Wang, J.; Liu, W.; Bu, D.P.; Liu, S.J.; Zhang, K.Z. Hydroxy-selenomethionine: A novel organic selenium source that improves antioxidant status and selenium concentrations in milk and serum of mid-lactation dairy cows. *J. Dairy Sci.* **2017**, *100*, 9602–9610. [CrossRef]
10. MOA (Ministry of Agriculture of P. R. China). *Feeding Standard of Dairy Cattle (NY/T 34-2004)*; MOA: Beijing, China, 2004.
11. West, J.W.; Mullinix, B.G.; Bernard, J.K. Effects of hot, humid weather on milk temperature, dry matter intake, and milk yield of lactating dairy cows. *J. Dairy Sci.* **2003**, *86*, 232–242. [CrossRef]
12. Wang, D.M.; Liu, H.Y.; Wang, C.; Liu, J.X.; Ferguson, J.D. Effects of rumen-protected gamma-aminobutyric acid on feed intake, performance and antioxidative status in transition cows. *Livest. Sci.* **2013**, *153*, 66–72. [CrossRef]
13. AOAC (Association of Official Analytical Chemists). *Official Methods of Analysis*, 15th ed.; AOAC: Arlington, VA, USA, 1990.
14. Van Soest, P.J.; Robertson, J.B.; Lewis, B.A. Symposium: Carbohydrate methodology, metabolism and nutritional implications in dairy cattle methods for dietary fiber, neutral detergent fiber and nonstarch polysaccharides in relation to animal nutrition. *J. Dairy Sci.* **1991**, *74*, 4377–4384. [CrossRef]
15. Wang, D.M.; Wang, C.; Liu, H.Y.; Liu, J.X.; Ferguson, J.D. Effects of rumen-protected γ-aminobutyric acid on feed intake, lactation performance, and antioxidative status in early lactating dairy cows. *J. Dairy Sci.* **2013**, *96*, 3222–3227. [CrossRef] [PubMed]
16. Laporte, M.F.; Paquin, P. Near-infrared analysis of fat, protein, and casein in cow's milk. *J. Agric. Food Chem.* **1999**, *47*, 2600–2605. [CrossRef] [PubMed]
17. Bashtani, M.; Farhangfar, H.; Naeimipour, H.; Asghari, M.R. Application of milk urea nitrogen index (MUN I) for monitoring protein nutrition status in lactating dairy cow. *J. Agric. Sci. Nat. Resour.* **2009**, *16*, 110–118.
18. Davidson, S.; Hopkins, B.A.; Odle, J.; Brownie, C.; Fellner, V.; Whitlow, L.W. Supplementing limited methionine diets with rumen-protected methionine, betaine, and choline in early lactation Holstein cows. *J. Dairy Sci.* **2008**, *91*, 1552–1559. [CrossRef]
19. Zhang, X.Y.; Tan, Y.L.; Cao, L.Y.; Wu, G.Y.; Xu, Q.; Shen, Y.; Zhou, D.F. Antioxidant enzymes and lipid peroxidation in different forms of schizophrenia treated with typical and atypical antipsychotics. *Schizophr. Res.* **2006**, *81*, 291–300. [CrossRef] [PubMed]
20. Faggio, C. Haematological and biochemical response of Mugil cephalus after acclimation to captivity. *Cah. De Biol. Mar.* **2014**, *55*, 31–36.
21. Silva, R.G.D.; Costa, M.J.R.P.D.; Sobrinho, A.G.S. Influence of hot environments on some blood variables of sheep. *Int. J. Biometeorol.* **1992**, *36*, 223–225. [CrossRef]
22. Arthur, J. The glutathione peroxidases. *Cell Mol Life Sci. CMLS.* **2001**, *57*, 1825–1835. [CrossRef]

23. Ran, L.; Wu, X.; Shen, X.; Zhang, K.; Ren, F.; Huang, K. Effects of selenium form on blood and milk selenium concentrations, milk component and milk fatty acid composition in dairy cows. *J. Sci. Food Agric.* **2010**, *90*, 2214–2219. [CrossRef]
24. Trevisi, E.; Amadori, M.; Cogrossi, S.; Razzuoli, E.; Bertoni, G. Metabolic stress and inflammatory response in high-yielding, periparturient dairy cows. *Res. Vet. Sci.* **2012**, *93*, 695–704. [CrossRef] [PubMed]
25. Serrapica, F.; Masucci, F.; Romano, R.; Napolitano, F.; Sabia, E.; Aiello, A.; Francia, A.D. Effects of chickpea in substitution of soybean meal on milk production, blood profile and reproductive response of primiparous buffaloes in early lactation. *Animals* **2020**, *10*, 515. [CrossRef] [PubMed]
26. Calamari, L.; Petrera, F.; Bertin, G. Effects of either sodium selenite or Se yeast (Sc CNCM I-3060) supplementation on selenium status and milk characteristics in dairy cows. *Livest. Sci.* **2010**, *128*, 154–165. [CrossRef]
27. Juniper, D.T.; Phipps, R.H.; Jones, A.K.; Bertin, G. Selenium supplementation of lactating dairy cows: Effect on selenium concentration in blood, milk, urine, and feces. *J. Dairy Sci.* **2006**, *89*, 3544–3551. [CrossRef]
28. Gong, J.; Ni, L.; Wang, D.; Shi, B.; Yan, S. Effect of dietary organic selenium on milk selenium concentration and antioxidant and immune status in midlactation dairy cows. *Livest. Sci.* **2014**, *170*, 84–90. [CrossRef]
29. Batistel, F.; Arroyo, J.M.; Bellingeri, A.; Wang, L.; Saremi, B.; Parys, C.; Trevisi, E.; Cardoso, F.C.; Loor, J. Ethyl-cellulose rumen-protected methionine enhances performance during the periparturient period and early lactation in Holstein dairy cows. *J. Dairy Sci.* **2017**, *100*, 7455–7467. [CrossRef]
30. Batistel, F.; Arroyo, J.M.; Garces, C.I.; Trevisi, M.E.; Parys, C.; Ballou, M.A.; Cardoso, F.C.; Loor, J.J. Ethyl-cellulose rumen-protected methionine alleviates inflammation and oxidative stress and improves neutrophil function during the periparturient period and early lactation in Holstein dairy cows. *J. Dairy Sci.* **2018**, *101*, 480–490. [CrossRef]
31. Sordillo, L.M.; Aitken, S.L. Impact of oxidative stress on the health and immune function of dairy cattle. *Vet. Immunol. Immunop.* **2009**, *128*, 104–109. [CrossRef]
32. Ibeagha, A.E.; Ibeagha-Awemu, E.M.; Mehrzad, J.; Baurhoo, B.; Kgwatalala, P.; Zhao, X. The effect of selenium sources and supplementation on neutrophil functions in dairy cows. *Animal* **2009**, *3*, 1037–1043. [CrossRef]
33. Hall, J.A.; Bobe, G.; Vorachek, W.R.; Kasper, K.; Traber, M.G.; Mosher, W.D.; Pirelli, G.J.; Gamroth, M. Effect of supranutritional organic selenium supplementation on postpartum blood micronutrients, antioxidants, metabolites, and inflammation biomarkers in selenium-replete dairy cows. *Biol. Trace Elem. Res.* **2014**, *161*, 272–287. [CrossRef] [PubMed]
34. Pilarczyk, B.; Jankowiak, D.; Tomza-Marciniak, A.; Pilarczyk, R.; Sablik, P.; Drozd, R.; Tylkowska, A.; Skólmowska, M. Selenium Concentration and Glutathione Peroxidase (GSH-Px) Activity in Serum of Cows at Different Stages of Lactation. *Biol. Trace Elem. Res.* **2012**, *147*, 91–96. [CrossRef] [PubMed]
35. Cao, J.; Guo, F.; Zhang, L.; Dong, B.; Gong, L. Effects of dietary selenomethionine supplementation on growth performance, antioxidant status, plasma selenium concentration, and immune function in weaning pigs. *J. Anim. Sci. Biotechnol.* **2014**, *5*, 46. [CrossRef]
36. Ortman, K.; Pehrson, B. Effect of selenate as a feed supplement to dairy cows in comparison to selenite and selenium yeast. *J. Anim. Sci.* **1999**, *77*, 3365–3370. [CrossRef] [PubMed]
37. Knowles, S.O.; Grace, N.; Wurms, K.; Lee, J. Significance of amount and form of dietary selenium on blood, milk, and casein selenium concentrations in grazing cows. *J. Dairy Sci.* **1999**, *82*, 429–437. [CrossRef]
38. Rao, J.R. Study on functions of red blood cell immunity in Kunming Holstein cows. *J. China Dairy Cattle* **1999**, *2*, 20–21.
39. Sivertsen, T.; Overnes, G.; Osterås, O.; Nymoen, U.; Lunder, T. Plasma vitamin E and blood selenium concentrations in Norwegian dairy cows: Regional differences and relations to feeding and health. *Acta Vet. Scand.* **2005**, *46*, 177–191. [CrossRef]
40. Gong, J.; Xiao, M. Selenium and antioxidant status in dairy cows at different stages of lactation. *Biol. Trace Elem. Res.* **2016**, *171*, 89–93. [CrossRef]
41. Fairweather-Tait, S.J.; Collings, R.; Hurst, R. Selenium bioavailability: Current knowledge and future research requirements. *Am. J. Clin. Nutr.* **2010**, *91*, 1484–1491. [CrossRef]