Effects of Cysteamine Hydrochloride on Fur Quality, Serum Biochemical Parameters, Hormone Indices, and Hepatic Gene Expression in Male Mink during the Winter Fur Growth Period (Postprint)

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Abstract

This experiment aimed to investigate the effects of dietary supplementation of cysteamine hydrochloride (CSH) on fur quality, serum biochemical and hormone indices, and liver-related gene expression in male mink during the winter fur period. Fifty-six healthy male mink at 160 days of age with similar body weight [(2.13±0.10) kg] were selected and randomly divided into 7 groups with 8 replicates per group and 1 mink per replicate. Each group was fed experimental diets supplemented with 0 (Group , control group), 60 (Group), 90 (Group), 120 (Group), 60 (Group), 90 (Group), and 120 mg/kg (Group) CSH in the basal diet; among them, Groups , , and were continuously supplemented, while Groups , , and were intermittently supplemented (continuous supplementation for 1 week, interval for 1 week). The preliminary period was 7 days, and the formal experimental period was 51 days. The results showed: 1) The pelt length, guard hair length, and underhair length of mink in Groups and were significantly or extremely significantly higher than those in the control group (P<0.05 or P<0.01). 2) The serum urea nitrogen content in Groups , , ,

, and was significantly or extremely significantly lower than that in the control group (P<0.05 or P<0.01), and the serum triglyceride content in Groups , , , , and was significantly or extremely significantly lower than that in the control group (P<0.05 or P<0.01). 3) The serum growth hormone content in Group was significantly higher than that in the control group and Group (P<0.05), the serum somatostatin content in Groups , , and was significantly lower than that in the control group and Group (P<0.05), the serum growth hormone receptor content in Groups , , , , , and was significantly or extremely significantly higher than that in the control group (P<0.05 or P<0.01), and the serum insulin-like growth factor-I content in Groups , , , , and was significantly higher than that in Group (P<0.05). 4) The liver insulin-like growth factor-I gene expression level in Group was significantly higher than that in the control group and Groups , , and (P<0.05), the liver insulin-like growth factor-I receptor gene expression level in Group was significantly higher than that in Groups , , and (P<0.05), and the liver growth hormone receptor gene expression level in Groups , , , , , and was significantly or extremely significantly higher than that in the control group (P<0.05 or P<0.01). In conclusion, under the conditions of this experiment, the appropriate supplementation level of CSH in the diet of male mink during the winter fur period was 90 mg/kg, and the appropriate supplementation method was intermittent supplementation.

Full Text

Effects of Cysteamine Hydrochloride on Fur Quality, Serum Biochemical and Hormone Parameters, and Liver-Related Gene Expression in Male Minks during the Winter Fur-Growing Period

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Abstract

This experiment was conducted to investigate the effects of dietary cysteamine hydrochloride (CSH) on fur quality, serum biochemical and hormone parameters, and liver-related gene expression in male minks during the winter fur-growing period. Fifty-six 160-day-old healthy male minks with similar body weight [(2.13±0.10) kg] were randomly divided into 7 groups, with 8 replicates per group and 1 mink per replicate. The groups were fed experimental diets supplemented with 0 (Group , control), 60 (Group), 90 (Group), 120 (Group

), 60 (Group), 90 (Group), and 120 mg/kg (Group) CSH, respectively. Groups , , and received continuous supplementation, while Groups , , and received interval supplementation (continuous for 1 week, interval for 1 week). The pre-experimental period lasted 7 days, and the experimental period lasted 51 days. The results showed: (1) The skin length, guard hair length, and underfur length of minks in Groups and were significantly or highly significantly higher than those in the control group (P<0.05 or P<0.01). (2) Serum urea nitrogen content in Groups , , , , and was significantly or highly significantly lower than that in the control group (P<0.05 or P<0.01), and serum triglyceride content in these groups was also significantly or highly significantly lower than that in the control group (P<0.05 or P<0.01). (3) Serum growth hormone content in Group was significantly higher than that in the control group and Group (P<0.05). Serum somatostatin content in Groups , , and was significantly lower than that in the control group and Group (P<0.05). Serum growth hormone receptor content in Groups , , , , , and was significantly or highly significantly higher than that in the control group (P<0.05 or P<0.01). Serum insulin-like growth factor-I content in Groups , , , , and was significantly higher than that in Group (P<0.05). (4) Liver insulin-like growth factor-I gene expression in Group was significantly higher than that in the control group and Groups , , and (P<0.05). Liver insulin-like growth factor-I receptor gene expression in Group was significantly higher than that in Groups , , and (P<0.05). Liver growth hormone receptor gene expression in Groups , , , , , and was significantly or highly significantly higher than that in the control group (P<0.05 or P<0.01). In conclusion, under the conditions of this experiment, the optimal dietary CSH supplementation level for male minks during the winter fur-growing period is 90 mg/kg, with interval supplementation being the appropriate method.

Keywords: cysteamine hydrochloride; minks; fur quality; serum parameters; gene expression

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Introduction

Cysteamine hydrochloride (CSH), as a functional feed additive, exhibits multiple biological functions, primarily manifested through regulating endocrine function and depleting somatostatin (SS) to promote animal growth [1]. This has been confirmed in poultry, swine, livestock, and aquaculture production. As an SS inhibitor, CSH has been widely applied in livestock and poultry production mainly because it can regulate animal growth through neuroendocrine pathways. CSH functions by inhibiting SS immunoreactivity and biological activity in peripheral and central nervous tissues, thereby relatively increasing growth hormone (GH) content in the body and promoting animal growth, making it a highly efficient SS inhibitor. Studies have shown that CSH can reduce pituitary prolactin content and inhibit dopamine- -hydroxylase activity [2-4]. Dopamine- -hydroxylase catalyzes the conversion of dopamine to norepinephrine, and inhibition of its activity leads to dopamine accumulation in the hypothalamus, thereby promoting GH synthesis and secretion and consequently stimulating animal growth. CSH can cause rapid loss of SS immunoreactivity in animal tissues (pancreas, digestive tract, and central nervous tissue) and serum [5-8]. In pancreatic tissue, CSH inhibits SS immunoreactivity in islet cells while preventing SS secretion from these cells [5-8]. McLeod et al. [9] found that CSH can increase the secretion of insulin, insulin-like growth factor-I (IGF-I), triiodothyronine (T3), and thyroxine (T4). These hormones are important for promoting growth and development and participating in anabolism, thus exerting growth-promoting effects on animals.

Feed nutrition is a critical factor affecting fur quality in fur-bearing animals, and nutritional regulation technology is key to improving pelt quality and farming efficiency. Wang [10] found that adding 70 mg/kg BW CSH to the diet at 5-day intervals increased average daily gain and feed conversion ratio in silver foxes, while also improving litter size during the reproductive period. Bai et al. [11] reported that dietary CSH supplementation increased average daily gain and serum GH, T3, T4, and IGF-I levels in growing male minks, with some improvement in fur quality. Huang [12] discovered that adding 20 mg/kg CSH to dry powder diets increased average daily gain, nutrient digestibility, feed conversion ratio, and fur quality in raccoon dogs, while elevating serum total protein (TP), cholesterol (CHO), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride (TG) levels. Xu et al. [13] found that dietary supplementation with 5 mg/d CSH promoted growth in nutrias and increased serum GH and IGF-I levels.

CSH demonstrates growth-promoting effects in fur-bearing animals, though its mechanism of action requires further investigation. Based on this background and considering the physiological characteristics of minks and the mechanism of CSH action, this experiment was designed to study the effects of dietary CSH supplementation on fur quality, serum biochemical and hormone parameters, and liver-related gene expression in male minks during the winter fur-growing period, aiming to provide a theoretical basis for CSH application in mink production.

1.1 Experimental Material

The CSH used in this experiment was -CD-CSH, provided by Shanghai Huakuoda Biochemical Technology Co., Ltd. This physiological metabolism regulation additive is produced using supramolecular technology, biomimetic membrane technology, and physiological homeostasis maintenance technology through a special process with -cyclodextrin and CSH as nutritional active substances, possessing certain stability with CSH active ingredient content 30%.

1.2 Experimental Design

The experiment was conducted at the Fur Animal Experimental Base of the Institute of Special Animal and Plant Sciences, Chinese Academy of Agricultural Sciences. A two-factor experimental design was employed, with CSH supplementation level and supplementation method as the factors. Fifty-six 160-day-old healthy male minks with similar body weight [(2.13±0.10) kg] were randomly divided into 7 groups, with 8 replicates per group and 1 mink per replicate. The pre-experimental period lasted 7 days, and the experimental period lasted 51 days.

1.3 Experimental Diets and Management

The basal diet was formulated according to the nutrient requirements for minks specified in NRC [14] (1982) and based on years of experimental experience from our research group. The composition and nutrient levels of the basal diet are shown in Table 1 . Each group was fed the basal diet supplemented with 0 (Group , control), 60 (Group), 90 (Group), 120 (Group), 60 (Group), 90 (Group), and 120 mg/kg (Group) CSH, respectively. Groups , , and received continuous supplementation, while Groups , , and received interval supplementation (continuous for 1 week, interval for 1 week). Experimental animals were housed individually in cages, managed by designated personnel, and fed at 08:00 and 15:00 daily with ad libitum access to feed and water. Animal health status was observed and recorded.

Table 1 Composition and Nutrient Levels of the Basal Diet (Air-Dry Basis)

Items	Content (%)
Ingredients	
Catfish	
Anglerfish	
Chicken liver	

Items	Content (%)
Chicken skeleton	
Glandular stomach	
Extruded corn	
Premix[1]	
Total	
Nutrient Levels	
Dry matter (DM)	
Crude protein (CP)	
Crude fat (EE)	
Metabolizable energy (ME, MJ/kg)[2]	

[1]The premix provided the following per kg of diet: VA 10,000 IU, VD 2,000 IU, VE 100 IU, VB 6 mg, VB 10 mg, VB 6 mg, VB 0.1 mg, VK 1 mg, VC 400 mg, nicotinic acid 30 mg, D-pantothenic acid 40 mg, biotin 0.2 mg, folic acid 1 mg, choline 400 mg, Fe 82 mg, Cu 20 mg, Mn 120 mg, Zn 50 mg, I 0.5 mg, Se 0.2 mg, Co 0.3 mg.
[2]ME was a calculated value, while others were measured values.

1.4 Sample Collection and Measurements

1.4.1 Fur Quality Measurements After the feeding trial, animals were euthanized by subcutaneous injection of succinylcholine chloride. After pelt collection, skin length was measured from nose tip to tail root during stretching, and guard hair length and underfur length at the mid-back region were measured using a precision ruler.

1.4.2 Serum Biochemical and Hormone Parameter Measurements After the feeding trial, 6 healthy minks were selected from each group, and 5 mL of blood was collected from each mink via cardiac puncture before slaughter into procoagulant tubes. Samples were immediately transported to the laboratory and centrifuged at 4,000 r/min for 10 min. Serum was separated into 1.5 mL EP tubes and stored at -20°C for later analysis. Serum biochemical parameters [TP, albumin (ALB), globulin (GLO), urea nitrogen (UN), TG, CHO] were measured using an automatic biochemical analyzer (Selectra E, Netherlands) with test kits from Zhongsheng Beikong Biotechnology Co., Ltd., following kit instructions strictly. Serum hormone parameters [GH, SS, growth hormone receptor (GHR), IGF-I, insulin-like growth factor-I receptor (IGF-IR), T3, T4] were measured using enzyme-linked immunosorbent assay (ELISA) kits from Nanjing Zhongsheng Beikong Biotechnology Co., Ltd., following kit instructions strictly.

1.4.3 Liver-Related Gene Expression Measurements After the feeding trial, experimental animals were euthanized. The liver (5-10 g) was dissected, placed in RNase-free cryotubes, immediately immersed in liquid nitrogen, and transferred to -80°C storage the next day. Reagents prepared included RNase-free and DNase-free water, chloroform, isopropanol, anhydrous ethanol, Trizol, reverse transcription kit, PCR kit, DNA Marker DL500, pMD™18-T Vector, agarose gel DNA recovery kit, and fluorescent quantitative PCR reaction kit. Total RNA from mink liver was extracted using the Trizol method. Reverse transcription was performed using a two-step method with TaKaRa reverse transcription kit: step 1 removed genomic DNA, and step 2 performed reverse transcription. -actin primers were designed according to Zhang [15]; specific primers for mink IGF-I (GenBank accession: FJ_472818.1), insulin-like growth factor-I receptor (IGF-IR) (GenBank accession: XM_004759809.1), and growth hormone receptor (GHR) (GenBank accession: XM_004737948.2) were designed using Primer 5.0. Primers were synthesized by Huada Gene, and PCR primer sequences are shown in Table 2 . Gene expression levels were calculated using the 2^(-ΔΔCT) method.

Table 2 Primer Sequences for PCR

Genes	Primer Sequence (5' -3')	Product Size (bp)
-actin	F: GCGTGACATCAAGGAAGAAGCR: CCGTCGGGTAGTTCGTAGCT	
IGF-I	F: TATTTCAACAAGCCCACGR: GTTTCCTGCACTCCCTCT	
IGF-IR	F: CTATACAGCCCGGATCCAGGR: TACAGCACTCCATTCCCCAG	
GHR	F: AAAGCCTTACCACTACCGCTR: AGTTGGTCTGTGCTCACGTA	

1.5 Statistical Analysis

Data were analyzed using two-way ANOVA with SAS 9.1 statistical software. Significant differences were determined using Duncan' s multiple comparison test, and multi-factor statistical analysis was performed using the GLM procedure. Data are expressed as mean ± standard deviation. P>0.05 indicated no significant difference, P<0.05 indicated significant difference, and P<0.01 indicated highly significant difference.

2.1 Effects of CSH on Fur Quality of Male Minks during Winter Fur-Growing Period

As shown in Table 3 , dietary CSH supplementation significantly affected mink skin length, guard hair length, and underfur length (P<0.05). Skin length increased with increasing CSH supplementation level, with Groups and being significantly higher than the control group (P<0.05). Guard hair length and underfur length were highest in Groups and , respectively, being highly significantly (P<0.01) and significantly (P<0.05) higher than the control group. CSH supplementation method highly significantly affected guard hair length (P<0.01), with the interval supplementation group being highly significantly higher than the continuous supplementation group (P<0.01). CSH supplementation level significantly affected guard hair length (P<0.05), with the 90 mg/kg group being significantly higher than the 60 and 120 mg/kg groups (P<0.05). CSH supplementation method and level showed significant or highly significant interactive effects on guard hair length and underfur length (P<0.05 or P<0.01).

Table 3 Effects of CSH on Fur Quality of Male Minks during Winter Fur-Growing Period

Items	Groups	Supplemental Level (mg/kg)	Supplemental Way	Skin Length (cm)	Guard Hair Length (mm)	Underfur Length (mm)
	(Control)	0	Continuous	57.30±1.77	22.01±0.98	16.09±0.65
		60	Continuous	58.43±2.15	22.89±0.98	16.57±0.45
		90	Continuous	58.83±1.94	23.31±1.09	16.44±0.20
		120	Continuous	59.50±2.43	21.73±0.66	16.12±0.68
		60	Interval	59.00±1.13	22.29±0.84	16.14±0.23
		90	Interval	59.92±1.34	23.91±1.11	16.89±0.68
		120	Interval	61.21±2.58	24.08±0.91	16.79±0.69
P-value						
Supplemental Way				0.0001	<0.0001	0.16
Supplemental Level				0.16	0.0001	0.02
Supplemental Way × Level				0.34	<0.0001	0.0001

In the same item and column, values with different lowercase superscripts indicate significant difference (P<0.05), different uppercase superscripts indicate highly significant difference (P<0.01), and same or no superscripts indicate no significant difference (P>0.05). The same applies below.

2.2 Effects of CSH on Serum Biochemical Parameters of Male Minks during Winter Fur-Growing Period

As shown in Table 4 , dietary CSH supplementation significantly affected serum UN and TG content (P<0.05). Specifically, serum UN content in Groups , , , and was highly significantly lower than that in the control group (P<0.01), while Group was significantly lower (P<0.05). Serum TG content in Groups , , and was highly significantly lower than that in the control group and Group

(P<0.01), and Groups and were significantly lower than the control group (P<0.05). CSH supplementation method highly significantly affected serum UN content (P<0.01), with the interval supplementation group being highly significantly lower than the continuous supplementation group (P<0.01). CSH supplementation level significantly or highly significantly affected serum UN and TG content (P<0.05 or P<0.01), with the 90 mg/kg group showing significantly lower serum UN content than the 60 and 120 mg/kg groups (P<0.05), and highly significantly lower serum TG content than the 120 mg/kg group (P<0.01). CSH supplementation method and level showed a significant interactive effect on serum TG content (P<0.05).

Table 4 Effects of CSH on Serum Biochemical Parameters of Male Minks during Winter Fur-Growing Period

Items	Groups	TP (g/L)	ALB (g/L)	GLO (g/L)	UN (mmol/L)	TG (mmol/L)	CHO (mmol/L)
	(Control)	79.16±1.53	39.10±1.33	40.06±1.60	17.90±1.22	4.15±0.47	5.34±0.94
		78.71±5.40	37.14±4.12	41.57±9.29	15.59±1.12	2.13±0.97	5.21±0.42
		79.75±5.39	38.34±0.56	41.41±5.95	14.25±0.64	1.91±0.51	4.76±0.07
		80.38±9.53	39.50±5.93	40.88±9.90	16.27±0.85	3.53±0.87	5.12±0.80
		77.89±5.59	39.70±4.15	38.20±6.57	14.57±1.93	2.46±0.73	4.94±0.50
		81.34±10.37	41.20±1.48	42.21±9.12	12.75±1.85	2.01±0.70	5.17±0.71
		82.42±4.45	40.03±2.95	42.40±6.57	13.62±1.14	2.41±0.53	5.01±0.88
P-value							
Supplemental Way		0.64	0.89	0.45	<0.0001	<0.0001	0.88
Supplemental Level		0.45	0.45	0.88	0.0001	0.0001	0.45
Supplemental Way × Level		0.88	0.45	0.88	0.02	0.02	0.88

2.3 Effects of CSH on Serum Hormone Parameters of Male Minks during Winter Fur-Growing Period

As shown in Table 5 , dietary CSH supplementation significantly or highly significantly affected serum GH, SS, GHR, and IGF-I content (P<0.05 or P<0.01). Specifically, serum GH content increased initially and then decreased with increasing CSH supplementation level, with Group being significantly higher than the control group and Group (P<0.05). Serum SS content in Groups , , and was significantly lower than that in Groups and (P<0.05). Serum

GHR content in Groups , , and was significantly higher than that in the control group (P<0.05), while Groups , , and were highly significantly higher (P<0.01). Serum IGF-I content in Groups , , , , and was significantly higher than that in Group (P<0.05). CSH supplementation method had no significant effect on serum hormone content (P>0.05). CSH supplementation level significantly affected serum SS content (P<0.05), with the 90 mg/kg group being significantly lower than the 120 mg/kg group. No significant interactive effect between CSH supplementation method and level was observed on serum hormone content (P>0.05).

Table 5 Effects of CSH on Serum Hormone Parameters of Male Minks during Winter Fur-Growing Period

Items	Groups	GH (ng/mL)	SS (ng/mL)	GHR (ng/mL)	IGF-I (ng/mL)	IGF-IR (ng/mL)	T3 (nmol/L)	T4 (nmol/L)
	(Control)	0.89±0.06	43.25±3.09	3.81±0.47	79.58±0.88	7.28±0.81	0.65±0.17	22.75±4.36
		0.97±0.11	35.96±9.51	4.92±0.71	82.64±11.96	6.76±0.82	0.66±0.16	22.97±4.42
		1.01±0.09	34.08±2.44	5.22±0.32	83.05±2.95	6.82±0.33	0.68±0.18	20.27±2.48
		0.94±0.04	42.37±5.13	4.66±0.77	73.29±7.74	6.46±0.80	0.62±0.15	21.14±4.03
		1.02±0.15	39.53±3.59	4.98±0.96	83.86±7.95	7.42±1.31	0.70±0.14	21.49±3.69
		1.09±0.06	35.44±2.47	5.30±0.11	84.72±3.38	7.26±0.26	0.66±0.06	21.70±4.09
		0.98±0.05	39.80±5.08	4.76±0.59	81.89±3.04	6.92±0.94	0.71±0.09	21.83±3.05
P-value								
Supplemental Way		0.45	0.45	0.45	0.45	0.45	0.45	
Supplemental Level		0.45	0.02	0.45	0.45	0.45	0.45	
Supplemental Way × Level		0.02	0.02	0.02	0.02	0.88	0.88	

2.4 Effects of CSH on Hepatic IGF-I, IGF-IR, and GHR Gene Expression in Male Minks during Winter Fur-Growing Period

As shown in Table 6 , dietary CSH supplementation significantly or highly significantly affected hepatic IGF-I, IGF-IR, and GHR gene expression (P<0.05 or P<0.01). Specifically, Group showed the highest hepatic IGF-I, IGF-IR, and GHR gene expression. Hepatic IGF-I gene expression in Group was significantly higher than that in the control group and Groups , , and (P<0.05), with no significant differences from other groups (P>0.05). Hepatic IGF-IR gene expression in Group was significantly higher than that in Groups , , and

(P<0.05), with no significant differences from other groups (P>0.05). Hepatic GHR gene expression in Groups and was significantly higher than that in the control group (P<0.05), while Groups , , , and were highly significantly higher (P<0.01). CSH supplementation method highly significantly affected hepatic IGF-IR gene expression (P<0.01), with the interval supplementation group being highly significantly higher than the continuous supplementation group (P<0.01). CSH supplementation level significantly or highly significantly affected hepatic IGF-I and IGF-IR gene expression (P<0.05 or P<0.01), with expression increasing initially and then decreasing as CSH supplementation level increased. The 90 mg/kg group showed significantly or highly significantly higher hepatic IGF-I and IGF-IR gene expression than the 60 and 120 mg/kg groups (P<0.05 or P<0.01). No significant interactive effect between CSH supplementation level and method was observed on hepatic IGF-I, IGF-IR, and GHR gene expression (P>0.05).

Table 6 Effects of CSH on IGF-I, IGF-IR, and GHR Gene Expressions of Male Minks during Winter Fur-Growing Period

Items	Groups	IGF-I	IGF-IR	GHR
	(Control)	1.00±0.31	1.00±0.45	1.00±0.21
		1.09±0.18	0.88±0.12	2.52±0.16
		1.24±0.07	1.02±0.22	2.46±0.81
		0.92±0.29	0.75±0.13	1.88±0.22
		0.97±0.05	0.90±0.13	1.92±0.40
		1.43±0.03	1.29±0.37	2.59±1.30
		1.24±0.50	1.03±0.03	2.15±0.25
P-value				
Supplemental Way		0.02	0.0001	0.45
Supplemental Level		0.02	0.0001	0.45
Supplemental Way × Level		0.45	0.45	0.45

3.1 Effects of CSH on Fur Quality of Minks during Winter Fur-Growing Period

The winter fur-growing period in minks is characterized primarily by fur growth and development, having passed the rapid skeletal growth phase and focusing mainly on muscle growth and fat deposition. Fur quality is a direct indicator for evaluating production performance during this period. This experiment measured skin length, guard hair length, and underfur length at the end of the winter fur-growing period. The results showed that CSH supplementation increased these parameters, with the best effects observed in Groups and . Guard hair length in the interval supplementation group was 3.4% higher than in the continuous supplementation group. Among different supplementation levels, 90 mg/kg showed the optimal effect. CSH demonstrated a positive effect on mink fur quality. Huang et al. [16] found that dietary CSH supplementation improved production performance and reduced feed-to-gain ratio in Northeast fine-wool sheep, with wool length increasing by 9.1%, fineness by 6.2%, and elasticity also improved, showing an initial increase followed by decrease with increasing CSH levels. Xu et al. [17] reported that interval CSH supplementation increased natural length of cashmere and wool by 32.2% and 34.8%, respectively, fiber diameter by 6.56%, and reduced cashmere fineness by 6.22% in Liaoning cashmere goats. Bai et al. [11] found that continuous CSH supplementation increased skin length and weight in male minks during winter fur-growing period, with pelt weight increasing by 23%. In summary, dietary CSH supplementation can improve fur quality in animals, possibly related to the active sulfhydryl groups within CSH molecules. Many factors affect fur quality, and sulfur supply becomes a limiting factor for keratin synthesis. Both organic and inorganic sulfur can promote fur quality [18]. CSH not only provides sulfur to the body but also participates in endocrine regulation, improving nutrient distribution. The combined effects may enhance mink production performance, though the specific mechanism requires further investigation.

3.2 Effects of CSH on Serum Biochemical and Hormone Parameters of Minks during Winter Fur-Growing Period

Protein is the most abundant solid component in blood, playing roles in nutrient transport, regulating physiological functions of transported substances, and modulating immunity. Its analysis helps understand nutritional status and immune function [19]. In this experiment, CSH supplementation significantly increased serum protein content compared to the control group, though it had no significant effect on serum ALB and GLO content. Interval supplementation groups showed higher serum TP and GLO content than continuous supplementation groups. UN is an important indicator of protein catabolism and the main form of nitrogen excretion in mammals, negatively correlating with nitrogen utilization efficiency [20]. In this experiment, CSH supplementation reduced serum UN content compared to the control group, indicating improved nitrogen retention in minks during winter fur-growing period, consistent with nitrogen metabolism study results [21]. During winter fur-growing period, minks have reached mature weight and are in a weight maintenance stage, but fur development, especially guard hair and underfur growth, remains active, with protein being the primary factor affecting fur growth. Elevated serum protein content helps improve nutrient transport, promotes protein deposition, enhances immunity, and consequently stimulates fur growth.

Dietary CSH supplementation significantly reduced serum TG content in male minks during winter fur-growing period, with content decreasing initially and then increasing as CSH supplementation level increased, while serum CHO content showed no significant changes. The liver is the primary source of serum TG synthesis, and hyperlipidemia is one of the main pathogenic factors for fatty liver disease [22]. In this experiment, CSH supplementation reduced serum TG content in minks, suggesting a protective effect on the liver. During winter fur-growing period, minks focus on fur growth and fat deposition for winter survival. Most dietary fat is deposited in subcutaneous adipose tissue. The reduced serum TG content in CSH supplementation groups suggests decreased fat mobilization from adipose tissue and correspondingly promoted fat deposition. Serum biochemical parameters reflect overall metabolic status and are influenced by multiple factors. CSH effects on animals are primarily based on endocrine regulation, which induces related physiological changes. Therefore, changes in serum protein and lipid content may be related to altered hormone secretion status caused by CSH, though the specific reasons require further investigation.

This experiment demonstrated that dietary CSH supplementation increased serum GH, GHR, and IGF-I content while reducing serum SS content in male minks during winter fur-growing period. Interval supplementation significantly increased serum GH content and reduced serum SS content, with 90 mg/kg being the optimal level. These results indicate that dietary CSH supplementation continues to promote the secretion of growth-promoting hormones during winter fur-growing period, particularly affecting IGF-I secretion. SS has physiological functions of inhibiting GH, IGF-I, thyroid-stimulating hormone, and related hormone secretion, while also suppressing gastrointestinal digestive enzyme secretion and activity, thereby inhibiting animal growth and development [23-25]. Hair follicle development is regulated by multiple growth factors, with IGF-I being particularly important [26]. Dietary CSH supplementation increased serum IGF-I content, suggesting that CSH promotes fur growth and development in minks during winter fur-growing period.

3.3 Effects of CSH on Hepatic IGF-I, IGF-IR, and GHR Gene Expression in Male Minks during Winter Fur-Growing Period

Animal growth is regulated by the GH-insulin-like growth factor (IGFs) axis, which mainly includes GH released from the pituitary and IGFs secreted by target organs such as the liver. This experiment investigated CSH effects on gene expression related to the growth axis in minks. The results showed that dietary CSH supplementation increased hepatic IGF-I, IGF-IR, and GHR gene expression, with interval supplementation being superior to continuous supplementation. Expression levels increased initially and then decreased with increasing CSH supplementation level. Li et al. [27] reported that continuous CSH supplementation increased pituitary GH and hepatic GHR gene expression in grouper, with expression increasing initially and then decreasing as CSH level increased. Ma et al. [28] found that intraperitoneal injection of 100 g/g CSH in Nile tilapia significantly increased pituitary GH gene expression while also elevating hepatic GHR and IGF-I gene expression. Ren et al. [29] reported that dietary CSH supplementation increased IGF-I gene expression in liver, muscle, and skin of Northeast fine-wool sheep, which decreased with increasing CSH levels. In summary, dietary CSH supplementation can increase expression of growth axis-related genes, though expression decreases when CSH reaches certain levels, indicating dose-dependency in production applications. Dietary CSH supplementation improved fur quality and increased serum growth-promoting hormone content in minks during winter fur-growing period, consistent with the gene expression results of the growth axis. Overall, dietary CSH supplementation improves fur production performance by regulating the endocrine system and increasing expression of growth axis-related genes, though the effect shows certain dose-time dependency.

This experiment demonstrated that interval supplementation was superior to continuous supplementation. Continuous CSH supplementation can cause gastric ulcers in animals. The growth-promoting mechanism of CSH mainly involves inhibiting SS secretion; however, SS provides significant protection against gastric damage caused by stress and CSH. The characteristic of stress- and CSH-induced ulcers is increased gastric acid and pepsin secretion [30-32].

Conclusions

1. Dietary CSH supplementation can improve fur quality, reduce serum UN content, and increase growth-promoting hormone levels in male minks during the winter fur-growing period.
2. Based on comprehensive evaluation of all indicators, under the conditions of this experiment, the optimal dietary CSH supplementation level for male minks during the winter fur-growing period is 90 mg/kg, with interval supplementation being the appropriate method.

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Note: Figure translations are in progress. See original paper for figures.