Research Progress on Cysteamine in Swine Nutrition: Postprint

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Abstract

Driven by the growing human demand for meat products, maximizing animal growth performance has become a focal point for researchers in animal science. Cysteamine (CS) is a non-hormonal physiological regulator that can exert growth-promoting effects by modulating the animal' s endocrine system, and it possesses multiple physiological functions including antioxidant activity, promotion of intestinal health, and immunomodulation. It has already been utilized as a feed additive in practical production. This article reviews the application of cysteamine in swine nutrition and its potential mechanisms of action, aiming to provide a reference for future scientific research.

Full Text

Review of Cysteamine on Swine Nutrition

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Abstract: With the growing demand for meat products, maximizing animal growth performance has become a key research focus in animal agriculture. Cysteamine (CS) is a non-hormonal physiological regulator that promotes growth by modulating the endocrine system of animals and possesses multiple physiological functions including antioxidant activity, promotion of intestinal health, and immunomodulation. CS has already been utilized as a feed additive in practical production. This review summarizes the application of cysteamine in swine nutrition and its potential mechanisms of action, aiming to provide a reference for future scientific research.

Keywords: cysteamine; pigs; growth performance; meat quality; gut health; stress; immunoregulation

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One of the primary objectives of animal husbandry is to provide more high-quality animal products for human consumption. Under similar nutritional and management conditions, the growth rate of pigs is primarily regulated by hormones related to the endocrine system [1]. Cysteamine (CS) can specifically bind to the disulfide bonds of somatostatin (SS), destroying its biological activity and thereby enhancing animal growth rate through endocrine modulation. Additionally, CS participates in the synthesis and metabolism of important bioactive substances such as cysteine, glutathione (GSH), hypotaurine, and taurine, contributing to the maintenance of the body' s antioxidant defense system. Therefore, CS holds significant importance as a novel feed additive in animal production.

1 Physicochemical Properties of CS

CS, also known as 2-mercaptoethylamine, has a melting point of 99 °C and is highly soluble in water and ethanol. CS is a natural product of coenzyme A degradation in animals. During this process, coenzyme A produces pantetheine, which is then hydrolyzed by pantetheinase to generate CS and pantothenic acid [2-3] [Figure 1: see original paper]. CS can be extracted from animal tissues or synthesized chemically. However, it is easily oxidized to cystamine under exposure to air, alkaline conditions, or in the presence of metal ions. In vivo, exogenous CS readily binds to plasma proteins or is degraded by free radicals [4]. Therefore, in commercial production, CS is typically formulated as cysteamine hydrochloride or encapsulated to ensure better physiological efficacy. Research has shown that encapsulated CS can resist gastric acid degradation while providing sustained release, thereby avoiding damage to the gastric mucosa [5].

2.1 Effects of CS on Growth Performance in Pigs

CS has been employed as a feed additive in pig production to improve growth performance, feed conversion efficiency, protein deposition, muscle growth in piglets and finishing pigs, and reproductive performance in sows. The European Agency for the Evaluation of Medicinal Products (EMEA) has classified CS as an "organic substance for which no maximum residue limit needs to be established" for use in mammals producing food products [6].

In piglet studies, Du et al. [7] demonstrated that dietary supplementation with 36 mg/kg CS (effective dose) fed to piglets from 15 to 35 days of age significantly increased feed intake and body weight gain. In growing-finishing pigs, however, application doses vary considerably. Liu et al. [8] found that supple-

menting finishing pig diets with 70 mg/kg CS for 47 days significantly improved growth performance, whereas other studies reported that an effective dose of 200 mg/kg was required to achieve growth-promoting effects [9-10]. These discrepancies may be related to dietary composition, management practices, and other factors. Additionally, the instability of free sulfhydryl groups in CS may cause partial oxidation and inactivation, reducing the effective dose, while crude CS products may contain off-odors that affect feed intake, leading to variable results. Research indicates that the optimal dose of CS should be appropriately increased with pig body weight during different finishing stages [11].

The growth-promoting mechanism of CS in animals is primarily achieved by inhibiting somatostatin activity. Somatostatin is a brain-gut peptide hormone synthesized and released by the hypothalamus, widely distributed in the gastrointestinal tract, central nervous system, and lymphoid tissues. It inhibits growth hormone (GH) secretion, digestive enzyme secretion in the gastrointestinal tract, peptide hormone release, and smooth muscle contraction, thereby hindering animal growth and nutrient digestion and absorption [12-14]. CS can specifically bind to somatostatin in vivo, disrupting its disulfide bonds and destroying its biological activity, which removes the inhibitory effects on GH and digestive enzyme secretion and promotes nutrient absorption and growth [15-19]. Furthermore, CS metabolites such as taurine can enhance the activities of digestive enzymes including amylase (AMY) and trypsin, indirectly promoting nutrient absorption [20]. However, the growth-promoting effects of CS are dose- and time-dependent, with efficacy diminishing over time. Whether administered orally or via rumen or duodenal fistula, CS' s inhibitory effect on somatostatin activity decreases gradually, returning to pre-treatment levels within approximately one week [21]. Consequently, some researchers have suggested administering CS to growing-finishing pigs every 5-7 days, though this method is cumbersome in practice [22]. Comparative studies have examined continuous versus intermittent supplementation. In growth performance studies, continuous supplementation of a low dose (18.22 mg/kg effective dose) throughout the 56-day finishing period yielded better growth performance than a stepwise increasing regimen (21.87 mg/kg for days 1-28 and 29.16 mg/kg for days 29-56), offering higher cost-effectiveness and greater practical applicability [23]. Another study investigating CS effects during the late finishing phase found that daily administration of 20 mg/kg CS for 20 days improved daily gain more effectively than the same dose administered every 5 days [24].

In sow studies, dietary CS supplementation during late gestation promoted fetal development, increased litter size, birth weight uniformity, and piglet birth weight while reducing the proportion of weak piglets [25-26]. This may be attributed to CS' s ability to regulate sex hormone secretion via the gonadal axis, improving maternal metabolic status and consequently nutrient supply to fetuses. Additionally, CS supplementation during lactation enhanced nutrient utilization, reduced body weight loss from milk production, shortened the weaning-to-estrus interval, and improved piglet survival rates by increasing immunoglobulin content in colostrum [27].

2.2 Effects of CS on Carcass and Meat Quality in Pigs

Research on CS effects on carcass and meat quality has focused primarily on growing-finishing pigs. Studies show that dietary supplementation with 70 mg/kg CS for 47 days significantly improved protein deposition [8]. Additionally, feeding a diet containing 180 mg/kg cysteamine hydrochloride (effective dose) during the late finishing period for 35 days significantly increased lean meat percentage and skeletal ratio while reducing fat percentage and improving meat color [28]. Supplementation with 70 mg/kg cysteamine hydrochloride for 21 days significantly decreased backfat thickness at the P2 site (last rib) [29], and 9.45 mg/kg CS for 29 days significantly increased deoxymyoglobin content while decreasing metmyoglobin content, delaying post-slaughter oxidative discoloration [30].

The mechanisms by which CS improves carcass quality and reduces fat deposition may involve several aspects. First, CS modulates the secretion of growth hormone, thyroid hormone, and glucagon [31-32,43], promoting nutrient repartitioning by reducing lipid synthesis in adipocytes and stimulating protein synthesis and lipolysis in muscle cells [33]. Second, CS regulates thyroid hormone and glucagon secretion, thereby promoting muscle tissue development and fat tissue decomposition [33]. Additionally, CS can reduce body fat deposition by increasing hormone-sensitive lipase activity and decreasing the expression of malate dehydrogenase, glucose-6-phosphate dehydrogenase, and isocitrate dehydrogenase [34-35].

2.3 Effects of CS on Nutrient Metabolism in Pigs

Dietary CS supplementation improves nutrient metabolism. Studies have shown that CS increases serum total protein (TP) content while decreasing serum urea nitrogen (UN) content [34,36]. Serum TP content is an important indicator of protein metabolism, playing crucial roles in maintaining plasma osmotic pressure, buffering blood pH, and providing nutritional supply [37], while also reflecting immune status. Serum UN is a metabolic product formed through the arginine cycle from proteins and amino acids, and its content is significantly negatively correlated with nitrogen retention rate and protein (or amino acid) utilization [38]. Higher TP and lower UN levels indicate stable amino acid metabolism, strong protein anabolism, and high dietary nitrogen utilization efficiency. Therefore, CS promotes protein metabolism and improves nitrogen utilization.

Regarding lipid and carbohydrate metabolism, CS reduces serum total cholesterol (TC), triglyceride (TG), and glucose (GLU) contents [39-40]. Since carbohydrate, protein, and lipid metabolism are all regulated by endocrine hormones, CS enhances glucose utilization by tissues through increased insulin activity. CS also accelerates adipose tissue decomposition, transporting blood cholesterol and triglycerides back to the liver for energy production to spare glucose, thereby reducing blood TC and TG levels. The underlying mechanism involves CS binding

to sulfur-containing amino acids in hepatic enzymes involved in cholesterol and triglyceride synthesis, inhibiting their activity and thus suppressing synthesis while promoting degradation [41].

Furthermore, different feeding modes affect nutrient metabolism differently. Research shows that continuous feeding of 37.5 mg/kg CS (effective dose) to finishing pigs resulted in higher serum activities of glutamate-pyruvate transaminase (GPT), glutamate-oxaloacetate transaminase (GOT), alkaline phosphatase (AKP), and amylase compared to intermittent feeding every 6 days. GPT and GOT reflect protein anabolic status, AKP participates in lipid metabolism, and amylase is involved in carbohydrate metabolism—all positively correlated with nutrient digestion and absorption. These results suggest that continuous CS supplementation is more effective in improving nutrient metabolism [42].

2.4 Effects of CS on Intestinal Health and Nutrient Absorption in Pigs

The small intestine is the primary site for nutrient digestion and absorption, making studies on CS' s intestinal effects crucial for pig production guidance. Dietary CS supplementation improves the apparent digestibility of dietary dry matter, nitrogen-free extract, crude protein, crude fat, crude fiber, calcium, and total phosphorus in growing pigs [43]. CS also significantly increases the activities of protease, lipase, and amylase in small intestinal contents and enhances trypsin activity [44]. This may occur because CS removes somatostatin' s inhibitory effects on secretin and cholecystokinin, thereby promoting pancreatic enzyme synthesis and secretion [45]. Additionally, CS increases the expression of sodium-glucose cotransporter 1 (SGLT1) in piglet small intestine, facilitating glucose absorption and utilization [46].

The intestinal antioxidant defense and immune systems play vital roles in maintaining gut health. Glutathione, glutathione peroxidase (GSH-Px), and superoxide dismutase (SOD) in intestinal mucosa are key components of the antioxidant defense system, while secreted immunoglobulin A (IgA), immunoglobulin M (IgM), and immunoglobulin G (IgG) reflect the defensive capacity of the intestinal immune system. Studies show that CS supplementation in finishing pigs increases jejunal mucosal glutathione content and GSH-Px activity while decreasing SOD activity, and significantly elevates secreted IgA, IgM, and IgG levels in jejunal mucosa [47]. These results demonstrate that CS maintains intestinal antioxidant defense and immune systems, promoting gut health.

Moreover, CS significantly enhances the expression of tight junction proteins Occludin, Claudin-1, and ZO-1 in jejunal mucosa [47], indicating its important role in maintaining intestinal barrier integrity and promoting intestinal epithelial development.

2.5 Role of CS in Alleviating Stress in Piglets

In modern swine production, early weaning of piglets often induces severe weaning stress, resulting in diarrhea and growth retardation. Insufficient gastric acid secretion is a major cause of growth retardation and diarrhea in weaned piglets [48]. Studies show that CS depletes somatostatin and promotes secretion of gastrin and ghrelin in gastric mucosa, thereby increasing endogenous gastric acid secretion [7,49]. Shi et al. [50] found that CS upregulates H+-K+-ATPase mRNA expression in gastric tissue, promoting gastric acid secretion in weaned piglets. Additionally, weaning stress increases serum cortisol, triiodothyronine (T3), and thyroxine (T4) levels [51], while CS supplementation significantly decreases cortisol and maintains stable T3 and T4 levels, reducing energy mobilization for stress response and alleviating weaning stress [52].

Beyond regulating gastric acid and hormone secretion, CS alleviates stress through antioxidant effects. Superoxide dismutase and glutathione peroxidase are essential components of the antioxidant defense system. Studies show that CS feeding significantly increases serum superoxide dismutase and glutathione peroxidase activities in piglets [53], enhancing their antioxidant defense capacity against external stress. The antioxidant mechanism of CS may involve several aspects: first, its active sulfhydryl groups can convert excess cystine in lysosomes to cysteine [54], which then synthesizes glutathione, indirectly exerting antioxidant effects by increasing glutathione content [30]; second, CS has been reported to be a more effective oxygen free radical scavenger than glutathione in the liver, alleviating various hepatic oxidative injuries induced by galactosamine, carbon tetrachloride (CCl4), and acetaminophen [55]; third, CS can be converted to taurine, which enhances catalase activity and antioxidant enzymes related to glutathione metabolism [56-57].

2.6 Immunomodulatory Function of CS

CS can modulate immune function in pigs to a certain extent. Liu et al. [58] reported that CS significantly increases serum immunoglobulin A and G contents, leukocyte phagocytic rate, and T-lymphocyte transformation rate in weaned piglets, thereby enhancing immunity. Liu et al. [59] found that the interaction between CS and N-carbamylglutamate benefits the recovery of foot-and-mouth disease antibody levels in weaned piglets, effectively avoiding interference from maternal antibodies and improving immune function. Additionally, CS supplementation in late gestation sow diets increases immunoglobulin G content in colostrum, indirectly enhancing piglet immune function [27]. Chang et al. [60] reported that piglets fed cysteamine hydrochloride preparations had significantly higher classical swine fever virus antibody blocking rates than control groups, suggesting that cysteamine hydrochloride preparations may enhance vaccine efficacy. Furthermore, CS increases complement 3 levels in finishing pig blood [61]; the complement system is a component of non-specific immunity that assists antibodies in phagocytosing pathogens [62].

The immunomodulatory mechanism of CS is related to somatostatin inhibition. Somatostatin suppresses immunoglobulin and cytokine synthesis [63], with inhibitory effects on immunoglobulin A synthesis reaching 20-50% [58]. By depleting somatostatin levels, CS promotes release of growth hormone and insulin-like growth factor-1, which facilitate glucose and amino acid uptake by lymphocytes, thereby promoting immunoglobulin synthesis [64].

3 Problems in CS Application

Despite its growth-promoting benefits, inappropriate dosing and administration methods can cause adverse effects. High doses of CS can induce duodenal ulcers and perforation in rats [65-66]. Additionally, CS can reduce duodenal mucosal blood flow in rats by promoting endothelin release, causing local tissue ischemia and hypoxia and compromising defense mechanisms [67]. High-dose CS also induces oxidative stress, causing direct cytotoxicity and necrosis [68].

4 Summary

Appropriate dietary supplementation of CS can effectively improve growth performance, carcass quality, meat quality, nutrient metabolism, intestinal health, stress response, and immune function in pigs. However, inconsistent results have been reported in animal production, likely due to variations in CS purity, effective dose, feeding duration, growth stage, environment, and breed. Therefore, further research is needed to determine optimal supplementation levels and methods for each growth stage. Although promoting growth performance through enhanced growth hormone secretion is effective, the safety of this direct approach has not been accepted by some countries, and its efficacy and potential toxic side effects in livestock production require further evaluation. Most existing studies have limitations including short experimental periods and small animal populations; more long-term, large-scale feeding trials are needed to assess sustained effects. Additionally, improvements in CS processing technology to reduce off-odors and enhance chemical stability for better physiological efficacy, as well as further investigation into its mechanisms of action in vivo, warrant continued research.

References:

[1] ETHERTON T D, WIGGINS J P, CHUNG C S, et al. Stimulation of pig growth performance by porcine growth hormone and growth hormone-releasing factor[J]. Journal of Animal Science, 1986, 63(5): 1389-1399.

[2] GALLEGO-VILLAR L, HANNIBAL L, H BERLE J, et al. Cysteamine revisited: repair of arginine to cysteine mutations[J]. Journal of Inherited Metabolic Disease, 2017, 40(4): 555-567.

[3] KHOMENKO T, SZABO S, DENG X, et al. Role of iron in the pathogenesis of cysteamine-induced duodenal ulceration in rats[J]. American Journal of

Physiology Gastrointestinal and Liver Physiology, 2009, 296(6): 1277-1286.

[4] BARNETT M C, HEGARTY R S. Cysteamine: a human health dietary additive with potential to improve livestock production efficiency[J]. Animal Production Science, 2016, 56(8): 1330-1338.

[5] RIOUX P, ZANKEL T C. Use of cysteamine and derivatives thereof to treat mitochondrial diseases: USA, US2014/064336[P]. 2015-05-14.

[6] 刘光芒. 半胱胺对动物生产性能及其营养生理效应研究 [D]. 博士学位论文. 雅安: 四川农业大学, 2010: 18.

[7] DU G, SHI Z, XIA D, et al. Cysteamine improves growth performance and gastric ghrelin expression in preweaning piglets[J]. Domestic Animal Endocrinology, 2012, 42(4): 203-209.

[8] LIU G M, WANG Z S, WU D, et al. Effects of dietary cysteamine supplementation on growth performance in finishing pigs[J]. Livestock Science, 2009, 122(1): 86-89.

[9] DUNSHEA F R. Porcine somatotropin and cysteamine hydrochloride improve growth performance and reduce back fat in finisher gilts[J]. Australian Journal of Experimental Agriculture, 2007, 47(7): 796-800.

[10] MILLER D W, PROSSER Z, CHEE E Y W, et al. Dietary stimulation of the endogenous somatotropic axis in weaner and grower-finisher pigs using medium chain triglycerides and cysteamine hydrochloride[J]. Journal of Animal Science and Biotechnology, 2016, 7(1): 61.

[11] 宋延飞. 不同剂量半胱胺对生长育肥猪生长性能的影响 [J]. 饲料工业, 2016, 37(6): 43-46.

[12] YANG W, WANG J, LIU L, et al. Effect of high dietary copper on somatostatin and growth hormone-releasing hormone levels in the hypothalami of growing pigs[J]. Biological Trace Element Research, 2011, 143(2): 893-900.

[13] RAMÍREZ J L, TORRONTERAS R, CASTAÑO J P, et al. Somatostatin plays a dual, stimulatory/inhibitory role in the control of growth hormone secretion by two somatotrope subpopulations from porcine pituitary[J]. Journal of Neuroendocrinology, 1997, 9(11): 841-848.

[14] RAMÍREZ J L, CASTAÑO J P, GRACIANA-NAVARRO F. Somatostatin at low doses stimulates growth hormone release from intact cultures of porcine pituitary cells[J]. Hormone & Metabolic Research, 1998, 30(4): 175-177.

[15] SZABO S, REICHLIN S. Somatostatin in rat tissues is depleted by cysteamine administration[J]. Endocrinology, 1981, 109(6): 2255-2257.

[16] MCLEOD K R, HARMON D L, SCHILLO K K, et al. Cysteamine-induced depletion of somatostatin in sheep: time course of depletion and changes in plasma metabolites, insulin, and growth hormone[J]. Journal of Animal Science, 1995, 73(1): 77-87.

[17] XIAO D, LIN H R. Effects of cysteamine—a somatostatin-inhibiting agent—on serum growth hormone levels and growth in juvenile grass carp (Ctenopharyngodon idellus)[J]. Comparative Biochemistry & Physiology Part A Molecular & Integrative Physiology, 2003, 134(1): 93-99.

[18] HALL T R, CHEUNG A, HARVEY S, et al. Somatostatin immunoneutralization affects plasma metabolite concentrations in the domestic fowl[J]. Comparative Biochemistry & Physiology Part A Physiology, 1986, 85(3): 489-494.

[19] MILLARD W J, SAGAR S M, MARTIN J B. Cysteamine-induced depletion of somatostatin and prolactin[J]. Federation proceedings, 1985, 44(9): 2546-2550.

[20] SALZE G, MCLEAN E, CRAIG S R. Dietary taurine enhances growth and digestive enzyme activities in larval cobia[J]. Aquaculture, 2012, 362-363(5): 44-49.

[21] 黄瑞林. 半胱胺的生理作用及其在养殖业中的应用 [J]. 饲料广角, 2002(3): 22-24.

[22] 唐好文, 李辉, 李婷. 半胱胺的动物营养研究进展 [J]. 中国畜牧兽医, 2008, 35(1): 33-36.

[23] 张晓峰, 柘丽, 余荣, 等. 包膜半胱胺对生长育肥猪生长性能的影响 [J]. 饲料博览, 2017(3): 1-5.

[24] 向德标, 姚元枝, 伍福. 半胱胺对宁乡猪肥育后期生产性能的影响 [J]. 怀化学院学报, 2005, 24(2): 76-78.

[25] 陈丛亮, 杨磊, 吕维远. 半胱胺盐酸盐对妊娠后期和泌乳母猪生产性能的影响 [J]. 饲料研究, 2009(2): 25-27, 34.

[26] 徐金先, 杨磊, 陆天水, 等. 强化保生灵在断奶母猪饲料中的应用效果 [J]. 饲料研究, 2005, 2005(7): 18-20.

[27] 田春庄, 肖成林, 黄飞若, 等. -CD-半胱胺对母猪繁殖性能和仔猪生长性能的影响 [J]. 动物营养学报, 2007, 19(5): 559-566.

[28] 韦习会, 夏东, 高勤学, 等. 半胱胺对育肥后期猪胴体性状和肉质性状的影响 [J]. 南京农业大学学报, 2003, 26(3): 73-75.

[29] ZHOU P, ZHANG L, LI J, et al. Effects of dietary crude protein levels and cysteamine supplementation on protein synthetic and derivative signaling in skeletal muscle of finishing pigs[J]. Plos One, 2015, 10(9): e0139393.

[30] BAI M, LIU H, XU K, et al. Effects of dietary coated cysteamine hydrochloride on pork color in finishing pigs[J]. Journal of the Science of Food and Agriculture, 2017, 48(1): 96-100.

[31] ETHERTON T D, WIGGINS J P, EVOCK C M, et al. Stimulation of pig growth performance by porcine growth hormone: determination of the dose-response relationship[J]. Journal of Animal Science, 1987, 64(2): 433-443.

[32] EBERT K M, LOW M J, OVERSTROM E W, et al. A Moloney MLV-rat somatotropin fusion gene produces biologically active somatotropin in a

transgenic pig[J]. Molecular Endocrinology, 1988, 2(3): 277-283.

[33] YANG C B, LI A K, YIN Y L, et al. Effects of dietary supplementation of cysteamine on growth performance, carcass quality, serum hormones and gastric ulcer in finishing pigs[J]. Journal of the Science of Food and Agriculture, 2005, 85(11): 1947-1952.

[34] 陈安国, 洪奇华, 吴林友. 半胱胺对生长肥育猪胴体品质的影响及其机理探讨 [J]. 中国畜牧杂志, 2004, 40(2): 11-13.

[35] 洪奇华, 吴林友, 陈安国. 半胱胺不同添加方式对生长肥育猪生产性能的影响 [J]. 养猪, 2003, (3): 22-23.

[36] 朱宇旌, 王浩然, 李方方, 等. 半胱胺螯合锌对仔猪生长性能、血清生化指标、养分消化率及粪中微生物菌群的影响 [J]. 动物营养学报, 2015, 27(10): 3225-3232.

[37] CAI D, JIA Y, LU J, et al. Maternal dietary betaine supplementation modifies hepatic expression of cholesterol metabolic genes via epigenetic mechanisms in newborn piglets[J]. British Journal of Nutrition, 2014, 112(9): 1459-1468.

[38] MAO X, ZENG X, HUANG Z, et al. Leptin and leucine synergistically regulate protein metabolism in C2C12 myotubes and mouse skeletal muscles[J]. British Journal of Nutrition, 2013, 110(2): 256-264.

[39] 张建斌, 杨升. 半胱胺和酵母铬对育肥猪内分泌激素和脂类代谢的影响 [J]. 天津农学院学报, 2006, 13(2): 7-10.

[40] 黄所含. 半胱胺、酵母铬对生长肥育猪和良凤肉鸡生长性能、胴体品质及血清生化指标的影响 [D]. 硕士学位论文. 南宁: 广西大学, 2006: 40.

[41] MCCARTY M F. Inhibition of acetyl-CoA carboxylase by cystamine may mediate the hypotriglyceridemic activity of pantethine[J]. Medical Hypotheses, 2001, 56(3): 314-317.

[42] 陶勇, 任善茂, 周春宝. 半胱胺不同添加方式对育肥猪胴体品质及血液生化指标的影响 [J]. 中国畜牧兽医文摘, 2006, 26(1): 39-40.

[43] 夏中生, 仵天培, 农志坚, 等. 半胱胺和酵母铬对生长猪饲粮养分消化代谢的影响 [J]. 粮食与饲料工业, 2012, 12(2): 53-55.

[44] 徐雪松, 吴金节, 李健, 等. 半胱胺对仔猪生长性能及小肠内容物消化酶活性的影响 [J]. 中国兽医学报, 2008, 28(9): 1088-1091.

[45] 洪奇华, 杨彩梅, 吴林友. 半胱胺对猪十二指肠内容物中消化酶活性和生产性能的影响 [J]. 中国饲料, 2003(16): 13-14.

[46] 张磊, 王丽娜, 石志敏, 等. 断奶前后仔猪十二指肠空肠和回肠 SGLT1 mRNA 表达的变化及半胱胺的影响 [J]. 农业生物技术学报, 2006, 14(6): 850-854.

[47] ZHOU P, LUO Y, ZHANG L, et al. Effects of cysteamine supplementation on the intestinal expression of amino acid and peptide transporters and intestinal health in finishing pigs[J]. Animal Science Journal, 2016, 88(2): 314-321.

[48] NABUURS M J A. Weaning piglets as a model for studying pathophysiology of diarrhea[J]. Veterinary Quarterly, 1998, 20(3): 42-45.

[49] 刘晢洁, 韩正康, 杨玉焕, 等. 半胱胺对香猪胃液分泌、血液胃泌素和生长抑素水平的影响 [J]. 畜牧与兽医, 1998, (3): 9-11.

[50] SHI Z M, DU G M, WEI X H, et al. Cysteamine increases expression and activity of H+-K+-ATPase of gastric mucosal cells in weaning piglets[J]. World Journal of Gastroenterology, 2005, 11(42): 6707-6712.

[51] CARROLL J A, VEUM T L, MATTERI R L. Endocrine responses to weaning and changes in post-weaning diet in the young pig[J]. Domestic Animal Endocrinology, 1998, 15(3): 183-194.

[52] 石志敏, 张磊, 韦习会, 等. 半胱胺对断奶前后仔猪血清皮质醇、T3、T4 和 IL-2 水平的影响 [J]. 动物学研究, 2005, 26(3): 317-321.

[53] 刘智. 半胱胺对仔猪免疫机能的影响及其机理研究 [D]. 硕士学位论文. 合肥: 安徽农业大学, 2007: 6.

[54] WILMER M J, KLUIJTMANS L A J, VAN D V, THEA J, et al. Cysteamine restores glutathione status in cultured cystinotic proximal tubular epithelial cells[J]. Biochimica et Biophysica Acta, 2011, 1812(6): 643-651.

[55] FERREIRA D W, NAQUET P, MANAUTOU J E. Influence of vanin-1 and catalytic products in liver during normal and oxidative stress conditions[J]. Current Medicinal Chemistry, 2015, 22(20): 2407-2416.

[56] SUMIZU K. Oxidation of hypotaurine in rat liver[J]. Biochimica et Biophysica Acta, 1962, 63(1): 210-212.

[57] SMITH L L, SHARMA R, KODAVANTI U P, et al. The uptake and metabolism of cystamine and taurine by isolated perfused rat and rabbit lungs[J]. International Journal of Biochemistry & Cell Biology, 1995, 27(7): 655-664.

[58] 刘智, 徐雪松, 刘丽, 等. 半胱胺对仔猪免疫机能的调节作用 [J]. 中国畜牧兽医, 2007, 34(5): 18-21.

[59] 刘巧婷. 半胱胺、N-氨甲酰谷氨酸对不同阶段生长育肥猪生长性能、血清生理化指标及免疫机能的影响 [D]. 硕士学位论文. 南宁: 广西大学, 2015: 4.

[60] 常文环, 江勇, 蔡辉益, 等. 免疫再生素对仔猪生产性能及免疫指标的研究 [J]. 饲料研究, 2007(2): 31-33.

[61] 李慧. 包膜半胱胺对肥育猪生长、胴体品质、肉质和消化的影响及其机理研究 [D]. 硕士学位论文. 杭州: 浙江大学, 2014.

[62] RICKLIN D, HAJISHENGALLIS G, YANG K, et al. Complement: a key system for immune surveillance and homeostasis[J]. Nature Immunology, 2010, 11(9): 785-797.

[63] TEN BOKUM A M, HOFLAND L J, VAN HAGEN P M. Somatostatin and somatostatin receptors in the immune system: a review[J]. European Cytokine

Network, 2000, 11(2): 161-176.

[64] FUKUHARA S, SUZUKI H, MASAOKA T, et al. Enhanced ghrelin secretion in rats with cysteamine-induced duodenal ulcers[J]. American Journal of Physiology Gastrointestinal and Liver Physiology, 2005, 289(1): 138-145.

[65] PRABHA T, DORABABU M, GOEL S, et al. Effect of methanolic extract of Pongamia pinnata Linn seed on gastro-duodenal ulceration and mucosal offensive and defensive factors in rats[J]. Indian Journal of Experimental Biology, 2009, 47(8): 649-659.

[66] DAS P K, PILLAI S, KAR D, et al. Pharmacological efficacy of Argemone mexicana plant extract against cysteamine-induced duodenal ulceration in rats[J]. Indian Journal of Medical Research, 2011, 65(3): 92-99.

[67] KHOMENKO T, DENG X, SANDOR Z, et al. Cysteamine alters redox state, HIF-1alpha transcriptional interactions and reduces duodenal mucosal oxygenation: novel insight into the mechanisms of duodenal ulceration[J]. Biochemical and Biophysical Research Communications, 2004, 317(1): 121-127.

[68] HUA L L, HALLIWELL B. Oxidation and generation of hydrogen peroxide by thiol compounds in commonly used cell culture media[J]. Biochemical and Biophysical Research Communications, 2001, 286(5): 991-994.

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