Effects of Resveratrol and Sanguinarine on Growth Performance, Serum Indices, and Diarrhea Status in Calves under 2 Months of Age (Postprint)

Authors: Zhang Weibing, Zhang Rong, Bi Yanliang, Tu Yan, Du Hanchang, Tian Zhonghong, Diao Qiyu

Date: 2018-12-24T00:00:00+00:00

Abstract

This study aimed to investigate the effects of resveratrol (RES) and sanguinarine (SAG) on growth performance, serum indices, and diarrhea status in Holstein calves under two months of age. Fifty-four 5-day-old Holstein heifer calves were randomly assigned to three treatments (n = 18 per treatment) and fed milk replacer (MR), MR + 0.05 mg/kg BW SAG, or MR + 4 mg/kg BW RES for 55 days. Body weight and body measurements were recorded at 5, 14, 28, 42, and 56 days of age, and diarrhea incidence was recorded daily. Blood samples were collected at 60 days of age for serum index determination. The results showed: 1) RES and SAG had no significant effects on total weight gain or dry matter intake ($P > 0.05$), age had a significant effect on body weight ($P < 0.0001$), but there was no interaction between age and treatment ($P = 0.8539$); 2) increases in chest girth and hip height were significantly greater in both RES and SAG treatments compared with the MR treatment ($P < 0.005$); 3) no significant differences in diarrhea rates were observed among treatments ($P > 0.05$); 4) serum concentrations of growth hormone (GH), epidermal growth factor (EGF), and insulin-like growth factor-I (IGF-I) were significantly higher in the RES treatment than in the other two treatments ($P < 0.05$); 5) serum malondialdehyde concentration was significantly higher in the SAG treatment than in the other two treatments ($P < 0.05$). In conclusion, supplementation of RES or SAG in milk replacer improved body measurements in calves under two months of age; RES supplementation significantly increased serum GH, EGF, and IGF-I concentrations; and both RES and SAG show potential as growth promoters for calves.

Full Text

Effects of Resveratrol and Sanguinarine on Growth Performance, Serum Indexes and Diarrhea Status of Calves under 2 Months of Age

ZHANG Weibing[1], ZHANG Rong[1], BI Yanliang[1], TU Yan[1], DU Hanchang[2], TIAN Zhonghong[2], DIAO Qiyu[1]*

[1]Key Laboratory of Feed Biotechnology of the Ministry of Agriculture, Beijing Key Laboratory for Dairy Cow Nutrition, Feed Research Institute, Chinese Academy of Agricultural Sciences, Beijing 100081, China
[2]Shandong Agricultural Biological Immune Technology Engineering Laboratory, Shandong Yinxiang Weiye Group Co., Ltd., Heze 274500, China

Abstract

This study investigated the effects of resveratrol (RES) and sanguinarine (SAG) on growth performance, serum indexes, and diarrhea status in Holstein calves under two months of age. Fifty-four 5-day-old female Holstein calves were randomly assigned to three treatments (n=18 per treatment) using a completely randomized design. The treatments consisted of a milk replacer (MR) control, MR supplemented with 0.05 mg/kg BW SAG, and MR supplemented with 4 mg/kg BW RES. The trial lasted 55 days. Body weight and body measurements were recorded at 5, 14, 28, 42, and 56 days of age, with daily monitoring of diarrhea status. Blood samples were collected at 60 days of age for serum analysis. The results showed: (1) RES and SAG had no significant effects on total weight gain or dry matter intake ($P>0.05$). Days of age significantly affected body weight ($P<0.0001$), but no interaction between age and treatment was observed ($P=0.8539$). (2) For body measurements, the increases in heart girth and hip height in both RES and SAG treatments were significantly greater than in the MR treatment ($P<0.005$). (3) No significant differences in diarrhea rates were detected among treatments ($P>0.05$). (4) The RES treatment exhibited significantly higher serum concentrations of growth hormone (GH), epidermal growth factor (EGF), and insulin-like growth factor-I (IGF-I) compared with the other two treatments ($P<0.05$). (5) Serum malondialdehyde (MDA) concentration in the SAG treatment was significantly higher than in the other treatments ($P<0.05$). In conclusion, supplementation of MR with RES or SAG can increase body size in calves under two months of age; RES supplementation significantly increases serum GH, EGF, and IGF-I concentrations; and both RES and SAG show potential as growth promoters for calves.

Keywords: calf; plant extracts; resveratrol; sanguinarine; calf breeding

Introduction

Calf rearing represents the most critical phase in cattle production, with the quality of calf management profoundly impacting subsequent growth and development. Therefore, implementing appropriate nutritional strategies to improve calf growth and health is essential. Conventional practice involves adding antibiotics to animal diets as growth promoters; however, the use of antibiotics as feed additives in ruminant diets is being phased out due to risks associated with improper use, including antimicrobial resistance and antibiotic residues, which have raised widespread societal concern. The World Health Organization has identified antimicrobial resistance as a growing public health problem in both human and veterinary medicine worldwide. Consequently, the European Union banned antibiotic growth promoters in January 2006 (EU Regulation 1831/2003/EC), and in July 2016, China' s Ministry of Agriculture announced a prohibition on using colistin sulfate as a growth promoter effective April 2017 (Announcement No. 2428). The livestock industry must identify economically effective growth promoters that enhance animal performance while addressing public health concerns.

In recent years, plant extracts have emerged as a research focus for animal growth promotion. Studies have demonstrated that tannins, saponins, and certain Chinese herbal extracts exert beneficial effects on rumen fermentation, nutrient digestibility, and growth performance in sheep and cattle. Resveratrol (RES) is a non-flavonoid polyphenol and natural phytoalexin found abundantly in grapes (particularly in skins and seeds), peanuts, and the traditional Chinese herb *Polygonum cuspidatum*. RES and its derivatives possess numerous biological and pharmacological activities, including antioxidant, neuroprotective, and cardioprotective properties. Sanguinarine (SAG), with the molecular formula C H O N, is a benzophenanthridine isoquinoline alkaloid primarily found in *Macleaya cordata*, *Chelidonium majus*, *Eomecon chionantha*, and *Corydalis* species. It exhibits antibacterial, antioxidant, and anti-inflammatory effects, and is used to control schistosomiasis as well as demonstrating antitumor properties.

While RES and SAG have been studied as feed additives in monogastric animals and fish, research in ruminants remains limited, particularly in young ruminants. Therefore, this experiment investigated the effects of RES and SAG on growth performance, serum indexes, and diarrhea status in Holstein calves under two months of age to provide a basis for their application in calf production.

Materials and Methods

Experimental Time and Location

The experiment was conducted from September to November 2015 at the Second Ranch of Yinxiang Weiye in Caoxian County, Heze City, Shandong Province. The average temperature and relative humidity ranged from 5–30°C and 30–60%, respectively.

Experimental Diets and Design

The milk replacer (MR) used in this study (Patent No. ZL 02128844.5) was provided by the Beijing Precision Animal Nutrition Research Center. SAG (>99% purity) and RES (>98% purity) were purchased from Hunan Meikeduo Biological Resources Co., Ltd. Fifty-four healthy 5-day-old Chinese Holstein female calves with similar genetic backgrounds and comparable body weights were housed individually in calf hutches (1.2 m × 2.0 m with sawdust bedding). Following a single-factor randomized design and based on body weight and age consistency, calves were randomly allocated to three treatments (n=18 per treatment): MR (control), MR + 0.05 mg/kg BW SAG, and MR + 4 mg/kg BW RES. Supplementation levels of SAG and RES were adjusted every two weeks as calf body weight increased.

The SAG dosage was selected based on Vieira et al., who reported that dietary supplementation of *Macleaya cordata* extract (containing 1.5% SAG) at 0.010–0.045 mg/kg BW improved feed conversion ratio and weight gain in broilers, with optimal results at 0.035 mg/kg BW. Additionally, Rao et al. reported effective dosages of 0.021–0.023 mg/kg BW in 8–25 kg piglets. Considering that some MR liquid may enter the rumen in calves, this study selected 0.05 mg/kg BW SAG. The RES dosage was based on recommendations from our laboratory' s previous work with sheep.

Feeding Management

Before the experiment, the entire facility was thoroughly disinfected with Qiangli Xiaoduling solution, with weekly repetition of disinfection for all pens and bi-monthly treatment with 10% lime solution. The MR contained no antibiotics or coccidiostats. During the transition period from 5 to 11 days of age, the ratio of MR to whole milk gradually increased from 1:3 to 3:1; from 12 days of age onward, calves received only MR. The MR was reconstituted to 12.5% dry matter (DM) using hot water boiled and cooled to 40–50°C, and fed as emulsion twice daily (08:00 and 17:00). Calves had ad libitum access to clean water 30 minutes after feeding. The daily feeding amount was set at 12% of calf body weight and adjusted regularly with growth. SAG and RES were added directly to the MR liquid before feeding.

At 14 days of age, all calves were moved from individual hutches to group pens (6 calves per pen, approximately 4 m^2 per calf). All calves received the same starter feed (without SAG or RES) and clean water for ad libitum consumption. Calves were weaned at 60 days of age. The composition of the starter feed and nutrient levels of MR and starter are presented in Table 1 .

Sample Collection

Feed Samples: Daily samples of MR and starter feed were collected, mixed thoroughly during the experimental period, and stored in sealed bags at -20°C.

Residual feed from each treatment was collected and weighed before morning feeding each day, with subsamples stored at -20°C for subsequent analysis.

Blood Samples: Blood samples (approximately 10 mL) were collected via jugular venipuncture before morning feeding at 60 days of age. Samples were placed at an angle to allow serum separation, then centrifuged at 1509.3×g for 10 minutes. Serum was harvested and stored at -20°C until analysis.

Diarrhea Rate: Diarrhea status was observed and recorded daily throughout the experimental period. Diarrhea rate was calculated as: Diarrhea rate (%) = [(number of diarrheic calves × diarrheic days) / (total number of calves × experimental days)] × 100.

Growth Performance: Body weight was measured before morning feeding at 5, 14, 28, and 56 days of age. Body measurements (body length, body height, heart girth, hip height, and hip width) were recorded at 5, 28, and 56 days of age.

Sample Analysis

Nutrient levels in MR and starter feed were determined using the following methods: gross energy (GE) by oxygen bomb calorimetry (C200, IKA Works Inc., Germany); dry matter (DM) by oven drying at 105°C for 6 hours (AOAC, 1990; 930.15); crude protein (CP) by Kjeldahl method (AOAC, 1990; 920.87); ether extract (EE) by Soxhlet extraction (AOAC, 1990; 920.85); crude ash by combustion at 600°C for 6 hours in a muffle furnace (AOAC, 1990; 924.05); calcium (Ca) by atomic absorption spectrophotometry (Perkin-Elmer M9W-700) according to AOAC (1990; 968.08); phosphorus (P) by molybdovanadate colorimetry (AOAC, 1990; 965.17); and neutral detergent fiber (NDF) and acid detergent fiber (ADF) according to Zhang Liying.

Serum indexes included biochemical, hormonal, and immune parameters. Concentrations of free fatty acids (FFA), immunoglobulin A (IgA), immunoglobulin G (IgG), immunoglobulin M (IgM), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), catalase (CAT), total antioxidant capacity (T-AOC), and malondialdehyde (MDA) were analyzed using an automatic biochemical analyzer (Hitachi 7160, Japan) with kits from Beijing Huaying Biotechnology Research Institute. Urea nitrogen (UN) was analyzed using the same analyzer with kits from Zhongsheng Beikong Co., Ltd. Insulin (INS) and norepinephrine (NE) concentrations were determined by radioimmunoassay (r-911) with kits from Beijing Huaying Biotechnology Research Institute. Cortisol (COR), interleukin-1 (IL-1), tumor necrosis factor- (TNF-), interferon- (-IFN), growth hormone (GH), insulin-like growth factor-I (IGF-I), and epidermal growth factor (EGF) concentrations were measured by enzyme-linked immunosorbent assay (STAT FAX 2100, USA) with kits from Beijing Huaying Biotechnology Research Institute.

Statistical Analysis

Raw data were initially processed using Excel 2013. Data for average daily gain (ADG), diarrhea rate, and serum indexes were analyzed using the GLM procedure in SAS 9.4, while other data were analyzed using the Mixed model. Significance was declared at $P<0.05$.

Results

Effects of RES and SAG on Growth Performance and Diarrhea Status

The effects of RES and SAG on calf growth performance are presented in Table 2 . The diet consisted of MR and starter feed. Compared with the MR treatment, RES and SAG treatments increased total weight gain by 1.44 kg and 1.85 kg, respectively, though differences among treatments were not significant ($P>0.05$). No significant differences in dry matter intake (DMI) were observed among treatments ($P>0.05$). Body weight increased with age, with significant effects of days of age ($P<0.0001$), but no interaction between age and treatment ($P=0.8539$).

Regarding body measurements, body length in the SAG treatment was significantly higher than in the other two treatments at 5 days of age ($P<0.05$), but this difference disappeared with age ($P>0.05$), and no significant differences were detected among treatments by 56 days of age ($P>0.05$). No significant treatment effects were observed for body height or hip width, and no age × treatment interactions were found ($P=0.1525$ and $P=0.4054$, respectively). At 5 days of age, heart girth in the MR treatment was significantly greater than in the SAG treatment ($P<0.05$), but by 56 days of age, the SAG treatment showed significantly greater heart girth than the MR treatment ($P<0.05$). Hip height in the MR treatment was significantly higher than in the RES treatment at 5 days of age ($P<0.05$), but differences among treatments diminished with age ($P>0.05$). For increases in heart girth and hip height, both RES and SAG treatments were significantly higher than the MR treatment ($P<0.005$).

The effects of RES and SAG on diarrhea status are shown in Table 3 . No significant differences in diarrhea rates were detected among the three treatments ($P>0.05$), though all treatments showed a decreasing trend with increasing age. Numerically, dietary SAG supplementation reduced diarrhea rate by 1.42 percentage points compared with the MR treatment.

Effects of RES and SAG on Serum Indexes

The effects of RES and SAG on serum indexes are presented in Table 4 and Table 5 . Among serum biochemical parameters, supplementation with RES and SAG significantly reduced serum FFA concentration compared with the MR treatment ($P<0.05$). The RES treatment exhibited significantly higher serum GH, EGF, and IGF-I concentrations than the other two treatments ($P<0.05$). Regarding serum immune parameters, the RES treatment showed significantly

lower serum IgA concentration than the MR treatment ($P<0.05$). For serum antioxidant parameters, the SAG treatment had significantly higher serum MDA concentration than the other two treatments ($P<0.05$). No significant differences were observed for other serum indexes ($P>0.05$).

Discussion

Effects of RES and SAG on Growth Performance and Diarrhea Status

At the conclusion of the 56-day experiment, RES and SAG increased total weight gain by over 1 kg, though differences among treatments did not reach statistical significance. This aligns with the findings of Yang Chuntao, who reported no significant effect of dietary mulberry leaf flavonoids on ADG in calves at 56 days of age. Additionally, RES supplementation did not significantly affect DMI, consistent with Sahin et al.' s observation of no significant change in quail DMI following RES supplementation. Research has shown that SAG supplementation significantly increased ADG and improved feed utilization efficiency in chickens without affecting DMI, which agrees with our results. The lack of effect on DMI suggests that these extracts do not negatively impact diet palatability.

Furthermore, dietary supplementation with SAG or its analogs significantly improved growth performance in weaned piglets and carp, particularly ADG in weaned piglets, which contrasts with our findings. While growth performance typically decreases under stress conditions, studies have confirmed that SAG or its analogs can improve growth performance in sheep under heat stress conditions. Although no significant differences were observed in total weight gain or body weight at various ages among treatments, SAG-treated calves exhibited significantly greater heart girth at 56 days of age compared with MR-treated calves. Moreover, both RES and SAG treatments showed significantly greater increases in heart girth and hip height than the MR treatment. This outcome may be attributed to SAG increasing the supply of non-ammonia nitrogen to the small intestine, thereby reducing feed protein degradation in the rumen and increasing microbial protein synthesis. Even though the effect of SAG on rumen microorganisms in vivo was not evaluated, the reduction in peptide degradation and amino acid deamination could be attributed to the selective antimicrobial action of SAG. SAG may affect hyper-ammonia-producing bacteria by inhibiting aromatic amino acid decarboxylase, while increased microbial protein synthesis may reflect the reduction or removal of protozoa from the rumen following SAG supplementation. Consequently, more nutrients are available for limb skeletal development, which may lay a foundation for superior performance in adulthood.

Diarrhea is a common disease in suckling calves, particularly prevalent within the first three weeks of age, and represents a major factor affecting calf growth and development. Our results showed a decreasing trend in diarrhea rate with increasing age, consistent with the findings of Dong Xiaoli and Yang Chuntao. As animals age, their digestive organs and immune functions gradually ma-

ture, leading to reduced diarrhea incidence. Although dietary supplementation with SAG and RES did not significantly reduce diarrhea rate, a decreasing trend was observed. Reports indicate that some plant extracts confer resistance to harmful compounds such as mycotoxins, which may improve digestive processes and ultimately enhance animal performance, particularly during early life stages. Additionally, plant extracts may influence animal health by enhancing endogenous enzyme secretion, improving intestinal environment and microbial community balance, and strengthening liver function to better utilize fats and proteins. SAG possesses antibacterial and anti-inflammatory properties that can effectively alleviate weaning stress, maintain intestinal health, and reduce diarrhea incidence in piglets.

Effects of RES and SAG on Serum Indexes

Serological parameters are valuable for evaluating nutrient metabolism and organ health status, providing guidance for disease prevention and treatment. While the effects of RES and SAG on calf serum indexes have not been extensively studied, our results demonstrate significant impacts under the experimental conditions. Serum UN, a metabolic product of protein metabolism, serves as an important indicator of protein metabolism and dietary amino acid balance. In this study, RES and SAG supplementation did not significantly affect serum UN concentration, consistent with the findings of Vakili et al. However, other studies have reported significant changes in serum UN concentration following dietary supplementation with plant essential oils. The lack of significant difference in our study may be attributed to similar protein intake levels among treatments.

Serum FFA represents an important energy substrate, and its metabolism sensitively reflects lipid metabolism status and nutritional condition. In this study, SAG and RES supplementation significantly reduced serum FFA concentration, consistent with Rivera et al.' s findings in obese Zucker rats where RES supplementation significantly decreased serum FFA concentration. Another study reported that dietary cinnamaldehyde supplementation in yearling steers significantly reduced serum FFA concentration compared with the control group. This effect was attributed to cinnamaldehyde potentially providing more energy to animals by increasing DMI, thereby favorably affecting energy balance.

INS is one of the most important hormones controlling nutrient metabolism. Significantly increased blood FFA and ketone body concentrations stimulate -cell INS release, which may represent a feedback mechanism to prevent excessive fat mobilization. In ruminant lipid metabolism studies, INS infusion in mature Suffolk ewes exerted lipogenic effects. INS inhibits gluconeogenesis and attenuates adipocyte lipolysis by reducing adenylate cyclase and hormone-sensitive lipase activity, leading to decreased serum glucose and non-esterified fatty acid concentrations. Research on RES effects on serum INS in normal, hyperinsulinemic, and diabetic rats has shown variable results depending on experimental conditions. In normal rats, oral administration of 50 mg/kg BW RES reduced

blood INS concentration after 30 minutes, consistent with our results. However, long-term RES administration had negligible effects on plasma INS in normal rats, differing from our findings, possibly due to species differences.

GH is a protein secreted by the anterior pituitary that promotes growth. Although treatment did not significantly affect total weight gain, numerical improvements were observed in RES and SAG treatments compared with MR. IGF-I is a multifunctional cell proliferation regulator and an essential active protein peptide required for GH to exert its physiological effects. Our results showed that RES treatment significantly increased serum GH, EGF, and IGF-I concentrations compared with the other treatments. This may be because resveratrol is an effective phytoestrogen that upregulates EGF and its receptors, activates phosphorylated extracellular regulatory kinase signaling cascades, promotes gastrointestinal epithelial cell proliferation and differentiation, repairs damaged mucosa, and enhances nutrient digestion and absorption.

While diarrhea rate provides direct observation of calf health status, serum immunoglobulins serve as a hidden indicator for evaluating internal immune capacity, and their combination facilitates comprehensive analysis of experimental results. Studies have shown that serum immunoglobulin concentrations are significantly higher in healthy calves than in diarrheic calves. Our results indicated that serum IgA concentration in the MR treatment was significantly higher than in the RES treatment, which may explain why diarrhea rate and total weight gain in the MR treatment did not differ significantly from the other treatments. RES and SAG supplementation did not significantly affect immune parameters.

Recent research has extensively investigated the relationship between growth performance and blood antioxidant status, with serum SOD or GSH activity and MDA concentration considered positive and negative indicators of antioxidant status, respectively. MDA, a metabolic product of lipid peroxides, is primarily produced when polyunsaturated fatty acids in cell membranes are attacked by free radicals, and its concentration indirectly reflects the degree of cell membrane damage. Our results showed that serum MDA concentration in the SAG treatment was significantly higher than in the other treatments, which contradicts Lee et al.' s findings that SAG supplementation reduced MDA concentration in broiler thigh muscle. This discrepancy may be due to differences in animal species and supplementation levels. Our results also differ from Sahin et al.' s findings that 400 mg/kg RES supplementation significantly reduced serum MDA concentration in quail, suggesting that RES possesses superior antioxidant properties compared with SAG.

Conclusion

1. RES and SAG supplementation significantly increased heart girth and hip height in calves and showed a trend toward increased feed intake.
2. RES and SAG did not significantly affect major serum immune parameters or antioxidant enzyme activities.

3. RES supplementation increased serum GH, EGF, and IGF-I concentrations.
4. Both RES and SAG demonstrate potential as growth promoters for calves.

References

[1] SEIFZADEH S, AGHJEHGHESHLAGH F M, ABDIBENEMAR H, et al. The effects of a medical plant mix and probiotic on performance and health status of suckling Holstein calves[J]. Italian Journal of Animal Science, 2017, 16(1): 44–51.

[2] DARWISH W S, ELDALY E A, EL-ABBASY M T, et al. Antibiotic residues in food: the African scenario[J]. The Japanese Journal of Veterinary Research, 2013, 61 Suppl: S13–S22.

[3] Z, ZHAO T, QIU al. Antibiotics crisis China[J]. Science, 2015, 348(6239): 1100–1101.

[4] VAN BOECKEL T P, GLENNON E E, CHEN D, et al. Reducing antimicrobial use in food animals[J]. Science, 2017, 357(6358): 1350–1352.

[5] ADEL M, AMIRI A A, ZORRIEHZAHRA J, et al. Effects of dietary peppermint (Mentha piperita) on growth performance, chemical body composition and hematological and immune parameters fry Caspian white (Rutilus frisii kutum)[J]. Fish & Shellfish Immunology, 2015, 45(2): 841–847.

[6] LILA Z A, MOHAMMED N, KANDA S, et al. Effect of sarsaponin on ruminal fermentation particular reference to methane production vitro[J]. Journal of Dairy Science, 2003, 86(10): 3330–3336.

[7] BUSQUET M, CALSAMIGLIA S, FERRE A, et al. Plant extracts affect in vitro rumen microbial fermentation[J]. Journal of Dairy Science, 2006, 89(2): 761–771.

[8] BEAUCHEMIN K A, MCGINN S M, MARTINEZ T F, et al. Use of condensed tannin extract from quebracho trees to reduce methane emissions from cattle[J]. Journal of Animal Science, 2007, 85(8): 1990–1996.

[9] BENCHAAR C, DUYNISVELD J L, CHARMLEY E. Effects of monensin and increasing dose levels of a mixture of essential oil compounds on intake, digestion and growth performance of beef cattle[J]. Canadian Journal of Animal Science, 2006, 86(1): 91–96.

[10] BENCHAAR C, MCALLISTER T A, CHOUINARD P Y. Digestion, ruminal fermentation, ciliate protozoal populations, and milk production from dairy cinnamaldehyde, quebracho condensed tannin, or Yucca schidigera saponin extracts[J]. Journal of Dairy Science, 2008, 91(12): 4765–4777.

[11] QIAO G H, SHAO T, YANG X, et al. Effects of supplemental Chinese herbs on growth performance, blood antioxidant function and immunity status

in Holstein dairy heifers fed high fibre diet[J]. Italian Journal of Animal Science, 2013, 12(1): e20.

[12] MA T, CHEN D D, TU Y, et al. Effect of dietary supplementation with resveratrol on nutrient digestibility, methanogenesis and ruminal microbial flora in sheep[J]. Journal of Animal Physiology and Animal Nutrition, 2015, 99(4): 676-683.

[13] AGUILAR-HERNÁNDEZ J A, URÍAS-ESTRADA J D, LÓPEZ-SOTO M A, et al. Evaluation isoquinoline alkaloid supplementation levels ruminal fermentation, characteristics of digestion, and microbial protein synthesis in steers fed a high-energy diet[J]. Journal of Animal Science, 2016, 94(1): 267-274.

[14] ESTRADA-ANGULO A, AGUILAR-HERNÁNDEZ J A, OSUNA-PÉREZ M, et al. Influence quaternary benzophenantridine protopine alkaloids growth performance, dietary energy, carcass traits, visceral mass, and rumen health in finishing ewes under conditions of severe temperature-humidity index[J]. Asian-Australasian Journal of Animal Sciences, 2016, 29(5): 652-658.

[15] JANG M, CAI L N, UDEANI G O, et al. Cancer chemopreventive activity of resveratrol, a natural product derived from grapes[J]. Science, 1997, 275(5297): 218-220.

[16] 张卫兵, 张蓉, 屠焰, 等. 白藜芦醇对动物表观遗传学调控的作用机制 [J]. 动物营养学报, 2016, 28(5): 1302-1308.

[17] 伍勇. 血根碱在大鼠、猪和鸡的体外代谢研究 [D]. 博士学位论文. 长沙: 湖南农业大学, 2013.

[18] VIEIRA S L, BERRES J, REIS R N, et al. Studies with sanguinarine like alkaloids as feed additive in broiler diets[J]. Brazilian Journal of Poultry Science, 2008, 10(1): 67-71.

[19] SAHIN K, AKDEMIR F, ORHAN C, et al. Effects of dietary resveratrol supplementation on egg production and antioxidant status[J]. Poultry Science, 2010, 89(6): 1190-1198.

[20] ABDELNABY E A, MOHAMED M F, GAMMAZ H A K. Pharmacological studies of feed additives (sanguinarine and Saccharomyces cerevisiae) on growth performance, haematological and intestinal bacterial count with challenge test by Aeromonas hydrophila in Cyprinus carpio[J]. Global Animal Science Journal, 2013, 1(1): 1154-1172.

[21] LEE K W, KIM J S, OH S T, et al. Effects of Dietary sanguinarine on growth performance, relative organ weight, cecal microflora, serum cholesterol level and meat quality in broiler chickens[J]. The Journal of Poultry Science, 2015, 52(1): 15-22.

[22] KANTAS D, PAPATSIROS V G, TASSIS P D, et al. The effect of a natural feed additive (Macleaya cordata), containing sanguinarine, on the performance

and health status of weaning pigs[J]. Animal Science Journal, 2015, 86(1): 92-98.

[23] 饶华, 蔡鹏, 周锡红, 等. 博落回提取物对断奶仔猪生长性能的影响 [J]. 中国兽药杂志, 2009, 43(11): 42-45.

[24] 张丽英. 饲料分析及饲料质量检测技术 [M]. 3 版. 北京: 中国农业大学出版社, 2007.

[25] 杨春涛. 热带假丝酵母与桑叶黄酮对犊牛生长和胃肠道发育的影响 [D]. 硕士学位论文. 北京: 中国农业科学院, 2016.

[26] DRSATA J, ULRICHOVÁ J, WALTEROVÁ D. Sanguinarine and chelerythrine as inhibitors of aromatic amino acid decarboxylase[J]. Journal of Enzyme Inhibition, 1996, 10(4): 231-237.

[27] 张蓉, 刁其玉. 碳水化合物组成对犊牛生长性能及消化代谢的影响 [J]. 塔里木大学学报, 2008, 28(3): 14-20.

[28] 董晓丽. 益生菌的筛选鉴定及其对断奶仔猪、犊牛生长和消化道微生物的影响 [D]. 博士学位论文. 北京: 中国农业科学院, 2013.

[29] TIMMERMAN H M, KONING C J M, MULDER L, et al. Monostrain, multistrain and multispecies probiotics-a comparison of functionality and efficacy[J]. International Journal of Food Microbiology, 2004, 96(3): 219-233.

[30] LEUNG A Y, FOSTER S. Encyclopedia of common natural ingredients used in food, drugs and cosmetics[M]. 2nd ed. New York: Wiley, 1996: 173-174.

[31] WILLIAMS P, LOSA R. The use of essential oils and their compounds in poultry nutrition[J]. World Poultry, 2001, 17(4): 14-15.

[32] 张卫兵, 张蓉, 屠焰, 等. 血根碱主要作用机制及其在动物营养上的应用效果 [J]. 动物营养学报, 2016, 29(1): 27-33.

[33] PICCIONE G, CASELLA S, LUTRI a1. Reference values haematological, haematochemical, and electrophoretic parameters in the Girgentana goat[J]. Turkish Journal of Veterinary and Animal Science, 2010, 34(2): 197-204.

[34] STANLEY C C, WILLIAMS C C, JENNY B F, et al. Effects of feeding milk replacer once versus twice daily on glucose metabolism in Holstein and Jersey calves[J]. Journal of Dairy Science, 2002, 85(9): 2335-2343.

[35] VAKILI A R, KHORRAMI B, MESGARAN M D, et al. The effects of thyme and cinnamon essential oils on performance, rumen fermentation and blood metabolites in Holstein calves consuming concentrate diet[J]. Asian-Australasian Journal Animal Sciences, 2013, 26(7): 935-944.

[36] TASSOUL M D, SHAVER R D. Effect of a mixture of supplemental dietary plant essential oils on performance of periparturient and early lactation dairy cows[J]. Journal of Dairy Science, 2009, 92(4): 1734-1740.

[37] ÖZDOĞAN M, ÖNENÇ S S, ÖNENÇ A. Fattening performance, blood parameters and slaughter traits of Karya lambs consuming blend of essential oil

compounds[J]. African Journal of Biotechnology, 2011, 10(34): 6663-6669.

[38] FRAYN N. Non-esterified fatty metabolism postprandial lipaemia[J]. Atherosclerosis, 1998, 141(Suppl.1): S41-S46.

[39] RIVERA L, MORÓN R, ZARZUELO A, et al. Long-term resveratrol administration reduces metabolic disturbances and lowers blood pressure in obese Zucker rats[J]. Biochemical Pharmacology, 2009, 77(6): 1053-1063.

[40] YANG W Z, AMETAI B N, BENCHAAR C, et al. Cinnamaldehyde in feedlot cattle diets: intake, growth performance, carcass characteristics, and blood metabolites[J]. Journal of Animal Science, 2010, 88(3): 1082-1092.

[41] FUKUMORI R, SUGINO T, SHINGU H, et al. Effects of fat-enriched diet and methionine on insulin sensitivity in lactating cows[J]. Journal of Animal Science, 2015, 93(6): 2778-2784.

[42] EL-SABAGH M, TANIGUCHI D, SUGINO T, et al. Insulin-independent actions glucagon-like peptide-1 in wethers[J]. Animal Science Journal, 2015, 86(4): 385-391.

[43] LAFONTAN M. Inhibition of epinephrine-induced lipolysis in isolated white adipocytes of aging rabbits increased alpha-adrenergic responsiveness[J]. Journal Lipid Research, 1979, 20(2): 208-216.

[44] LIEN T F, HORNG Y M, YANG K H. Performance, serum characteristics, carcase traits and lipid metabolism of broilers as affected by supplement of chromium picolinate[J]. British Poultry Science, 1999, 40(3): 357-363.

[45] SZKUDELSKA K, SZKUDELSKI T. Resveratrol, obesity and diabetes[J]. European Journal of Pharmacology, 2010, 635(1/2/3): 1-8.

[46] SZKUDELSKI T. The insulin-suppressive effect of resveratrol-an in vitro and in vivo phenomenon[J]. Life Science, 2008, 82(7/8): 430-435.

[47] ETHERTON T D, BAUMAN D E. Biology of somatotropin in growth and lactation of domestic animals[J]. Physiological Reviews, 1998, 78(3): 745-761.

[48] 王杰, 崔凯, 王世琴, 等. 饲粮蛋氨酸水平对湖羊公羔营养物质消化、胃肠道 pH 及血清指标的影响 [J]. 动物营养学报, 2017, 29(8): 3004-3013.

[49] SERRERO G, LU R Q. Effect of resveratrol on the expression of autocrine growth modulators in human breast cancer cells[J]. Antioxidants & Redox Signaling, 2001, 3(6): 969-979.

[50] PENNER G B, STEELE M A, ASCHENBACH J R, et al. Ruminant nutrition symposium: molecular adaptation of ruminal epithelia to highly fermentable diets[J]. Journal of Animal Science, 2011, 89(4): 1108-1119.

[51] STOTT G H, FELLAH A. Colostral immunoglobulin absorption linearly related to concentration for Calves[J]. Journal of Dairy Science, 1983, 66(6): 1319-1328.