Animal Feed Science and Technology 256 (2019) 114261

Contents lists available at ScienceDirect

Animal Feed Science and Technology

journal homepage: www.elsevier.com/locate/anifeedsci

Effects of *Acremonium terricola* culture on production performance, antioxidant status, and blood biochemistry in transition dairy cows

Yi-Zhen Wang[a,1], Yang Li[a,1], Qing-Biao Xu[b,1], Xing-Yi Zhang[a], Guang-Ning Zhang[a], Cong Lin[a], Yong-Gen Zhang[a,*]

[a] *College of Animal Sciences and Technology, Northeast Agricultural University, 150030, PR China*
[b] *College of Animal Sciences and Technology, Huazhong Agricultural University, Wuhan, 430070, PR China*

ARTICLE INFO

Keywords:
Acremonium terricola culture
Transition dairy cow
Energy balance
Antioxidant

ABSTRACT

The effects of supplementing transition dairy cows with *Acremonium terricola* culture (ATC) in the transition period were investigated. Ten dairy cows received a dietary supplement of 30 g/cow/d ATC from 14 d prior to their estimated calving date to 21 d postpartum, and 10 did not. The cows that receiving ATC showed greater milk production, energy-corrected milk yield, and feed efficiency, and had a lower somatic milk cell count and body mass change than the non-supplemented cows ($P < 0.05$). Cows that consumed ATC also had significantly higher plasma concentrations of superoxide dismutase, glutathione peroxidase, and total antioxidant capacity than the controls ($P < 0.05$). In addition, they had significantly higher blood glucose and lower plasma β-hydroxybutyrate, non-esterified fatty acid, and cholesterol concentrations ($P < 0.05$). This study demonstrates that dietary supplementation with ATC improved production, antioxidant status, and energy balance in transition cows, with no obvious adverse effects.

1. Introduction

Transition in dairy cows is defined as the period between 3 wk before and 3 wk after calving (Grummer, 1995). The dramatic changes that occur during this period are associated with a substantial metabolic challenge in dairy cows, which is characterized by a negative energy balance (NEB) (Bell, 1995). A reduction in nutrient intake during the transition period is key to the development of metabolic disorders (Ropstad et al., 1989). Furthermore, delivery, lactation, and changes in nutrition during the transition period are often followed by metabolic disease or mastitis (Weiss et al., 1990).

The use of feed additives can be an effective strategy for the prevention of various diseases in transition cows. *Cordyceps gunnii (Berk.)* is an important pathogenic fungus that belongs to Ascomycota, Pyrenomycetes, Sphaeriales, and Clavicipitaceae and parasitizes the larvae of hepialid insects. Its active ingredient is similar to that of *C. sinensis (Berk.) Sacc*. and contains *Cordyceps* polysaccharides, proteins, amino acids, D-mannitol, alkaloids, and antibacterial substances. *Cordyceps* species, in particular *Cordyceps*

Abbreviations: ALB, albumin; ALP, alkaline phosphatase; ALT, alanine transaminase; ATC, *Acremonium terricola* culture; BHBA, β-hydroxybutyric acid; BUN, blood urea nitrogen; CAT, catalase; CHOL, cholesterol; CP, crude protein; DM, dry matter; DMI, dry matter intake; GLB, globulin; GLU, glucose; GPx, glutathione peroxidase; HDL, high-density lipoprotein-cholesterol; LDL, low-density lipoprotein-cholesterol; MDA, malondialdehyde; NEB, negative energy balance; NDF, neutral detergent fiber; NEFA, non-esterified fatty acids; OH, hydroxyl radical inhibitory capacity; SCS, somatic cell score; SOD, superoxide dismutase; T-AOC, total antioxidant capacity; TG, triglyceride; TP, total protein

* Corresponding author.
E-mail address: zhangyonggen@sina.com (Y.-G. Zhang).

[1] These authors contributed equally to this article.

https://doi.org/10.1016/j.anifeedsci.2019.114261
Received 3 January 2019; Received in revised form 18 August 2019; Accepted 20 August 2019
0377-8401/

gunnii, have beneficial effects, which include immunoregulatory (Koh et al., 2002), anti-inflammatory (Yu et al., 2004), and anti-tumor (Nakamura et al., 1999) effects. However, its high cost and the obsolete processing method that is required limit its application in livestock production.

The *Acremonium terricola* culture (ATC) used in this experiment was extracted from *Cordyceps gunnii* and then subjected to artificial culture. ATC was used instead of *Cordyceps gunnii* because it contains similar functional components, but it is less expensive. ATC has been shown to improve the immunity of piglets and to promote their growth (Wei et al., 2009). Cordycepin from ATC has a significant immune regulatory effect, which promotes the production of specific antibodies and enhances the humoral immune response (Wu et al., 2007). An increase in rumen fermentation, gas, and volatile fatty acid production, and improved digestion of cellulose filter paper, has been reported in dairy cows when rumen fluid is supplemented with *Cordyceps sinensis* (Joonmo et al., 2009).

Although ATC may also be beneficial in transition cows, the effects of dietary supplementation with ATC have not been investigated fully. However, the market value for the milk and meat derived from such cows could be improved if the bioactive components of ATC have similar effects to those tested previously. The objective of this study was to assess the effects of ATC supplementation on the productivity, antioxidant status, and blood biochemistry of transition cows.

2. Materials and methods

This study was conducted in accordance with the principles and guidelines of the Northeast Agricultural University Animal Science and Technology College Animal Care and Use Committee (approval number: NEAU-[2011]-9). Approval was obtained before commencement of the study.

2.1. Experimental design, cows, and diets

Acremonium terricola culture (ATC) was provided by Hefei Micro. Biological Engineering Co. Ltd. (Hefei, China). The preservation number of the ATC according to the China General Microbiological Culture Collection Center was 0346. *Acremonium terricola* culture was obtained by processing the bacteria using artificial solid fermentation. Briefly, *Acremonium terricola* was inoculated onto sterile solid medium that contained 200 g/kg soybean meal, 100 g/kg wheat bran, 699 g/kg corn, 0.8 g/kg KH_2PO_4, and 0.2 g/kg $MgSO_4$, and it was incubated at 25 °C in 800–900 g/kg relative humidity for 76 h. The medium was then dried at 80 °C for 1 h, and passed through a 0.15 mm mesh screen.

Acremonium terricola culture had the following composition: cordycepic acid (D-mannitol; 84.50 g/kg dry matter (DM)), *Cordyceps* polysaccharide (galactomannan; 44.60 g/kg DM), cordycepin (3′-deoxyadenosine; 0.432 g/kg DM), ergosterol (0.597 g/kg DM), and total amino acid content (218.10 g/kg DM). It contained 56 g/kg moisture, 50 g/kg crude fiber (CF), 40.4 g/kg crude ash, 30.6 g/kg ether extract (EE), 245.3 g/kg crude protein (CP), and 633.7 g/kg nitrogen-free extract (NFE).

The concentrations of cordycepic acid, *Cordyceps* polysaccharide, cordycepin, and ergosterol in the ATC were determined using high-performance liquid chromatography. The total amino acid content was determined using a Hitachi L-8800 automatic amino acid analyzer (Hitachi Co., Tokyo, Japan). *Acremonium terricola* culture was analyzed for its DM (method 930.15), crude fiber (method 993.21), crude ash (method 942.05), EE (method 920.39), and CP (method 976.05), according to the methods of the Association of Official Analytical Chemists (AOAC, 2000).

The feeding experiment was performed at Zonghe Dairy Farms in Harbin (Heilongjiang Province, China). Twenty Holstein cows (parity = 3, body mass = 600 ± 25 kg) were allocated to two groups on the basis of their previous 305 d milk yield and anticipated calving date, half of which received the ATC between 14 ± 3 d before their predicted calving date and 21 d postpartum. This experiment consisted of a 2 wk adaptation period and a 5 wk collection period. The cows were kept in a tie-stall barn and were fed a total mixed ration *ad libitum* (50 g refusals/kg) twice daily (0700 and 1900 h) until calving, when it was changed to a diet suitable for postpartum use, and throughout the trial period water was available *ad libitum*. Ten cows were given daily 30 g ATC (on DM basis) per cow, which was the level of supplementation recommended by the manufacturer, and this was mixed with 100 g of the standard diet and fed to the test cows before the standard morning feed. The control cows received 100 g of the standard diet without ATC (Table 1).

2.2. Dry matter intake

The amount of feed offered was recorded, and the orts were collected and weighed every day before the next feed to determine the dry matter intake (DMI), and they were then analyzed for dry matter (DM), neutral detergent fiber (NDF), and crude protein (CP) content. NDF was quantified according to the method described by Soest et al. (1991). The DM (method 930.15) and CP (method 976.05) were determined using the techniques specified by the Association of Official Analytical Chemists (AOAC, 2000).

2.3. Milk yield and composition

Cows were milked twice daily at 05:00 and 17:00 h, and the milk production per cow was recorded. Milk samples were collected in the morning and afternoon, 7, 14, and 21 d after calving calving for analysis of fat, protein, lactose, total solid content (MilkoScanFT120, Foss), and somatic cell count (Fossomatic 400, Foss Electric). The somatic cell count was converted into a somatic cell score (SCS) using the formula: SCS = $\log_2$ (somatic cell counts/100) + 3 (Shook, 1993).

Table 1
Composition of the diets.

Item	Prepartum	Postpartum
Ingredient, g/kg DM[a]		
Corn silage	570	280
Alfalfa silage		265
Wheat straw	200	25
Soybean meal, 470 g/kg, solvent-extracted	188	154
Dry ground-shelled corn		232
Megalac protected fat[b]	2	14
Calcium sulfate	10	
Calcium bicarbonate		9
Sodium bicarbonate		9
Magnesium sulfate	10	
Magnesium oxide	5	2
Monocalcium phosphate	5	3
Trace mineral salts[c]	5	5
Vitamin premix[d]	5	2
Nutrient composition, g/kg DM		
DM	502	524
CP[e]	166	185
NDF[f]	427	285
NDF from forage	407	220
Starch	165	232
Ether extract	26	49
Ash	78	84

[a] DM = dry matter.
[b] Volac International, Liverpool, UK.
[c] Preparation contained (g/kg of DM unless otherwise noted) 880 NaCl, 3.25 Cu, 0.04 Co, 0.175 I, 0.20 Fe, 10 Mn, 0.065 Se, and 14 Zn.
[d] Preparation contained 3,300,000 IU vitamin A, 1,100,000 IU IU vitamin D, and 25,000 IU vitamin E per kg.
[e] CP = crude protein.
[f] NDF = neutral detergent fiber.

2.4. Antioxidant status and blood biochemistry

Every 7 d, before the morning feed, blood samples were collected from the tail vein of each cow using 10 ml evacuated blood collection tubes that contained heparin sodium, which were then centrifuged at 2000 × g for 10 min. The derived plasma was frozen at −20°C until analysis. The activities of plasma glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT), and total antioxidant capacity (T-AOC), and hydroxyl radical inhibitory capacity (OH) were determined using commercial colorimetric analysis kits (Nanjing Jiancheng Institute of Bioengineering, Nanjing). A commercial thiobarbituric acid kit (Nanjing Jiancheng Institute of Bioengineering, Nanjing) was used to measure the plasma malondialdehyde (MDA) concentration. All these analyses were conducted in accordance with the manufacturers' instructions. The plasma concentrations of total protein (TP), glucose (GLU), globulin (GLB), albumin (ALB), ALB/GLB (A/G), triglyceride (TG), cholesterol (CHOL), alanine transaminase (ALT), alkaline phosphatase (ALP), high-density lipoprotein (HDL), low-density lipoprotein (LDL), blood urea nitrogen (BUN), β-hydroxybutyric acid (BHBA) and non-esterified fatty acid (NEFA) were measured using a fully automatic biochemical analyzer provided by Biosino Biotec (Beijing).

2.5. Statistical analysis

The Proc Mixed procedure of SAS version 9.0 (SAS Institute Inc., Cary, NC) was used to analyze the data in a randomized block design, which included repeated measures (DMI, SCS, feed efficiency, milk yield, and composition, and plasma metabolites). The statistical model included fixed effects of block, treatment, time, and two- and three-way interactions, with the identity of the cow used as a random effect. No block, block × treatment, block × time, or block × treatment × time effects were identified. The time point was used as a repeated measure in the first-order autoregressive covariance structure, which provided the best fit according to Schwartz's Bayesian information criterion. Degrees of freedom were calculated using the Kenward-Roger option, and the means were determined using the least squares means statement. The significance level was defined as $P < 0.05$ and a trend was accepted when $0.05 < P < 0.10$.

Table 2
Effect of *Acremonium terricola* culture (**ATC**) supplementation on DMI and production in transition dairy cows.

Item	Treatment		SEM[c]	*P*-value		
	Control (n[a] = 10)	ATC[b] (n = 10)		Treatment	Time	Treatment × Time
DMI[d] (kg/d)	14.3	15.7	0.66	0.17	< 0.01	0.15
CP[e] intake (kg/d)	2.40	2.45	0.07	0.63	< 0.01	0.21
NDF[f] intake (kg/d)	8.06	9.10	0.37	0.08	< 0.01	0.02
Milk yield (kg/d)	21.1	24.7	0.43	< 0.01	< 0.01	0.02
ECM[g] (kg/d)	23.6	27.8	0.47	< 0.01	< 0.01	0.004
Efficiency (ECM/DMI)	1.61	1.65	0.01	< 0.01	< 0.01	< 0.01
SCS[h]	5.72	5.54	0.03	< 0.01	< 0.01	0.15
Fat (g/kg)	40.8	40.6	0.25	0.96	< 0.01	0.74
Protein (g/kg)	33.5	34.5	0.12	0.56	< 0.01	0.67
Lactose (g/kg)	45.5	47.2	0.06	0.07	< 0.01	0.31
Total solids (g/kg)	122	124	0.23	0.54	< 0.01	0.73
BW change[i] (kg)	−20.1	−18.6	0.50	0.04		

[a] n = number of cows.
[b] ATC = 30g of ATC/cow/d.
[c] SEM = standard error of the mean.
[d] DMI = dry matter intake.
[e] CP = crude protein.
[f] NDF = neutral detergent fiber.
[g] ECM= 0.327 × milk (kg) + 12.95 × fat (kg) + 7.65 × protein (kg; Dairy Records Management Systems, 2011).
[h] SCS = log2 (somatic cell counts/100) + 3.
[i] Difference between calving data and data at 21 d postcalving.

3. Results

3.1. DMI and performance

Compared with the control group, ATC supplementation significantly increased the milk yield, ECM, and feed efficiency ($P < 0.05$), and it reduced the SCS and body mass change ($P < 0.05$) (Table 2). In addition, NDF intake tended to be higher ($P = 0.08$) in cows that consumed ATC during the trial period. However, no significant differences were found in milk fat (%), protein (%), lactose (%), total solids (%), CP intake, or DMI between the groups ($P > 0.05$).

3.2. Antioxidant status

The activities of SOD and GPx were significantly higher in cows that had received ATC ($P < 0.01$), and the plasma T-AOC concentration was also significantly higher ($P < 0.01$) (Table 3). A significant ATC × time interaction was observed with respect to GPx activity ($P < 0.05$), but there was no significant effect of ATC or an ATC × time interaction with respect to the activities of CAT or OH during the study ($P > 0.05$).

Table 3
Effect of ATC supplementation on antioxidant parameters in transition cows.

Item	Treatment		SEM[c]	*P*-value		
	Control (n[a] = 10)	ATC[b] (n = 10)		Treatment	Time	Treatment × Time
CAT[d] (U/mL)	3.21	2.35	0.43	0.20	0.43	0.18
SOD[e] (U/mL)	160	183	3.47	< 0.01	0.03	0.11
MDA[f] (nmol/L)	3.19	2.91	0.14	0.18	0.46	0.84
GPx[g] (U/mL)	423	451	3.00	< 0.01	< 0.01	0.03
OH[h] (U/mL)	739	669	25.61	0.09	0.04	0.94
T-AOC[i] (U/mL)	2.49	3.28	0.13	< 0.01	< 0.01	0.42

[a] n = number of cows.
[b] ATC = 30g of ATC/cow/d.
[c] SEM = standard error of the mean.
[d] CAT = catalase.
[e] SOD = superoxide dismutase.
[f] MDA = malondialdehyde.
[g] GPx = glutathione peroxidase.
[h] OH = hydroxyl radical inhibitory capacity.
[i] T-AOC = total antioxidant capacity.

3.3. Blood biochemistry

Cows that received ATC had a significantly higher GLU concentration and a lower CHOL concentration than the controls ($P < 0.05$) (Table 4). In addition, plasma BHBA and NEFA concentrations were also significantly lower in the treatment group ($P < 0.01$). Across the entire experimental period, significant ATC × time interactions were found with respect to plasma BHBA ($P < 0.05$) and NEFA ($P < 0.01$) concentrations. There were no significant effects of ATC or ATC × time interactions with respect to the concentrations of TP, ALB, GLB, ALT, ALP, HDL, LDL, or BUN (all $P > 0.05$).

4. Discussion

4.1. DMI and performance

The substantial drop in the DMI of cows in both groups during the weeks preceding calving was consistent with previously published results (Dann et al., 1999), and this may be a result of the physical limitations and endocrine changes that are associated with parturition and lactogenesis (Grummer, 1993). During the prepartum period, the feed intake was similar in the control and ATC groups, but 21 d after calving, the DMI of cows supplemented with ATC tended to be higher, which suggested that consuming ATC improved feed digestibility and the health status of the cows and may have beneficial effects on postpartum DMI. In general, DMI increases with an increase in the apparent digestibility of feed nutrients. Our previous studies have also demonstrated that ATC increased milk yield and the apparent digestibility of the feed, and it promoted immune function, both in lactating dairy cows (Li et al., 2018) and their calves (Li et al., 2016a), which suggested that ATC was beneficial for transitioning dairy cows.

Dairy cows often develop diseases that are related to oxidative stress during the transition period, which lead to a decline in milk production and mastitis. In particular, mastitis can reduce milk yield (Natzke et al., 1972) and lactose content (Shuster et al., 1991). Ilie et al. (2011) demonstrated that SCS increased as milk production decreased, which was consistent with other reports that showed a negative correlation between somatic cell count and milk yield (Cinar et al., 2015). In the present study, the increase in milk production and the decrease in SCS might at least partially be due to the alleviation of mammary inflammation and positive effects on the immune system associated with ATC administration because milk production tends to increase with improvements in immune

Table 4
Effect of ATC supplementation on blood biochemistry in transition cows.

Item	Treatment		SEM[c]	P-value		
	Control (n[a] = 10)	ATC[b] (n = 10)		Treatment	Time	Treatment × Time
GLU[d] (mmol/L)	3.59	3.83	0.07	0.03	< 0.01	0.23
TP[e] (g/L)	63.9	65.7	1.57	0.45	< 0.01	0.44
ALB[f] (g/L)	26.3	27.9	0.59	0.11	< 0.01	0.20
GLB[g] (g/L)	36.7	36.7	1.42	0.98	< 0.01	0.84
A/G[h] ratio	0.78	0.80	0.04	0.67	< 0.01	0.81
ALT[i] (IU/L)	21.6	22.1	0.98	0.72	0.05	0.91
ALP[j] (IU/L)	63.9	59.1	4.58	0.48	< 0.01	0.45
TG[k] (mmol/L)	0.24	0.24	0.01	0.94	< 0.01	0.03
CHOL[l] (mmol/L)	2.95	2.49	0.13	0.04	< 0.01	0.27
HDL[m] (mmol/L)	0.78	0.94	0.05	0.06	< 0.01	0.20
LDL[n] (mmol/L)	0.56	0.50	0.08	0.62	0.01	0.24
BUN[o] (mmol/L)	4.59	4.69	0.16	0.67	< 0.01	0.76
BHBA[p] (mmol/L)	0.68	0.65	0.01	0.01	< 0.01	0.049
NEFA[q] (μmol/L)	553	531	3.63	< 0.01	< 0.01	< 0.01

[a] n = number of cows.
[b] ATC = 30g of ATC/cow/d.
[c] SEM = standard error of the mea.
[d] GLU = glucose.
[e] TP = total protein.
[f] ALB = albumin.
[g] GLB = globulin.
[h] A/G = ALB/GLB.
[i] ALT = alanine transaminase.
[j] ALP = alkaline phosphatase.
[k] TG = triglyceride.
[l] CHOL = cholesterol.
[m] HDL = high-density lipoprotein.
[n] LDL = low-density lipoprotein.
[o] BUN = blood urea nitrogen.
[p] BHBA = β-hydroxybutyric acid.
[q] NEFA = non-esterified fatty acid.

function (Mukherjee, 2008). In addition, anti-inflammatory effects of functional components of ATC have been demonstrated (Koh et al., 2002). Previous studies have also shown that ATC improved production performance in piglets (Wei et al., 2009) and chickens (Sun et al., 2011), and follow-up studies have shown that the productivity of broilers (Han et al., 2015) and layers (Wang et al., 2015) can be improved by supplementing their diets with the fermentation products of *Cordyceps* or the byproducts of *Cordyceps sinensis*.

Furthermore, the increase in milk yield was also related closely to the increase in efficiency in our study. Although few studies have been conducted on the response of dairy cows to ATC, studies conducted in an aquatic animal (Deng et al., 2015) have demonstrated that ATC and its functional components improved feed efficiency and health status, which was consistent with beneficial effects of ATC on animal growth. During the postpartum period, we found that cows that were fed ATC exhibited fewer changes in body mass. We believe that this was because ATC increased the propionic acid concentration in the rumen, which enhanced gluconeogenesis and blood glucose concentration and availability, thereby reducing the necessity for the mobilization of body fat. Previous studies have also shown that ATC supplementation increased the concentration of volatile fatty acids and propionic acid, specifically in the rumen of dairy cows (Li et al., 2018; Zhang et al., 2016). Therefore, we contend that ATC supplementation has great potential for the amelioration of negative energy balance, improvement of milk yield, and reduction of the somatic cell count in transition cows, and that these effects are not associated with obvious adverse effects.

4.2. Antioxidant status

Oxidative stress develops when there is an imbalance between oxidation and the antioxidant system, which occurs in response to a number of stimuli. In this situation, free radicals, such as the active oxygen free radical and the active nitrogen radical are present in excess of the scavenging ability of the antioxidant system (Lushchak, 2014). Transition cows are particularly vulnerable to oxidative stress and the resulting damage (Bouwstra et al., 2008). Oxidative stress underlies a number of disorders that affect cows during the transition period, such as mastitis, ovarian cysts, abomasal displacement, and ketosis. These diseases are all associated with reductions in milk yield and quality, which result in economic loss.

T-AOC is a relatively independent index that describes the dynamic balance between oxidation and antioxidant activity in the circulation, and SOD, CAT, and GPx also play key roles in the maintenance of oxidative balance and the repair of oxidative damage (Dong et al., 2009). The present study showed that ATC supplementation increased plasma T-AOC, SOD, and GPx activity, which suggests that ATC improved antioxidant capacity by reducing oxidative stress and enhancing antioxidant enzyme activity. These findings are consistent with those of previous studies that demonstrated that ATC supplementation increased the activity of T-AOC, SOD, and GPx and reduced MDA concentration in the serum of weaned calves (Li et al., 2016b). Furthermore, another study identified similar effects in the liver and serum of rats (Li et al., 2016a).

Cordyceps and its functional components have potential antioxidant effects and reduce lipid peroxidation (Yu et al., 2000). Our results are consistent with previous studies that showed that *Cordyceps militaris* exhibited antioxidant effects in mice (Liu et al., 2016) and improved SOD and GPx activity in white shrimp (Deng et al., 2015). In addition, *Cordyceps* polysaccharide and other immunopolysaccharides, which are the principal active components of ATC, improved SOD and GPx activity (Kobayashi et al., 1994; Li et al., 2012). Earlier studies also demonstrated that *Cordyceps* polysaccharides enhanced the activity of GPx and inhibited the formation of the lipid peroxide MDA, which reduced damage caused by carbon tetrachloride in liver cells (Yu et al., 2011). The mechanism that underpins the effect of ATC is still unclear; however, biological functions of the proposed active ingredients of ATC have been demonstrated. Therefore, the effects of ATC on antioxidant status are worthy of further exploration. In the present study, ATC had a positive effect on the antioxidant status of transition cows, and all the measured associated values were within the normal range.

4.3. Blood biochemistry

During the transition period, a reduction in nutrient intake and an increase in demand led to NEB in dairy cows. When in a state of NEB, the blood GLU concentration is low because of inadequate gluconeogenesis, and, therefore, body fat is used to meet the energy requirement for lactation. This involves the release of NEFA into the circulation, but when its circulating concentration exceeds a threshold it cannot all undergo β-oxidation; instead, ketone bodies are generated. When the capacity of the animal to metabolize these is exceeded, they accumulate, which leads to fatty liver, ketosis, and other metabolic diseases (Li, 2015). Thus, high concentrations of serum NEFA and BHBA are indicative of severe NEB and ketosis (Roche et al., 2008). Our results showed that ATC reduced concentrations of NEFA and BHBA in the blood and reduced fluctuations in body mass, which implied that it has the ability to ameliorate the NEB and prevent metabolic disease in transition cows. Similarly, Chanjula and Cherdthong (2018) reported that *Cordyceps sinensis* lowered the circulating concentrations of NEFA and BHBA in goats. ATC contains *Cordyceps* polysaccharide, which effectively reduced serum CHOL and NEFA in rats (Wang et al., 2010), and previous studies have shown that dietary supplementation with polysaccharides from the cultured mycelium of *Cordyceps sinensis* reduced serum NEFA in mice (Liu et al., 2011).

The beneficial effect of ATC might also be due to the higher concentration of blood GLU in the present study. A low concentration of GLU was associated with high serum NEFA and BHBA concentrations (Li et al., 2018), and the values were negatively correlated in cows (Chi, 2007), which implied a close relationship between these metabolites. Propionic acid is the principal gluconeogenic substrate in dairy cows, and its generation is therefore crucial for the maintenance of blood GLU (Sauer et al., 1989). Previous studies reported an increase in blood GLU and a reduction in serum NEFA concentration following propionic acid infusion (Oba and Allen, 2003). It inhibited fatty acid oxidation by reducing the activity of fatty acyl-CoA dehydrogenase (Shaw and Engel, 1985) or by reducing fatty acid transport to mitochondria (Jesse et al., 1986), thereby reducing lipolysis in adipose tissue. Previous studies have observed a large increase in propionic acid in the rumen of dairy cows supplemented with ATC (Zhang et al., 2016), probably because it had a positive effect on the growth of rumen bacteria and protozoa, which improved the degradation of dietary protein and carbohydrates (Li et al., 2018). Therefore, it is likely that the amelioration of the NEB in transition cows may be related to an enhancement of rumen fermentation efficiency.

An increase in blood CHOL may impair the health of dairy cows (Drackley et al., 1992). In the present study, ATC supplementation reduced serum CHOL, which may also be beneficial for the health of transition cows. Administration of the ATC functional ingredient *Cordyceps* polysaccharide may maintain a lower level of CHOL (Yu et al., 2011), and *Cordyceps sinensis* has been shown to similarly reduce plasma CHOL concentration in mice (Liu and Zhao, 2004) and goats (Chanjula and Cherdthong, 2018). CsB-851 is a product derived from *Cordyceps sinensis* mycelium using resin separation, and Li et al. (1992) found that CsB-851 might be an inhibitor of endogenous cholesterol synthesis. Therefore, it may be that ATC and its functional components improve the health status of transition cows by influencing CHOL metabolism, although the potential mechanisms involved require further elucidation.

5. Conclusion

Dietary supplementation with ATC could improve the production and antioxidant capacity, and ameliorate the NEB, in transition cows. The results of the present study showed that ATC represented a valuable new feed additive, and it had no obvious adverse effects on the cows when used at 30 g/d.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

This study was financially supported by the China Agriculture Research System (CARS-36), the Postdoctoral Foundation in Heilongjiang Province (LBH-Z17035), the Young Talents Project of the Northeast Agricultural University (18QC35), and the China Postdoctoral Science Foundation Grant for the 65nd batch (2019M651252). The authors thank the staff of Zonghe farm for their help with animal care.

References

AOAC International, 2000. Official Methods of Analysis, 17th ed. Off. Anal. Chem., Arlington, VA.
Bell, A.W., 1995. Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation. J. Anim. Sci. 73, 2804–2819.
Bouwstra, R.J., Goselink, R.M.A., Dobbelaar, P., Nielen, M., Newbold, J.R., Werven, T.V., 2008. The relationship between oxidative damage and vitamin E concentration in blood, milk, and liver tissue from vitamin E supplemented and nonsupplemented periparturient heifers. J. Dairy Sci. 91, 0–987.
Chanjula, P., Cherdthong, A., 2018. Effects of spent mushroom *Cordyceps* militaris supplementation on apparent digestibility, rumen fermentation, and blood metabolite parameters of goats. J. Anim. Sci. 96, 1150–1158.
Chi, J.B., 2007. Research on the Blood Biochemical Indexes of Cow Suffering From Ketone Disease, Fatty Liver Disease during Perinatology. Chinese Academy of Agricultural Sciences.
Cinar, M., Serbester, U., Ceyhan, A., Gorgulu, M., 2015. Effect of somatic cell count on milk yield and composition of first and second lactation dairy cows. Ital. J. Anim. Sci. 14, 105–108.
Dann, H.M., Varga, G.A., Putnam, D.E., 1999. Improving energy supply to late gestation and early postpartum dairy cows. J. Dairy Sci. 82, 1765–1778.
Deng, B., Wang, Z.P., Tao, W.J., Li, W.F., Wang, C., Wang, M.Q., Ye, S.S., Du, Y.J., Wu, X.X., Wu, D., 2015. Effects of polysaccharides from mycelia of *Cordyceps sinensis* on growth performance, immunity and antioxidant indicators of the white shrimp L itopenaeus vannamei. Aquacult. Nutr 21, 173–179.
Dong, C.H., Zhao, J.M., Song, L.S., Wang, L.L., Qiu, L.M., Zheng, P.L., Li, L., Gai, Y.C., Yang, G.P., 2009. The immune responses in Chinese mitten crab eriocheir sinensis challenged with double-stranded RNA. Fish Shellfish Immunol. 26, 438–442.
Drackley, J.K., Richard, M.J., Beitz, D.C., Young, J.W., 1992. Metabolic changes in dairy cows with ketonemia in response to feed restriction and dietary 1,3-butanediol. J. Dairy Sci. 75, 1622–1634.
Grummer, R.R., 1995. Impact of changes in organic nutrient metabolism on feeding the transition dairy cow. J. Anim. Sci. 73, 2820–2833.
Grummer, R.R., 1993. Etiology of lipid-related metabolic disorders in periparturient dairy cows. J. Dairy Sci. 76, 3882–3896.
Han, J.C., Qu, H.X., Wang, J.G., Yan, Y.F., Zhang, J.L., Yang, L., Zhang, M., Cheng, Y.H., 2015. Effects of fermentation products of on growth performance and bone mineralization of broiler chicks. J. Appl. Anim. Res. 43, 236–241.
Jesse, B.W., Emery, R.S., Thomas, J.W., 1986. Control of bovine hepatic fatty acid oxidation. J. Dairy Sci. 69, 2290–2297.
Joonmo, Y., Shinja, L., Sangmin, L., Sunghwan, S., Sunghoon, L., Jongk, H., Wanyoung, K., Sungsill, L., 2009. Effects of *Cordyceps* militaris mycelia on in vitro rumen microbial fermentation. Asian Austral. J. Anim. 22, 201–205.
Kobayashi, Y., Kariya, K., Saigenji, K., Nakamura, K., 1994. Oxidative stress relief for cancer-bearing hosts by the protein-bound polysaccharide of coriolus versicolor QUEL with SOD mimicking activity. Cancer Biother. Radiopharm. 9, 55–62.
Koh, J.H., Yu, K.W., Suh, H.J., Choi, Y.M., Ahn, T.S., 2002. Activation of macrophages and the intestinal immune system by an orally administered decoction from cultured mycelia of *Cordyceps sinensis*. Biosci. Biotechnol. Biochem. 66, 407–411.
Li, C.H., 2015. Research on negative energy balance and energy metabolism disorders of transition cows. Chinese J. Anim. Husb. Vet. Med. 7, 69–70.
Li, L., Bao, T.T., Song, Z.Y., 1992. Mechanism of the hypocholesterolemic effect of csb-851 (a fraction separated from fermented mycelium of *Cordyceps sinensis*) in mice. Pharmacol. Clin. Chinese Materia Medica. 2, 6–10.
Li, X.T., Li, H.C., Li, C.B., Dou, D.Q., Gao, M.B., 2012. Protective effects on mitochondria and anti-aging activity of polysaccharides from cultivated fruiting bodies of *Cordyceps* militaris. Am. J. Chinese Med. 38, 1093–1106.
Li, Y., Lin, C., Xu, W.B., Zhang, X.Y., Wang, Y.Z., Gao, H., Dou, X.J., Hao, X.Y., Zhang, Y.G., 2016b. Effects of *Acremonium terricola* culture on growth performance antioxidant and immune indexes of serum and liver in sprague dawley rats. Chin. J. Anim. Nur. 28, 2657–2666.
Li, Y., Sun, Y.K., Li, X., Zhang, G.N., Xin, H.S., Xu, H.J., Zhang, L.Y., Li, X.X., Zhang, Y.G., 2018. Effects of *Acremonium terricola* culture on performance, milk composition, rumen fermentation and immune functions in dairy cows. Anim. Feed Sci. Technol. 240, 40–51.
Li, Y., Wang, Y.Z., Ding, X., Zhang, Y.G., Xue, S.C., Lin, C., Xu, W.B., Dou, X.J., Zhang, L.Y., 2016a. Effects of *Acremonium terricola* culture on growth performance, antioxidant status and immune functions in weaned calves. Livest. Sci. 193, 66–70.

Liu, J.Y., Feng, C.P., Li, X., Chang, M.C., Meng, J.L., Xu, L.J., 2016. Immunomodulatory and antioxidative activity of *Cordyceps* militaris polysaccharides in mice. Int. J. Biol. Macromol. 86, 594–598.
Liu, X.C., Zhao, Y.X., 2004. The cholesterol lowering activity of hot water extract of *Cordyceps* mycelium. J. Tradit. Chin. Med. 26, 305–306.
Liu, X.Q., Yu, M., Zhang, Y., Wei, L.L., 2011. Effect of polysaccharides from cultured mycelium of *Cordyceps sinensis* on insulin resistance in T2DM mice. Herald Med. 30, 5–8.
Ilie, L.I., Galis, A.M., Tudor, L., 2011. Relationship of somatic cell count with milk yield and composition in holstein and romanian spotted cow crossbreed population. Curr. Opin. Biotechnol. 22 S96-S96.
Lushchak, V.I., 2014. Free radicals, reactive oxygen species, oxidative stress and its classification. Chem-Biol. Interact. 224, 164–175.
Mukherjee, R., 2008. Selenium and vitamin E increases polymorphonuclear cell phagocytosis and antioxidant levels during acute mastitis in riverine buffaloes. Vet. Res. Commun. 32, 305–313.
Nakamura, K., Yamaguchi, Y., Kagota, S., Kwon, Y.M., Shinozuka, K., Kunitomo, M., 1999. Inhibitory effect of *Cordyceps sinensis* on spontaneous liver metastasis of lewis lung carcinoma and B16 melanoma cells in syngeneic mice. Jpn. J. Pharmacol. 79, 335–341.
Natzke, R.P., Everett, R.W., Guthrie, R.S., Keown, J.F., Meek, A.M., Merrill, W.G., Roberts, S.J., Schmidt, G.H., 1972. Mastitis control program: effect on milk production. J. Dairy Sci. 55, 1256–1260.
Oba, M., Allen, M.S., 2003. Dose-response effects of intrauminal infusion of propionate on feeding behavior of lactating cows in early or midlactation. J. Dairy Sci. 86, 2922–2931.
Roche, J.R., Sheahan, A.J., Chagas, L.M., Boston, R.C., 2008. Short communication: change in plasma ghrelin in dairy cows following an intravenous glucose challenge. J. Dairy Sci. 91, 1005–1010.
Ropstad, E., Larsen, H.J., Refsdal, A.O., 1989. Immune function in dairy cows related to energy balance and metabolic status in early lactation. Acta Vet. Scand. 30, 209–219.
Sauer, F.D., Kramer, J.K.G., Cantwell, W.J., 1989. Antiketogenic effects of monensin in early lactation. J. Dairy Sci. 72, 436–442.
Shaw, L., Engel, P.C., 1985. The suicide inactivation of ox liver short-chain acyl-CoA dehydrogenase by propionyl-CoA. Formation of an FAD adduct. Biochem. J. 230, 723–731.
Shook, G.E., 1993. Genetic improvement of mastitis through selection on somatic cell count. Vet. Clin. N. Am-food A 9, 563–581.
Shuster, D.E., Harmon, R.J., Jackson, J.A., Hemken, R.W., 1991. Suppression of milk production during endotoxin-induced mastitis. J. Dairy Sci. 74, 3763–3774.
Soest, P.J.V., Robertson, J.B., Lewis, B.A., 1991. Methods for dietary fiber, neutral detergent fiber, and nonstarch polysaccharides in relation to animal nutrition. J. Dairy Sci. 74, 3583–3597.
Sun, H.J., Li, X.X., Ding, Q., Zhu, Y., Chen, Z., 2011. Effects of *Cordyceps* feed additive on production performance and egg quality of laying ducks (in Chinese). J. Anhui Agri. Sci. 39, 3618–3620.
Wang, C.L., Chiang, C.J., Chao, Y.P., Yu, B., Lee, T.T., 2015. Effect of *Cordyceps* militaris waster medium on production performance, egg traits and egg yolk cholesterol of laying hens. J. Poult. Sci. 52, 188–196.
Wang, J.F., Li, X.L., Zhang, X., Fu, J., Zhao, Q., Xue, C.H., 2010. The mechanism of the mixture of apostichopus japonicus and *Cordyceps* militaris on protection of renal injury in diabetic rats. Chinese Pharmacol. Bulletin 26, 1238–1242.
Wei, J.Z., Zhang, W., Li, Y., Fan, M.Z., Wang, G.J., Yang, D.K., 2009. Effects of the culture of *Acrermonium terricolaon* performance and immunity of piglets. China Anim. Husb. Vet. Med. 36, 33–35.
Weiss, W.P., Todhunter, D.A., Hogan, J.S., Smith, K.L., 1990. Effect of duration of supplementation of selenium and vitamin E on periparturient dairy cows. J. Dairy Sci. 73, 3187–3194.
Wu, W.C., Hsiao, J.R., Lian, Y.Y., Lin, C.Y., Huang, B.M., 2007. The apoptotic effect of cordycepin on human OEC-M1 oral cancer cell line. Cancer Chemoth. Pharm. 60, 103–111.
Yu, B.C., Tang, L., Mao, X.X., Li, X.J., 2011. Research progress of pharmacological study on *Cordyceps* polysaccharide. World Sci. Technol. 13, 585–590.
Yu, R.M., Song, L.Y., Zhao, Y., Bin, W., Wang, L., Zhang, H., Wu, Y.H., Ye, W.C., Yao, X.S., 2004. Isolation and biological properties of polysaccharide CPS-1 from cultured *Cordyceps* militaris. Fitoterapia 75, 465–472.
Yu, Y., Kagota, S., Nakamura, K., Shinozuka, K., Kunitomo, M., 2000. Antioxidant activity of the extracts from fruiting bodies of cultured *Cordyceps sinensis*. Phytother. Res. 14, 647–649.
Zhang, Y.G., Wang, Y.Z., Li, Y., Zhang, X.Y., Lin, C., Zhang, G.N., 2016. Effect of *Acremonium terricola* culture on ruminal fermentation, microflora and blood biochemical parameters in dairy cows. J. Northeast Agri. Univ. 47, 60–66.