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Original Research Article

Oral administration of dibutyryl adenosine cyclophosphate improved growth performance in weaning piglets by enhancing lipid fatty acids metabolism

Guanya Li [a, b], Ling Chang [a], Guanglei Zhang [a], Zehe Song [a], Dan Wan [b], Chunyan Xie [a, *], Hong Wang [c], Zhiyong Fan [a, *]

[a] Hunan Co-Innovation Center of Safety Animal Production, College of Animal Science and Technology and College of Bioscience and Biotechnology, Hunan Agricultural University, Changsha, 410128, China
[b] Key Laboratory of Agro-Ecological Processes in Subtropical Region, Institute of Subtropical Agriculture, The Chinese Academy of Sciences, National Engineering Laboratory for Pollution Control and Waste Utilization in Livestock and Poultry Production, Hunan Provincial Engineering Research Center for Healthy Livestock and Poultry Production, Changsha, 410125, China
[c] Meiya Hai'an Pharmaceutical Co., Ltd., Hai'an, 226600, China

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ABSTRACT

Dibutyryl adenosine cyclophosphate (dbcAMP-Ca), an analog of cyclic adenosine monophosphate (cAMP), plays greater roles in regulating physiological activities and energy metabolism than cAMP. The aim of this study was to investigate the effect of oral administration of dbcAMP-Ca on growth performance and fatty acids metabolism in weaning piglets. A total of 14 early weaning piglets (7 ± 1 d of age, 3.31 ± 0.09 kg, Landrace × Large White × Duroc) were randomly divided into 2 groups: control group and dbcAMP-Ca group, and the piglets received 7 mL of 0.9% NaCl or 1.5 mg dbcAMP-Ca dissolved in 7 mL of 0.9% NaCl per day for 10 d, respectively. The results showed that the average daily gain (ADG) increased by 109.17% ($P < 0.05$) in the dbcAMP-Ca group compared with the control group. Besides, dbcAMP-Ca significantly decreased blood high density lipoprotein cholesterol (HDLC) concentration ($P < 0.05$) and significantly increased blood low density lipoprotein cholesterol (LDLC) concentration ($P < 0.05$) compared with the control group. Further, liver C18:2n6t content significantly increased in dbcAMP-Ca group ($P < 0.05$) compared with the control group. With the increase of C18:2n6t content, the mRNA expression levels of peroxisome proliferator-activated receptor α (*PPARα*) and hormone sensitive glycerol three lipase (*HSL*), of which genes are related to lipid metabolism, were also significantly increased ($P < 0.05$ or $P < 0.01$). All of the results indicated that dbcAMP-Ca improved the ADG, which was probably done by regulating fatty acids metabolism in the liver of weaning piglets.

1. Introduction

Neonatal piglets face heavy challenge to adapt to the shift between intrauterine and extrauterine environments because of weak gut absorptive capacity, low immunity and adaptability, etc (Tanghe et al., 2014; Wang et al., 2017). Normally, weaning usually occurred in an early period at around 21 d of age. However, under the integrated production, weaning time of piglets gets earlier and earlier. Weaning in piglets may lead to worse situation and result in weaning stress in piglets, thus may affect their health and welfare with a decline in feed intake and be vulnerable to disease (Duan et al., 2015).

* Corresponding authors.
E-mail addresses: xiechunyan@hunau.edu.cn (C. Xie), fzyong04@163.com (Z. Fan).

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Milk lipids are the main sources of energy for sucking piglets. An earlier study has found that respiratory entropy of newborn piglets was reduced after birth which indicated that piglets used large amounts of fatty acids to provide energy (Hales, 1997). A former study also showed that lipids in the milk provided nearly 50% of the energy for suckling piglets (Hobbins, 1997). However, it has been reported that the activity of pancreatic lipase increased with age but weaning made it sharply decline (Aumaitre and Corring, 1978; Cera et al., 1990). Therefore, fatty acid, 1 of the 3 major nutrients, plays significant roles in growth, metabolism and physiological functions in newborn mammals because of their considerable energy needs and defective dietary capacity (Gruppuso et al., 1994; Hardy and Kleinman, 1994; Goodyer et al., 2001). Herein, the decomposition and utilization of fatty acids are of great significance to newborn piglets.

Interestingly, cyclic adenosine monophosphate (cAMP), which has been shown to mediate the hormonal regulation of lipid metabolism (Butcher et al., 1968; Gagelin et al., 1999), is vital in regulating and utilizing fatty acids (Luiken et al., 2002; Madsen et al., 2008). Moreover, dibutyryl adenosine cyclophosphate calcium (dbcAMP-Ca, Fig. 1), an analog of cAMP, can regulate the lipid metabolism remarkably in growing and finishing pigs (Gao et al., 2004), and affect the differentiation of sheep inguinal preadipocytes (Kong et al., 2017). However, little is known about how dbcAMP affects the metabolism of fatty acids and the growth performance in weaning piglets. Therefore, the present study was intended to seek the effect of oral administration of dbcAMP-Ca on growth performance and lipid fatty acids metabolism in weaning piglets.

2. Materials and methods

2.1. Animals and treatments

The animal experiment was approved by the Protocol Management and Review Committee of the institute of Subtropical Agriculture, Chinese Academy of Science. Pigs were cared for and slaughtered according to the guidelines of the institute of Subtropical Agriculture on Animal Care, Changsha, China. Dibutyryl adenosine cyclophosphate (dbcAMP-Ca) ($C_{18}H_{23}N_5O_8PCa$, molecular weight 507.00 g/mol, purity 98.00%) was provided by Meiya Haian pharmaceutical Co., Ltd (Haian 226600, China).

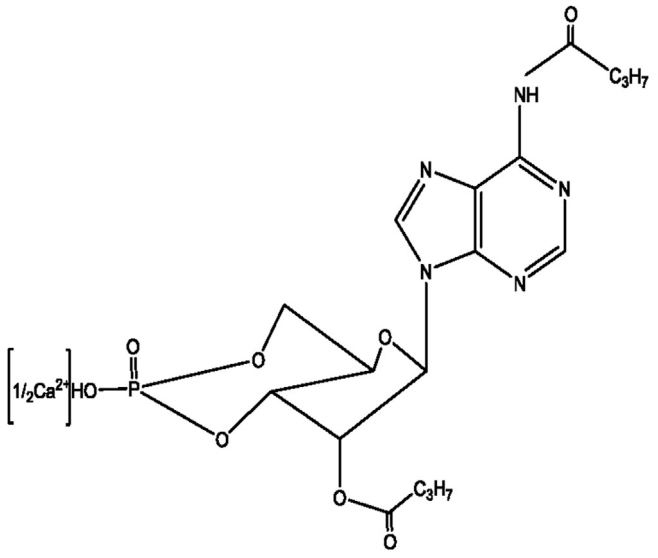

Fig. 1. The structural formula of dibutyryl adenosine cyclophosphate (dbcAMP-Ca).

Fourteen 7-day-old weaning piglets (Landrace × Large White × Duroc) with mean body weight at 3.31 ± 0.09 kg were randomly divided into 2 groups: control group and dbcAMP-Ca group. The piglets received 7 mL of 0.9% NaCl or 1.5 mg dbcAMP-Ca dissolved in 7 mL of 0.9% NaCl by oral administration at indicated times per day for 10 days, respectively. Ingredients and nutrient levels of the basal milk are shown in Table 1. All the piglets were fed by artificial breast feeder and had *ad libitum* access to water and the basal milk.

2.2. Samples collection

Before slaughter, 5 mL blood samples were collected from the jugular vein, and plasma samples were obtained by centrifugation at 3,000 × *g* for 10 min at 4 °C, followed by being immediately stored at −80 °C for later lipid profiles analysis (Wu et al., 2016). Liver samples were taken from each animal, followed by being flash frozen in liquid nitrogen and stored at −80 °C prior to RNA isolation and at −20 °C for fatty acid analysis, respectively.

2.3. Fatty acids analysis in liver of piglets

The extraction of fatty acids from 500 mg of the liver tissue and the methylation were performed. The concentration of individual fatty acids was quantified according the peak area and expressed as a percentage of total fatty acids by gas chromatography (GC-2010, Shimadzu Corp, Japan) as previously described (Tan et al., 2009; Raj et al., 2010).

2.4. RNA extraction and cDNA synthesis

About 100 mg of the liver tissue was pulverized in liquid nitrogen. Total RNA was isolated from the homogenate using TRIzol reagent (Invitrogen, CA, USA). The concentration of total RNA was quantified spectrophotometrically (NanoDrop ND-1000; Thermo Fisher Scientific, DE, USA) at 260 nm, and the ratio of 260 nm to 280 nm was used to assess RNA quality, then cDNA synthesis was carried out using a PrimeScript RT reagent Kit With gDNA Eraser (TaKaRa, Dalian, China). Primers (Table 2) were designed by Primer 5.0 based on GenBank (http://www.ncbi.nlm.nih.gov/pubmed/), and Oligo Synthesis was conducted by Sangon Biotech (Shanghai, China). β-actin was chosen as a reference gene.

Table 1
Ingredients (%) and nutrient levels (%) of the basal milk (air-dry basis).

Ingredients	Content	Nutrient levels	Content
Skimmed milk powder	85.0	DE, MJ/kg	14.65
Dried whey	5.0	CP	20.50
Glucose	2.5	Ca	0.70
Plasma proteins	3.5	Total P	0.60
Premix[1]	4.0	Lys	1.45
Total	100.0	Met	0.48
		Try	0.29

[1] The premix provided the following for per kg of the basal milk: vitamin A_1 500 IU, vitamin D_3 200 IU, vitamin E 85 IU, D-pantothenic acid 35 mg, vitamin B_2 12 mg, folic acid 1.5 mg, nicotinic acid 35 mg, vitamin B 13.5 mg, vitamin B_6 2.5 mg, biotin 0.2 mg, vitamin B_{12} 0.05 mg, copper (as copper sulfate) 15 mg, ferrum (as ferrous sulfate) 100 mg, manganese (as manganese sulfate) 20 mg, iodate (as calcium iodate) 1.0 mg, selenium (as sodium selenite) 0.35 mg, cobalt (as cobalt sulfate) 0.2 mg, and chromium (as chromium picolinate) 0.2 mg.