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Dietary supplementation with garcinol during late gestation and lactation facilitates acid–base balance and improves the performance of sows and newborn piglets[1]

Tongxin Wang, Weilei Yao, Jun Xia, Juan Li, Yafei Shao, and Feiruo Huang[2]

Department of Animal Nutrition and Feed Science, College of Animal Science and Technology, Huazhong Agricultural University, Wuhan 430070, China

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[2]Corresponding author: huangfeiruo@mail.hzau.edu.cn

ORCiD number: 0000-0001-5404-8091 (Feiruo Huang).

Abstract

The present study was conducted to evaluate the effects of dietary garcinol supplementation during late gestation (from the 90th day of pregnancy; day 90) and lactation on the acid–base balance of the umbilical cord blood and performance of sows and piglets. Sixty sows (Duroc × Yorkshire × Landrace; second- or third-parity; $n = 20$) were randomly divided into 3 gestation (day 90 of pregnancy) or lactation treatments, control diet (CON; basal diet), basal diet with 200 mg garcinol, and basal diet with 600 mg garcinol per kg of feed. The body weight (BW); backfat thickness and litter size of the sows; and birth weight, weaning weight, and mortality of piglets were recorded. Sows' blood and piglets' umbilical cord blood were collected for the measurements of hematological parameters and antioxidative and immune indexes, and acid–base balance parameters, respectively. The colostrum and milk and fecal samples of the sows were also collected for analysis of milk composition and apparent total tract nutrient digestibility. Garcinol had no effect on the BW and backfat thickness of the sows but significantly increased the birth weight and weaning weight of piglets ($P < 0.05$) and decreased the mortality ($P < 0.05$). Moreover, the white blood cell counts and neutrophil count, mean cell hemoglobin, superoxide dismutase (**SOD**), glutathione peroxidase (**GSH-Px**), and catalase (**CAT**) activity in the plasma of the sows were increased more significantly ($P < 0.05$) in the garcinol groups than that in the CON group, whereas the malondialdehyde (**MDA**) content was decreased ($P < 0.05$). The garcinol treatment significantly increased the pH, HCO_3^- and base excess values ($P < 0.05$), whereas it decreased the p_{CO2} and lactate content ($P < 0.05$) in the umbilical blood. Dry matter (**DM**), ash, and ether extract in the colostrum were similar between groups ($P > 0.05$), whereas the garcinol significantly increased the crude protein (CP) in the milk. In addition, the content of immunoglobulin A (**IgA**) and immunoglobulin G (**IgG**) in the plasma of piglets and in colostrum and milk of sows were increased more significantly ($P < 0.05$) in the garcinol groups than that in the CON group. The apparent total tract nutrient digestibility was similar between treatments. Collectively, this study indicates that sows fed with garcinol in late gestation and lactation showed improved maternal health and antioxidative status, milk protein content, acid–base balance in the umbilical cord blood, and growth performance in piglets, showing promise in natural plant extract nutrition for sows.

Key words: acid–base balance, garcinol, late gestation and lactation, newborn piglets, performance, sows

Introduction

Acidosis is a common phenomenon in all fetuses during delivery (Mexico, 2007). In the uterus, the fetus is easily exposed to risk factors which may result in disrupted oxygen flow in the umbilical cord, leading to fetal hypoxia and metabolic acidosis (Alonso-Spilsbury et al., 2005). These conditions and factors are proved to be crucial causes of intrapartum mortality and neonatal death, among which the degree of acidosis is considered to be the main factor and danger signal in determining the outcome of newborn (Gjerris et al., 2008).

Clinically, the rational management of acid–base metabolism is critical to the survival of critically ill patients (Fencl et al., 2000). Recently, increasing number of studies have raised concerns about the prognostic value of lactic acidemia in severe hypoxic neonates (Nordström et al., 2001; Wiberg et al., 2010). In human infants, metabolic acidosis is caused by excessive accumulation of metabolic acids (especially the lactate) during hypoxemia, and it was shown to cause serious complications in newborns (Low et al., 1994). However, in polytocous animals, like pigs, metabolic acidosis is different and interesting on account of the diversity and wild range of acid–base values from different newborn of the same litter at birth. Previous studies have indicated that viability of piglets was negatively correlated with the lactate content and positively correlated with the pH value in the blood (Herpin et al., 1996; Zanardo et al., 2015). In addition, lactic acid concentrations in the mother and fetus increased significantly with the duration of the second stage of labor, especially in the mother (Nordström et al., 2001).

There is limited number of researches on the relation between acid–base balance at birth and viability or performance of piglets. In addition, it is difficult to find an effective management to alleviate metabolic acidosis and facilitate acid–base balance. Although the timing of umbilical cord clamping has been used for this purpose in human delivery, this management is difficult to carry out in pigs (Friedlich and Seri, 2004). Remarkably, it has been widely believed that the pregnancy of sows is usually accompanied by the occurrence of oxidative stress, along with the aggravation of glycolysis and lactate accumulation (Père, 1995; Berchieri-Ronchi et al., 2011). Therefore, studies about alleviating oxidative stress and facilitating acid–base balance in pregnant sows can be relevant. Recently, numerous studies focus on improving the performance of sows and newborn piglets through dietary supplementation with antioxidative nutrients, such as resveratrol and oregano essential oils (Ariza-Nieto et al., 2011; Meng et al., 2018). As an excellent antioxidative plant extract, garcinol has been widely used in dietary supplementation of rodents (Yoshida et al., 2005; Lee et al., 2019). However, the effect of dietary supplementation with garcinol during late gestation and lactation on the performance of sows and newborn piglets, as well as on the acid-base balance in blood, has rarely been reported.

To date, blood samples from newborn piglets for acid–base balance analysis have ranged from carotid artery, cranial vein, umbilical artery to umbilical cord (mixed blood) (Randall, 1972; Linderkamp et al., 1981; Andren, 1982; Chiang and Rodway, 1997). But a previous study of umbilical blood in pigs indicated that there is a clear relation between acid–base balance values and the delivery progress (Van Dijk et al., 2006). Here, the aim of this study was to evaluate the effect of dietary supplementation with garcinol in late gestation and lactation on the acid–base balance in umbilical cord blood and the performance of sows and newborn piglets.

Material and Methods

Animals and Diets

This experiment was approved by the Animal Care and Use Committee of College of Animal Sciences and Technology, Huazhong Agricultural University, and was in compliance with the National Research Council's Guide for the Care and Use of Laboratory Animals. Sixty second- and third-parity sows (Duroc × Yorkshire × Landrace) were used in this study. The sows were randomly allotted to 3 dietary treatments: control diet (CON; n = 20), CON + 200 mg/kg garcinol (LOW; n = 20), and CON + 600 mg/kg garcinol (HIGH; n = 20) on day 90 of gestation until the end of lactation (day 21 postpartum). During gestation, sows were housed in individual gestation crates (0.58 × 2.1 m). Each crate was equipped with a stainless steel nipple for water and a concrete trough into which 2 kg of gestation diet was dropped daily (0800 h) from a timer-controlled automatic feeding system. Sow feed intake during the gestational treatment was restricted and adjusted so that daily protein intake and metabolizable energy are basically the same among the groups. From days 90 to 100 of gestation, sows in the CON, LOW, and HIFH groups received 2.4 kg of feed in 1 daily meal, whereas from day 101 until farrowing, they were fed 3.5 kg/d of feed. After gestation, sows received 1 kg of feed on day 1(after farrowing), 3 kg on day 2, 5 kg on day 3, 7 kg on day 4, and 9 kg on day 5 and were fed ad libitum as of day 6. Water was freely available to sows and piglets throughout the experimental period. All experimental diets were formulated according to National Research Council (2012) requirements (Table 1). Representative feed samples from experimental diets were taken regularly throughout the project for compositional analyses. The dry matter (DM) (method 930.15; AOAC International, 2005), crude protein (CP) (method 984.13; AOAC International, 2005), ether extract (EE) (method 920.39A; AOAC International, 2005), and ash (method 942.05; AOAC International, 2005) concentration were analyzed. During lactation, sows were provided with fresh feed 2 times (0800 and 1600 h) and any residual feed was weighed daily for feed intake record. The body weight and backfat thickness were measured at days 90 and 110 of gestation, and days 1, 7, 14, and 21 of lactation. On the day of farrowing, sows were moved to farrowing crates (2.4 × 2.4 m), and farm workers provided birth assistance during farrowing. Sows were inspected every 45 min during farrowing for the presence of newborn wet piglets or the presence of expelled placenta, as a standard procedure in the farrowing unit. In addition, farrowing sows were supervised once during the middle of the night. For piglets handling, after farrowing (within 24 h), litter size were recorded at birth (total and alive) and standardized (within dietary treatment group) to 10 ± 1 piglets. Then, the piglets were weighed after standardization and day 21 of lactation, the piglet mortality was also recorded at day 21 of lactation.

Blood Sample Collection and Analysis

Umbilical cord blood samples were collected according to previously described method (Dennis et al., 2014). Briefly, the blood samples were collected during apnea of breathing by clamping the umbilical cord both at the placental end and 7 cm from the piglets. About 1.5- to 2-mL blood from umbilical artery and vein of each fetus was collected and transferred into a heparinized blood vacutainer tubes for acid–base analysis, then kept on ice for 2 h before analysis. Umbilical artery and vein pH, p_{CO_2}%, HCO_3^-, and base excess were analyzed using an automatic

Table 1. Ingredient and chemical composition of the gestation and lactation diets

Item	Gestation[1]	Lactation[2]
Ingredient, %		
Corn	67.0	62.6
Soybean meal, dehulled	14.0	22.0
Wheat bran	15.4	6.0
Fish meal	0.6	4.0
Soybean oil	–	2.7
Dicalcium phosphate	1.2	1.0
Limestone	0.9	0.8
L-Lysine HCl (78%)	–	0.1
Salt	0.38	0.3
Premix[3]	0.52	0.5
Total	100	100
Calculated composition		
GE, MJ/kg	13.28	12.42
DM, %	88.6	89.2
CP, %	13.6	19.4
Ca, %	0.95	1.06
Total P, %	0.61	0.65
Analyzed composition		
DM, %	87.4	88.1
CP, %	12.4	18.9
Ash, %	5.3	4.9
EE, %	1.8	2.7

[1]Gestation, from days 90 to 110.
[2]Lactation, from delivery to day 21 postpartum.
[3]Premix supplied the following per kilogram of diet: Zn, 90.31 mg as Zn oxide; Mn, 18.01 mg as Mn sulfate; Fe, 53.96 mg as ferrous sulfate; Cu, 5.40 mg as Cu sulfate; Se, 0.30 mg as Na selenite; I, 2.20 mg as K iodate; niacin, 55.07 mg; pantothenic acid, 33.04 mg; vitamin A, 11,013 IU; vitamin D, 2,753 IU; vitamin E, 55 IU; riboflavin, 9.9 mg; vitamin K, 4.41 mg; vitamin B 12, 0.06 mg; choline, 495 mg; pyridoxine, 1.65 mg; folic acid, 1.65 mg; thiamine, 1.01 mg.

blood gas analyzer (GEM3500, Werfen, USA), and lactate in the blood was determined by using an automatic analyzer (YLS9-BIOSEN C line, Zhongxi Yuanda Technology, Beijing) Jugular venous blood of sows was sampled on days 90, 110, and 21 of lactation by jugular puncture for hematological parameters measurement. Piglet blood samples were collected at days 1, 7, and 14 of lactation via jugular venipuncture for immunoglobulin A (**IgA**) and immunoglobulin G (**IgG**) measurement. Blood was collected into heparin-treated tubes for hematological counts (CL-7200, Shimadzu, Japan), and then centrifuged at 3,500 × *g* for 10 min, the plasma was stored at –80 °C for further analysis.

Colostrum and Milk Collection and Analysis

Colostrum samples (approximately 20 mL) were collected from the second, third, and fourth pairs of sows teats within 3 h after farrowing. After giving 1 mL of oxytocin (1 U/mL) behind one ear to stimulate milk release, milk samples (approximately 10 mL) were also collected from the second, third, and fourth pairs of sows teats on day 17 of lactation. Piglets were separated from their dam for 45 min before oxytocin was injected. Milk and colostrum samples were collected and kept for measurement of DM (method 930.15; AOAC International, 2005), CP (method 984.13; AOAC International, 2005), and ether extract (method 920.39A; AOAC International, 2005) concentration. Ash of colostrum and milk were measured by oven-drying 5 g of samples at 105 °C for 16 h in crucibles and then placing them in a muffle furnace for 8 h at 550 °C, and reweighing them (Shen et al., 2011).

IgA, IgG, and Antioxidative Enzyme Measurement

Concentrations of IgA and IgG in colostrum, milk, and plasma were determined by ELISA using commercially available kits (Nanjing Jiancheng Bioengineering company, Jiangsu, China) following the manufacturer's procedures. Briefly, plates were coated with anti-swine IgG (4 μg/mL) or anti-swine IgA (10 μg/mL) and incubated them overnight at 4 °C. Plates were washed 4 times and blocked for 1 h. Diluted samples were added to the plates and incubated for 1 h before washing 4 times and adding the secondary antibody. The secondary antibody was incubated for 1 h in the dark; the plates were then washed 4 times and read on a microplate reader (Thermolab System, Multiskan FC, USA) at 540 nm.

The activities of antioxidative enzymes, including glutathione peroxidase (**GSH-Px**), catalase (**CAT**) and superoxide dismutase (**SOD**), and total antioxidant capacity (**T-AOC**) in plasma of sows were measured by using commercial kits (Nanjing Jiancheng Bioengineering company, Jiangsu, China) following the manufacturer's procedures and colorimetric methods with a spectrophotometer (Mepda instrument Co. Ltd, Shanghai, China). The content of the malondialdehyde (**MDA**) was measured by the thiobarbituric acid reaction, according to previous publication (Draper et al., 1993). All samples were assayed in 3 times under appropriate dilution conditions, to determine the enzyme activity within the linear range of the standard curve for pure enzymes.

Apparent Total Tract Nutrient Digestibility Measurement

The sows were fed diets with 0.25% chromic oxide to determine the apparent nutrient digestibility from days 4 to 10 of lactation, and fecal samples from each sow were collected for 12 h from 0800 to 2100 h on days 8, 9, and 10. Once collected, the fecal samples were mixed with HCl at a concentration of 10% to limit microbial growth and reduce the loss of ammonia. Then, the fecal samples were immediately stored at –20 °C. At the end of the collection period, fecal samples from each pig were pooled and dried in an oven at 65 °C for 72 h. After drying and grinding, subsamples were obtained from the total collected fecal samples for chemical analysis. The nutrient digestibility for DM, CP, ash, and ether extract were measured according AOAC (method 966.23; AOAC, 2005), using the following equation: 100 – [(the nutrient content of diet/the nutrient content of fecal) × (the content of chromium in fecal/the content of chromium in diet)] × 100.

Statistical Analysis

All the results from experiment were analyzed by using the one-way ANOVA, performed using the MIXED procedure of SAS (SAS Inst., Inc., Cary, NC). The sow or litter was the experimental unit. The results in the tables are shown with the means + SEM, and other figure results are presented with means + SE. Means are considered significantly different at $P < 0.05$.

Results

Effects of Dietary Garcinol on Performance of Sows and Newborn Piglets During Late Gestation and Lactation

The performance of sows and newborn piglets during late gestation and lactation is shown in Table 2. Dietary supplementation with garcinol had no effect on sows body

Table 2. Effects of dietary garcinol on performance of sows and newborn piglets during late gestation and lactation

Item	CON[1]	LOW[1]	HIGH[1]	SEM	*P*-value
Number of sows, *n*	20	20	20	–	–
Sow performance					
Parity	1.62	1.63	1.71	0.45	0.578
BW, kg					
Gestation					
Day 90	217.2	216.2	216.4	3.1	0.454
Day 110	230.2	228.7	230.2	4.9	0.573
Lactation					
Day 1	215.8	212.3	216.4	2.8	0.214
Day 7	208.1	207.2	208.8	7.2	0.689
Day 14	203.4	202.6	204.9	4.7	0.297
Day 21	198.6	197.1	200.3	3.6	0.882
Backfat, mm					
Gestation					
Day 90	13.9	13.6	13.3	0.5	0.213
Day 110	15.2	14.9	14.8	0.5	0.198
Lactation					
Day 1	13.8	13.6	13.0	0.6	0.214
Day 7	13.2	12.9	12.7	0.5	0.112
Day 14	12.6	12.2	11.9	0.6	0.101
Day 21	11.8	11.4	11.0	0.5	0.231
BW gain, kg					
Gestation (days 90 to 110)	13.0	12.5	13.8	6.4	0.521
Lactation (days 1 to 21)	−17.2	−15.2	−16.1	3.7	0.414
Backfat gain, mm					
Gestation (days 90 to 110)	1.33	1.28	1.47	0.54	0.098
Lactation (days 1 to 21)	−1.98	−2.18	−1.97	0.46	0.211
ADFI, kg	5.31	5.28	5.30	0.11	0.524
Litter performance					
Litter size at birth, total	11.6	12.0	12.4	0.2	0.178
Litter size at birth, live	10.2	11.3	11.9	0.3	0.562
Litter size at weaning	9.4	10.0	10.6	0.1	0.407
Litter birth wt, kg	16.2[a]	16.7[ab]	17.2[b]	0.6	0.041
Litter weaning wt, kg	56.9[a]	61.2[b]	64.1[b]	1.4	0.021
Litter gain, kg	40.7[a]	44.5[b]	46.9[b]	1.1	0.048
Pig BW at birth, kg	1.59	1.56	1.52	0.21	0.778
Pig BW at weaning, kg	6.05	6.12	6.04	0.15	0.662
Piglet mortality, %	8.7[a]	8.1[b]	7.4[b]	0.7	0.042

[1]Dietary treatment: CON = control diet; LOW = control diet with 200mg/kg garcinol; HIGH = control diet with 600mg/kg garcinol.
SEM = standard error of means; BW = body weight.

[a,b]Means with different superscripts in the same row differ ($P < 0.05$).

weight, backfat thickness, and average daily feed intake (ADFI) during gestation and lactation ($P > 0.05$). However, the litter weight of piglets at birth and at weaning showed a significant increase with the increase of dietary supplementation with garcinol ($P < 0.05$). The numbers of born alive piglets did not differ among treatments. Notably, the newborn piglets in the garcinol treatment significantly decreased mortality compared with the CON treatment ($P < 0.05$).

Effects of Dietary Garcinol on Hematological Parameters and Oxidative Stability of Sows During Late Gestation and Lactation

As shown in Table 3, dietary supplementation with garcinol had no effect on lymphocytes, monocytes, eosonophils, basophils, red blood cells, and hemoglobin on days 90, 110 of gestation and day 21 of lactation ($P > 0.05$). However, both low and high dietary supplementation with garcinol significantly decreased the white blood cell counts on day 110 of gestation, and neutrophil counts on day 21 of lactation compared with the CON treatment ($P < 0.05$). In addition, dietary garcinol significantly increased the mean cell hemoglobin on day 21 of lactation ($P < 0.05$). Furthermore, the antioxidative enzyme activities, T-AOC, and MDA content of sows during late gestation and lactation are shown in Table 4. SOD, GSH-Px, T-AOC, and CAT activity were significantly greater for sows, whereas the MDA content was decreased in the garcinol treatment on day 110 of gestation and day 21 of lactation compared with sows in the CON treatment ($P < 0.05$)

Effects of Dietary Garcinol on Acid–Base Balance Parameters and IgA and IgG Content of Piglets During Lactation

The pH, p_{CO2}, HCO_3^-, and base excess values in the umbilical venous and arterial blood at birth were used to evaluate the acid–base balance, and the results are shown in Table 5. Nearly all blood values (pH, p_{CO2}, HCO_3^-, and base excess) were

Table 3. Effects of dietary garcinol on hematological parameters of sows during late gestation and lactation

Item	CON[1]	LOW[1]	HIGH[1]	SEM	*P*-value
Number of sows, *n*	20	20	20	–	–
Day 90 of gestation					
White blood cells, 10^3cells/μL	11.7	11.6	11.2	0.2	0.378
Neutrophils, 10^3 cells/μL	6.14	5.77	5.01	0.44	0.525
Lymphocytes, 10^3 cells/μL	4.50	4.63	4.88	0.14	0.301
Monocytes, 10^3 cells/μL	0.33	0.28	0.27	0.12	0.555
Eosonophils, 10^3 cells/μL	1.07	0.82	0.79	0.04	0.486
Basophils, 10^3 cells/μL	0.03	0.01	0.0078	0.01	0.113
Red blood cells, 10^6 cells/μL	6.72	6.40	6.23	0.18	0.078
Hemoglobin, g/dL	15.9	14.7	13.8	0.62	0.504
Mean cell hemoglobin, pg	24.9	25.7	26.6	0.51	0.712
Day 110 of gestation					
White blood cells, 10^3cells/μL	11.3[a]	10.2[b]	9.4[b]	0.8	0.031
Neutrophils, 10^3 cells/μL	6.87	5.99	5.73	0.61	0.111
Lymphocytes, 10^3 cells/μL	4.21	3.98	3.74	0.18	0.247
Monocytes, 10^3 cells/μL	0.26	0.24	0.22	0.17	0.445
Eosonophils, 10^3 cells/μL	0.59	0.55	0.52	0.24	0.114
Basophils, 10^3 cells/μL	0.004	0.002	0.001	0.33	0.411
Red blood cells, 10^6 cells/μL	6.07	6.01	5.77	0.48	0.797
Hemoglobin, g/dL	15.4	14.3	13.6	0.51	0.177
Mean cell hemoglobin, pg	27.5	29.8	31.2	0.54	0.705
Day 21 of lactation					
White blood cells, 10^3cells/μL	10.9	10.4	10.2	0.54	0.624
Neutrophils, 10^3 cells/μL	6.15[a]	5.32[b]	4.73[b]	0.30	0.042
Lymphocytes, 10^3 cells/μL	3.82	4.15	4.33	0.47	0.062
Monocytes, 10^3 cells/μL	0.23	0.24	0.28	0.04	0.428
Eosonophils, 10^3 cells/μL	0.72	0.78	0.83	0.11	0.078
Basophils, 10^3 cells/μL	0.01	0.015	0.012	0.97	0.862
Red blood cells, 10^6 cells/μL	5.89	5.76	5.54	1.24	0.257
Hemoglobin, g/dL	16.9	17.8	18.9	1.42	0.748
Mean cell hemoglobin, pg	28.4[a]	31.2[b]	33.6[b]	0.77	0.042

[1]Dietary treatment: CON = control diet; LOW = control diet with 200mg/kg garcinol; HIGH = control diet with 600mg/kg garcinol.
SEM = standard error of means.

[a,b]Means with different superscripts in the same row differ ($P < 0.05$).

Table 4. Effects of dietary garcinol on plasma antioxidant index of sows during late gestation and lactation

Item	CON[1]	LOW[1]	HIGH[1]	SEM	*P*-value
Day 110 of gestation					
MDA, nmol/mL	2.42[a]	1.88[b]	1.62[b]	0.13	0.0012
T-AOC, U/mL	1.68[a]	1.72[b]	1.79[b]	0.44	0.026
SOD, U/mL	76.87[a]	82.48[ab]	87.31[b]	4.51	0.034
CAT, U/mL	18.82[a]	19.21[b]	21.64[b]	2.42	0.046
GSH- Px, U/mL	672.4[a]	698.5[b]	714.3[b]	31.8	0.033
Day 21 of lactation					
MDA, nmol/mL	2.21[a]	1.94[b]	1.72[b]	0.46	0.029
T-AOC, U/mL	1.13[a]	1.08[ab]	1.01[b]	0.33	0.025
SOD, U/mL	69.46[a]	73.08[b]	77.44[b]	2.74	0.014
CAT, U/mL	14.62[a]	15.87[b]	17.36[b]	4.33	0.049
GSH-Px, U/mL	560.1[a]	573.8[b]	591.9[b]	35.4	0.001

[1]Dietary treatment: CON = control diet; LOW = control diet with 200mg/kg garcinol; HIGH = control diet with 600mg/kg garcinol.
MDA = malondialdehyde; T-AOC = total antioxidant capacity; SOD = superoxide dismutase; CAT = catalase; GSH-Px = glutathione peroxidase; UA = umbilical artery; UV = umbilical vein.

[a,b]Means with different superscripts in the same row differ ($P < 0.05$).

significantly affected by the garcinol treatment. Dietary garcinol treatment significantly increased the pH, HCO_3^-, and base excess values ($P < 0.05$), whereas it decreased the p_{CO2} ($P < 0.05$) in the umbilical venous and arterial blood. Additionally, the results of lactate concentration in umbilical cord blood are shown in Figure 1. The lactate contents in both the low and high levels of dietary garcinol were significantly lower than those of the CON group in the umbilical venous and arterial blood. The results of IgA and IgG content of piglets during lactation are shown in Table 6. The IgA and IgG content in piglets with both low and

Table 5. Effects of dietary garcinol on acid–base balance parameters in the umbilical venous and arterial blood of newborn piglets

Item	Mean (SD)			P-value	Range (min–max)
	CON[1]	LOW[1]	HIGH[1]		
UA pH	7.25 (0.05)[a]	7.35 (0.26)[b]	7.58 (0.14)[b]	0.048	6.72–7.63
UA p_{CO2}%, mm Hg	67.2 (1.4)[a]	61.8 (2.3)[b]	58.3 (5.9)[b]	0.029	56.2–73.1
UA base excess, mEq·L^{-1}	−1 (4)[a]	2 (2)[b]	3 (2)[b]	0.012	(−21)–(16)
UA HCO_3^-, mmol/L	30 (6)[a]	35 (4)[b]	40 (5)[b]	0.018	12–42
UV pH	7.36 (0.13)[a]	7.41 (0.29)[b]	7.67 (0.08)[b]	0.023	6.84–7.76
UV p_{CO2}%, mm Hg	48.9 (4.2)[a]	45.4 (1.9)[ab]	37.1 (6.2)[b]	0.035	28.4–59.5
UV base excess, mEq·L^{-1}	2 (6)[a]	3 (1)[b]	3 (3)[b]	0.0144	(-18)-(9)
UV HCO_3^-, mmol/L	15 (4)[a]	21 (6)[ab]	29 (2)[b]	0.036	9–35

[1]Dietary treatment: CON = control diet; LOW = control diet with 200 mg/kg garcinol; HIGH = control diet with 600 mg/kg garcinol.
UA = Umbilical artery; UV = Umbilical vein.

[a,b]Means with different superscripts in the same row differ ($P < 0.05$).

high dietary garcinol treatment had an increased trend on day 7 of lactation ($P > 0.05$) and increased significantly on day 14 of lactation ($P < 0.05$), compared with those in CON treatment.

Effects of Dietary Garcinol on Colostrum and Milk Composition and Apparent Total Tract Nutrient Digestibility in Lactation Sows

The results of colostrum (day 1 of lactation) and milk (day 17 of lactation) composition and apparent total tract nutrient digestibility of lactation sows are shown in Tables 7 and 8. Dietary supplementation with garcinol had no effect on DM, CP, ash, and ether extract concentrations in the colostrum ($P > 0.05$). However, the dietary garcinol significantly increased the CP in comparison with the CON treatment in the milk. The IgA and IgG contents in both colostrum and milk in the garcinol treatment were significantly greater than those in the CON treatment ($P < 0.05$). Moreover, the apparent total tract nutrient digestibility were similar between treatments ($P > 0.05$).

Discussion

The aim of the present study was to evaluate the effect of dietary supplementation with garcinol in late gestation on the acid-base balance in the umbilical cord blood and performance of sows and newborn piglets. Supplementation with plant extracts (including oregano oil, glycitein, resveratrol, etc.) during late pregnancy and lactation is well-established to have a beneficial effect on the performance of the sows and piglets (Ariza-Nieto et al., 2011; Hu et al., 2015; Meng et al., 2018). Recently, more and more antioxidative additives are being used in the diets of pregnant sows, and this may be due to oxidative stress status occurring in late pregnancy (Berchieri-Ronchi et al., 2011). Previous studies have characterized pregnant animals with severe oxidative stress as showing placental production of reactive oxygen species, including superoxide and hydrogen peroxide (Al-Gubory et al., 2010). Moreover, plenty of studies indicated that oxidative stress directly induces the abnormal glycolysis and lactate accumulation. The accumulation of lactate may not only reduce growth performance of mater but also affect the development of offspring (Randall, 1971; Mexico, 2007). Garcinol is the main medicinal component of the dried fruit rind of *Garcinia indica* and is known to have effective antioxidant properties (Padhye et al., 2009). Additionally, as a natural inhibitor of histone acetyltransferase, the garcinol was shown to have the ability to affect the metabolism of glucose and lipids (Madhuri and Naik, 2017; Lee et al., 2019). Among all the research about the antioxidative additive of feed, this study is the first, to the best of our knowledge, to describe the effect of dietary supplementation with garcinol on sows and piglets. According to the dosage of garcinol in mice (100 and 500 mg/kg) (Lee et al., 2019), we choose the dosage of dietary supplementation with garcinol 200 and 600 mg/kg in pigs. Besides, according to the study in mice to evaluate the safety profile of garcinol, it is reported that garcinol did not show any adverse effects at a high single dose of 2000 mg/kg in an acute safety study of Wistar rats (Majeed et al., 2018). In addition, a 90-d repeated dose oral toxicity and reproductive/developmental toxicity study including a histopathological examination showed that there were no treatment-related changes in growth performance, feed intake, and hematological and biochemical variables induced by garcinol, all indicating that garcinol is not harmful, even at very high dosages (Majeed et al., 2018).

In many cases, acid–base disorders is often considered complicated by the mixed metabolic and respiratory origins of the disorder, whereas metabolic acidosis is predominantly due to increased lactate (Gjerris et al., 2008). The umbilical cord blood acid–base status and the level of lactate accumulation at birth, especially, are regarded as important for use in evaluating the risk of developing later motor and cognitive defects (Low et al., 1994; Van Dijk et al., 2006). In the present study, nearly all blood values were significantly affected by garcinol treatment. The pH, HCO_3^-, and base excess values were increased by garcinol. Consistent with our results in the umbilical cord blood lactate content, dietary garcinol significantly decreased the lactate concentration both in the umbilical artery and venous blood, which may be the reason of the increase of pH and reduction of acidosis after dietary supplementation with garcinol in the late gestation of sows. Therefore, these results indicated that dietary supplementation with garcinol improves the acid–base balance.

It is known that the acid–base balance may be an indicator of growth performance of the mother and the development of the offspring (Nordström et al., 2001). Further study was conducted to evaluate the effect of garcinol on the performance of sows and newborn piglets during gestation and lactation. The results showed that garcinol had no effect on the feed intake of sows, which was consistent with other research about effect of antioxidative additive on the feed intake of sows (Ariza-Nieto et al., 2011). Thus, the effects of the garcinol on lactating sows may be the improvement of the health and metabolism of sows.

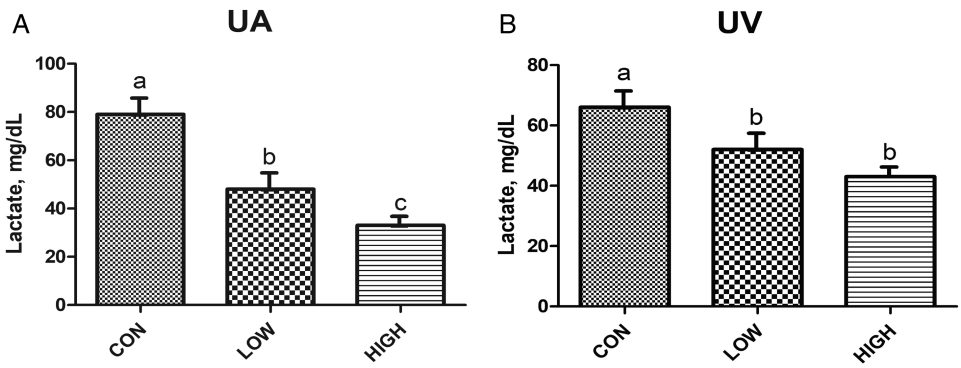

Figure 1. Effects of dietary garcinol on lactate concentration in umbilical cord blood of piglets. (A) Lactate concentration in umbilical arterial blood. (B) Lactate concentration in umbilical venous blood. UA = Umbilical artery; UV = Umbilical vein. CON = control diet; LOW = control diet with 200 mg/kg garcinol; HIGH = control diet with 600 mg/kg garcinol. Means with different superscripts in the same row differ ($P < 0.05$).

Table 6. Effects of dietary garcinol on plasma IgA and IgG content in piglets during lactation

Item	CON[1]	LOW[1]	HIGH[1]	SEM	*P*-value
Day 1 of lactation					
IgA, mg/mL	31.71	30.61	32.42	0.21	0.378
IgG, mg/mL	4.84	4.77	5.01	0.44	0.525
Day 7 of lactation					
IgA, mg/mL	42.32	45.28	44.27	0.12	0.555
IgG, mg/mL	7.47	7.82	7.79	0.04	0.486
Day 14 of lactation					
IgA, mg/mL	51.02[a]	57.40[b]	61.23[b]	0.18	0.038
IgG, mg/mL	9.12[a]	9.47[b]	9.85[b]	0.62	0.044

[1]Dietary treatment: CON = control diet; LOW = control diet with 200 mg/kg garcinol; HIGH = control diet with 600 mg/kg garcinol.
SEM = standard error of means; IgA = immunoglobulin A; IgG = immunoglobulin G.

[a,b]Means with different superscripts in the same row differ ($P < 0.05$).

This is supported by the reduced plasma neutrophils of sows that we observed in the garcinol treatment during lactation. Despite the similarity of growth performance (ADFI, BW gain, and backfat gain) of sows between CON and the different levels of garcinol groups, the litter weight of piglets at birth and at weaning showed a significant increase with the increase of dietary supplementation with garcinol. This may depend on the time length of supplementation with garcinol. In this study, the garcinol was supplemented not only during breeding periods, but from late gestation. It always takes time for nutrients to influence the performance of sows and piglets, especially the litter weight gain during late gestation and lactation (Shen et al., 2011). Moreover, it was observed that the white blood cells count and neutrophil count were affected on day 110 of gestation, which indicated that supplementation of this garcinol may need a conditioning time to affect the performance of sows. Moreover, the newborn piglet in the garcinol treatment tended to show decreased mortality compared with the CON treatment. The reason may be because the garcinol improved the acid–base status in the umbilical cord blood. It was demonstrated that the acid–base balance, as well as the lactate in the umbilical cord blood showed a clear relation with the progress of delivery and mortality of newborn (Herpin et al., 1996; Wiberg et al., 2008). In addition, the metabolic acidosis occurred during the gestation, which may directly lead to the perinatal asphyxia of piglets (Low et al., 1994). Our results showed that garcinol significantly decreased the lactate in the blood, and facilitated the acid–base balance, which is one possible reason for decreasing mortality and increasing litter weight of piglets at weaning.

Furthermore, we also tested the the blood cell composition of sow plasma during the gestation and lactation periods. The results in the present study showed that dietary garcinol supplementing decreased plasma white blood cells count and neutrophil count on day 110 of gestation and neutrophils on day 21 of lactation. It indicates that, on some level, the garcinol may function as an immune system regulator. This is consistent with some previous studies about the other functional nutritional additive and garcinol on the immune system of animals (Liao et al., 2004; Shen et al., 2011). The garcinol was shown to have an anti-inflammatory effect (Liu et al., 2015). As shown in a previous study, the tendency toward decreasing inflammatory challenge may be due to improved gut health; therefore, a reduced of neutrophils, which has been regarded as an inflammatory challenge, could also be the reason for the benefit of dietary garcinol supplementation on the health of sow and litter gain (Shen et al., 2011). As we know, because of dietary insufficiency and the resultant catabolic state during late pregnancy and lactation, the highly prolific sows always suffer systemic oxidative stress. In this period, due to the increase of nutrients requirement of offspring and mother, as well as the milk production, the rates of digestion, absorption, and metabolism of sows are excessively increased, along with the overproduction of free radicals which may cause the oxidative stress in sows (Al-Gubory et al., 2010). Despite the anti-inflammatory effect,

Table 7. Effects of dietary garcinol on colostrum and milk composition of sows during lactation

Item	CON [1]	LOW [1]	HIGH [1]	SEM	P-value
Number of sows, *n*	20	20	20	–	–
Colostrum, day 1 of lactation					
DM	22.6	23.7	24.5	0.92	0.105
Ash, % (DM basis)	14.6	15.7	16.6	0.88	0.226
CP, % (DM basis)	51.2	48.6	47.2	2.2	0.445
Ether extract, % (DM basis)	24.6	19.4	16.5	1.9	0.778
IgG, mg/mL	48.04[a]	51.65[b]	53.44[b]	0.21	0.045
IgA, mg/mL	8.82[a]	9.21[b]	9.37[b]	0.88	0.022
Milk, day 17 of lactation					
DM	18.9	17.5	16.5	0.35	0.441
Ash, % (DM basis)	9.62	8.87	7.52	0.41	0.126
CP, % (DM basis)	27.8[a]	29.2[b]	31.5[b]	0.28	0.041
Ether extract, % (DM basis)	45.6	42.6	38.7	1.4	0.114
IgG, mg/mL	51.88[a]	54.92[b]	55.41[b]	0.25	0.043
IgA, mg/mL	9.44[a]	9.68[b]	9.85[b]	0.94	0.033

[1]Dietary treatment: CON = control diet; LOW = control diet with 200 mg/kg garcinol; HIGH = control diet with 600 mg/kg garcinol.
SEM = standard error of means; DM = dry matter; CP = crude protein; IgA = immunoglobulin A; IgG = immunoglobulin G.
[a,b]Means with different superscripts in the same row differ ($P < 0.05$).

Table 8. Effects of dietary garcinol on apparent total tract nutrient digestibility in lactation sows

Item	CON[1]	LOW[1]	HIGH[1]	SEM	P-value
N	20	20	20	–	–
DM, %	75.6	73.7	74.2	0.33	0.355
Ash, %	78.2	77.6	78.4	5.2	0.778
CP, %	66.9	68.7	67.4	3.4	0.493
Ether extract, %	63.5	61.7	61.4	1.6	0.584

[1]Dietary treatment: CON = control diet; LOW = control diet with 200 mg/kg garcinol; HIGH = control diet with 600 mg/kg garcinol.
SEM = standard error of means; DM = dry matter; CP = crude protein.

according to the previous study, the garcinol mainly showed an antioxidative effect because of its free radical scavenging activity (Yamaguchi et al., 2000). However, little is known about whether the garcinol could have affected the oxidative status of the sows and litters. Our results showed supplementing sow diets with garcinol resulted in the improvement of antioxidative indices. These results provide the first version of data about the antioxidative effect of garcinol on sows.

This study also tested the concentrations of IgA and IgG in the plasma of piglets and in colostrum and milk of sows during lactation. The results of the present study showed that both IgA and IgG in piglets were increased in garcinol treatment groups, as well as in colostrum and milk of sows. IgA and IgG are widely believed to be predominantly involved in the immune response, whereas a previous study reported that the supplementation of garcinol in vivo supported the immune response (Sailhamer et al., 2008), and this may be the reason why IgA and IgG concentrations are different among the treatments. In addition, we also tested the apparent nutrient digestibility of sows after supplementation with of garcinol. No differences were found between the groups, a finding consistent with some other feed additive research, such as that on yeast culture and *Saccharomyces cerevisiae* fermentation products (Shen et al., 2011). Moreover, it was observed that dietary supplementation with garcinol had no effect on the the ash, DM, and ether extract contents of colostrum and milk. However, the crude protein content of milk in garcinol treatment was increased in early lactation. This result is consistent with the ideas of previous studies that the early lactation is the main period for synthesizing milk, and it absolutely depends on the body condition of the sows (Boyd et al., 1995). As far as we know, there is no study that provides the evidence that dietary garcinol supplementation improves the protein of the animals milk. However, a few studies support the idea that the oxidative status is related to the synthesis of the milk composition and N utilization (Castillo et al., 2005; Albera and Kankofer, 2009). In this case, a change in the oxidative status of the sows' bodies by garcinol may be one of the explanations of synthesizing of milk protein during early lactation. In addition, the increase of sows antioxidant status by dietary garcinol may be served as the reason that garcinol improves the the daily weight gain of piglets at weaning. Because the improved antioxidant status of the sows fed garcinol may be reflected in the milk, as the protein content in the milk was elevated, this may provided benefits to increase protein intake of piglets and enhance the growth performance of suckling piglets.

To sum up, the present study provides the first evidence that dietary supplementation with garcinol during late gestation and lactation improved the acid–base balance of sows and piglets, as shown in a reduced lactate concentration in umbilical cord blood and piglet mortality; improved maternal immune and oxidative status, as shown in the improvement of hematological parameters and antioxidant values in blood; and improved the milk quality as well as the piglets growth performance during lactation, as shown in the improvement crude protein of the milk and the litter weight gain at weaning. Together, these results indicate that garcinol may be a promising natural plant

extractive of nutrition for sows especially during late pregnancy and lactation.

Ethical Statement

The animal studies were approved by the Animal Care and Use Committee of College of Animal Sciences and Technology, Huazhong Agricultural University and performed in accordance with relevant regulations and guidelines.

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Literature Cited

Albera, E., and M. Kankofer. 2009. Antioxidants in colostrum and milk of sows and cows. *Reprod. Domest. Anim.* **44**:606–611. doi:10.1111/j.1439-0531.2007.01027.x

Al-Gubory, K. H., P. A. Fowler, and C. Garrel. 2010. The roles of cellular reactive oxygen species, oxidative stress and antioxidants in pregnancy outcomes. *Int. J. Biochem. Cell Biol.* **42**:1634–1650. doi:10.1016/j.biocel.2010.06.001

Alonso-Spilsbury, M., D. Mota-Rojas, D. Villanueva-García, J. Martínez-Burnes, H. Orozco, R. Ramírez-Necoechea, A. L. Mayagoitia, and M. E. Trujillo. 2005. Perinatal asphyxia pathophysiology in pig and human: a review. *Anim. Reprod. Sci.* **90**:1–30. doi:10.1016/j.anireprosci.2005.01.007.

Andren, B. 1982. Arterial acid-base measurements in 1–3 days old piglets [arterial blood]. *Acta Vet Scand.***23**(4):581–91.

AOAC International. 2005. *Official methods of analysis of AOAC International. Current through revision* 4. 18 th ed. AOAC Int., Gaithersburg, MD.

Ariza-Nieto, C., M. Bandrick, S. K. Baidoo, L. Anil, T. W. Molitor, and M. R. Hathaway. 2011. Effect of dietary supplementation of oregano essential oils to sows on colostrum and milk composition, growth pattern and immune status of suckling pigs. *J. Anim. Sci.* **89**:1079–1089. doi:10.2527/jas.2010-3514

Berchieri-Ronchi, C. B., S. W. Kim, Y. Zhao, C. R. Correa, K. J. Yeum, and A. L. Ferreira. 2011. Oxidative stress status of highly prolific sows during gestation and lactation. *Animal.* **5**:1774–1779. doi:10.1017/S1751731111000772

Boyd, D. R., R. S. Kensinger, R. J. Harrell, and D. E. Bauman. 1995. Nutrient uptake and endocrine regulation of milk synthesis by mammary tissue of lactating sows. *J. Anim Sci.* **73**:36–56. doi:10.2527/1995.73suppl_236x

Castillo, C., J. Hernandez, A. Bravo, M. Lopez-Alonso, V. Pereira, and J. L. Benedito. 2005. Oxidative status during late pregnancy and early lactation in dairy cows. *Vet. J.* **169**:286–292. doi:10.1016/j.tvjl.2004.02.001

Chiang, F. E., and R. G. Rodway. 1997. Determinations of umbilical cord beta-endorphin concentration and blood gas parameters in newborn piglets. *Res. Vet. Sci.* **63**:107–111. doi:10.1016/S0034-5288(97)90001-1

Dennis, R. L., K. A. McMunn, H. W. Cheng, J. N. Marchant-Forde, and D. C. Lay, Jr. 2014. Serotonin's role in piglet mortality and thriftiness. *J. Anim. Sci.* **92**:4888–4896. doi:10.2527/jas.2014-7835

Draper, H. H., E. J. Squires, H. Mahmoodi, J. Wu, S. Agarwal, and M. Hadley. 1993. A comparative evaluation of thiobarbituric acid methods for the determination of malondialdehyde in biological materials. *Free Radic. Biol. Med.* **15**:353–363. doi:10.1016/0891-5849(93)90035-s

Fencl, V., A. Jabor, A. Kazda, and J. Figge. 2000. Diagnosis of metabolic acid-base disturbances in critically ill patients. *Am. J. Respir. Crit. Care Med.* **162**:2246–2251. doi:10.1164/ajrccm.162.6.9904099

Friedlich, P. S., and I. Seri. 2004. Chapter 142 – regulation of acid-base balance in the fetus and neonate. In: Polin, R. A., W. W. Fox, and S. H. Abman, editors. In: Polin, R. A., W. W. Fox, and S. H. Abman, editors. *Fetal & Neonatal Physiol.* St. Louis, MO: Saunders. p. 1361–1364. doi:10.1016/B978-0-7216-9654-6.50145-4

Gjerris, A. C., J. Staer-Jensen, J. S. Jørgensen, T. Bergholt, and C. Nickelsen. 2008. Umbilical cord blood lactate: a valuable tool in the assessment of fetal metabolic acidosis. *Eur. J. Obstet. Gynecol. Reprod. Biol.* **139**:16–20. doi:10.1016/j.ejogrb.2007.10.004

Herpin, P., J. Le Dividich, J. C. Hulin, M. Fillaut, F. De Marco, and R. Bertin. 1996. Effects of the level of asphyxia during delivery on viability at birth and early postnatal vitality of newborn pigs. *J. Anim. Sci.* **74**:2067–2075. doi:10.2527/1996.7492067x

Hu, Y. J., K. G. Gao, C. T. Zheng, Z. J. Wu, X. F. Yang, L. Wang, X. Y. Ma, A. G. Zhou, and Z. J. Jiang. 2015. Effect of dietary supplementation with glycitein during late pregnancy and lactation on antioxidative indices and performance of primiparous sows. *J. Anim. Sci.* **93**:2246–2254. doi:10.2527/jas.2014-7767

Lee, P. S., C. Y. Teng, N. Kalyanam, C. T. Ho, and M. H. Pan. 2019. Garcinol reduces obesity in high-fat-diet-fed mice by modulating gut microbiota composition. *Mol. Nutr. Food Res.* **63**:e1800390. doi:10.1002/mnfr.201800390

Liao, C. H., S. Sang, Y. C. Liang, C. T. Ho, and J. K. Lin. 2004. Suppression of inducible nitric oxide synthase and cyclooxygenase-2 in downregulating nuclear factor-kappa B pathway by Garcinol. Published in cooperation with the University of Texas MD Anderson Cancer Center. *Mol. Carcinog.* **41**:140–149. doi:10.1002/mc.20050

Linderkamp, O., K. Betke, M. Güntner, G. H. Jap, K. P. Riegel, and K. Walser. 1981. Blood volume in newborn piglets: effects of time of natural cord rupture, intra-uterine growth retardation, asphyxia, and prostaglandin-induced prematurity. *Pediatr. Res.* **15**:53–57. doi:10.1203/00006450-198101000-00013

Liu, C., P. C. Ho, F. C. Wong, G. Sethi, L. Z. Wang, and B. C. Goh. 2015. Garcinol: Current status of its anti-oxidative, anti-inflammatory and anti-cancer effects. *Cancer Lett.* **362**:8–14. doi:10.1016/j.canlet.2015.03.019

Low, J. A., C. Panagiotopoulos, and E. J. Derrick. 1994. Newborn complications after intrapartum asphyxia with metabolic acidosis in the term fetus. *Am. J. Obstet. Gynecol.* **170**:1081–1087. doi:10.1016/s0002-9378(94)70101-6

Madhuri, K., and P. R. Naik. 2017. Modulatory effect of garcinol in streptozotocin-induced diabetic Wistar rats. *Arch. Physiol. Biochem.* **123**:322–329. doi:10.1080/13813455.2017.1336632

Majeed, M., S. Bani, B. Bhat, A. Pandey, L. Mundkur, and P. Neupane. 2018. Safety profile of 40% Garcinol from Garcinia indica in experimental rodents. *Toxicol. Rep.* **5**:750–758. doi:10.1016/j.toxrep.2018.06.009

Meng, Q., T. Guo, G. Li, S. Sun, S. He, B. Cheng, B. Shi, and A. Shan. 2018. Dietary resveratrol improves antioxidant status of sows and piglets and regulates antioxidant gene expression in placenta by Keap1-Nrf2 pathway and Sirt1. *J. Anim. Sci. Biotechno.* **9**:34. doi:CNKI:SUN:XMSW.0.2018-03-012

Mexico, N. S. Z. 2007. Importance of blood gas measurements in perinatal asphyxia and alternatives to restore the acid base balance status to improve the newborn performance. *Am. J. Biotechno. Biochem.* **3**:131–140. doi:10.3844/ajbbsp.2007.131.140

National Research Council. 2012. Nutrient requirements of swine: Washington, DC: The National Academies Press. doi:10.17226/13298

Nordström, L., S. Achanna, K. Naka, and S. Arulkumaran. 2001. Fetal and maternal lactate increase during active second stage of labour. BJOG: Int. J. Obstet. & Gy. **108**:263–268. doi:10.1016/s0306-5456(00)00034-6

Padhye, S., A. Ahmad, N. Oswal, and F. H. Sarkar. 2009. Emerging role of Garcinol, the antioxidant chalcone from Garcinia

indica choisy and its synthetic analogs. *J. Hematol. Oncol.* **2**:38. doi:10.1186/1756-8722-2-38

Père, M. C. 1995. Maternal and fetal blood levels of glucose, lactate, fructose, and insulin in the conscious pig. *J. Anim. Sci.* **73**:2994–2999. doi:10.2527/1995.73102994x

Randall, G. C. 1971. The relationship of arterial blood pH and pCO2 to the viability of the newborn piglet. *Can. J. Comp. Med.* **35**:141–146. doi:10.1038/365188a0

Randall, G. C. 1972. pH values and blood-gas tensions in the normal piglet during the first 48 hours of life. *Biol. Neonate* **20**:68–73. doi:10.1159/000240447

Sailhamer, E. A., Y. Li, E. J. Smith, F. Shuja, C. Shults, B. Liu, C. Soupir, M. deMoya, G. Velmahos, and H. B. Alam. 2008. Acetylation: a novel method for modulation of the immune response following trauma/hemorrhage and inflammatory second hit in animals and humans. *Surgery* **144**:204–216. doi:10.1016/j.surg.2008.03.034.

Shen, Y. B., J. A. Carroll, I. Yoon, R. D. Mateo, and S. W. Kim. 2011. Effects of supplementing *Saccharomyces cerevisiae* fermentation product in sow diets on performance of sows and nursing piglets. *J. Anim. Sci.* **89**:2462–2471. doi:10.2527/jas.2010-3642

Van Dijk, A. J., T. van der Lende, and M. A. Taverne. 2006. Acid-base balance of umbilical artery blood of liveborn piglets at birth and its relation with factors affecting delivery of individual piglets. *Theriogenology* **66**:1824–1833. doi:10.1016/j.theriogenology.2006.04.035

Wiberg, N., K. Källén, A. Herbst, A. Aberg, and P. Olofsson. 2008. Lactate concentration in umbilical cord blood is gestational age-dependent: a population-based study of 17 867 newborns. *Bjog.* **115**:704–709. doi:10.1111/j.1471-0528.2008.01707.x

Wiberg, N., K. Källén, A. Herbst, A. Aberg, and P. Olofsson. 2010. Lactate concentration in umbilical cord blood is gestational age-dependent: a population-based study of 17 867 newborns. *Bjog.* **115**:704–709. doi:10.1111/j.1471-0528.2008.01707.x

Yamaguchi, F., M. Saito, T. Ariga, Y. Yoshimura, and H. Nakazawa. 2000. Free radical scavenging activity and antiulcer activity of garcinol from Garcinia indica fruit rind. *J. Agric. Food Chem.* **48**:2320–2325. doi:10.1021/jf990908c

Yoshida, K., T. Tanaka, Y. Hirose, F. Yamaguchi, H. Kohno, M. Toida, A. Hara, S. Sugie, T. Shibata, and H. Mori. 2005. Dietary garcinol inhibits 4-nitroquinoline 1-oxide-induced tongue carcinogenesis in rats. *Cancer Lett.* **221**:29–39. doi:10.1016/j.canlet.2004.08.016

Zanardo, V., G. Mari, F. de Luca, G. Scambia, P. Guerrini, and G. Straface. 2015. Lactate in cord blood and its relation to fetal gluconeogenesis in at term deliveries. *Early Hum. Dev.* **91**:165–168. doi:10.1016/j.earlhumdev.2015.01.003