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Effects of silymarin supplementation during transition and lactation on reproductive performance, milk composition and haematological parameters in sows

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Abstract

Silymarin has been shown to be a multiple-functional plant extract having antioxidant, hepatoprotective, hypolipidemic, antihypertensive, antidiabetic and anti-obesity effects. In recent years, the galactagogue effects of silymarin in animals and humans have also been revealed. This research was conducted to test whether dietary inclusion of silymarin during transition and lactation could impact reproductive performance of sows and to explore the underlying mechanisms. From day 108 of gestation to weaning, sows were randomly assigned to receive dietary treatment of silymarin (40 g/day) or not and were designated as control group (CGP, $n = 55$) or treatment group (TGP, $n = 55$). The results showed that piglets' average daily gain and average weaning weight were higher in TGP than CGP sows. In comparison with the CGP sows, the TGP sows had higher serum concentrations of catalase (CAT) on day 18 of lactation and glutathione peroxidase (GSH-Px) on day 7 of lactation. The TGP sows had lower concentration of TNF-α on day 7 of lactation and significantly lower concentration of IL-1β on day 18 of lactation than CGP sows. There was significantly higher serum concentration of PRL on day 7 of lactation in sows consuming silymarin than sows from the CGP group. On day 18 of lactation, the protein and urea contents in milk were significantly increased while the serum urea concentration was significantly decreased in TGP sows. In summary, our results indicate that silymarin supplementation during transition and lactation can increase circulating concentrations of PRL transiently, reduce oxidative stress, increase feed intake and enhance protein metabolism, thereby significantly increasing milk yield of sows and subsequently improving growth performance of their offsprings.

KEYWORDS

cytokines, oxidative status, prolactin, silymarin, sow

XiaoJun Jiang and Sen Lin contributed equally to this work.

1 | INTRODUCTION

In recent decades, with advances in pig breeding techniques, litter size of sows has increased dramatically (Baxter et al., 2013). Large litter size (Milligan, Fraser, & Kramer, 2001) and insufficient colostrum intake (Decaluwe et al., 2014) have become important causes of pre-weaning death. Furthermore, additional supplementation of milk to suckling piglets was shown to significantly increase litter performance (Miller, Wiley, Chen, Bagnell, & Bartol, 2013). As a result, milk yield of the sow is the most critical factor determining piglets' growth performance (Harrell, Thomas, & Boyd, 1993). In spite of its short duration, the peripartum is a critical period for growth of mammary gland and production of colostrum (Theil, 2015).

Silymarin, an extract from milk thistle, includes several flavonolignans: silybin, silydianin, silychristin and isosilybin. The flavonolignans are bioflavonoid phytoestrogens. Recent studies have revealed the galactogogue effects of silymarin in lactating cows and women (Di Pierro, Callegari, Carotenuto, & Tapia, 2008; Serrao, Corsello, Romagnoli, D'Andrea, & Zecca, 2018; Zecca et al., 2016). One underlying mechanism is that silymarin can decrease insulin resistance (Sayin et al., 2016), which may increase feed intake in lactation. Another underlying mechanism may be correlated with its role in promoting PRL secretion (Capasso, 2014), which showed a dose-related response as the concentration of PRL doubled when silymarin supplemented increased from 25 to 200 mg/kg. Furthermore, silymarin can enhance mammary cell proliferation and up-regulate the expression of β-casein gene (Starvaggi Cucuzza et al., 2010). In gestating gilts, supplementation of 8 g/day silymarin starting from day 90 of gestation tended to increase the secretion of PRL on day 94 of gestation (Farmer, Lapointe, & Palin, 2014). However, in other two studies in sows, the serum concentrations of PRL were unaffected in response to dietary inclusion of silymarin, which was believed to be associated with inadequate inclusion of silymarin in diets (Farmer, Lapointe, & Cormier, 2017; Loisel, Quesnel, & Farmer, 2013). Only 23%–47% of oral silymarin can be finally absorbed, and its bioavailability is very low (Xie, Zhang, Zhang, & Yuan, 2019). Consequently, it is worth investigating whether increasing the dose of silymarin in diets leads to improved outcomes. Consequently, this study was aimed to investigate whether dietary inclusion of higher doses of silymarin has beneficial effects on PRL secretion, oxidative capacity, inflammatory responses, feed intake, milk yield and performance of sows and their litters.

2 | MATERIALS AND METHODS

2.1 | Animals and diets

A total of 110 Landrace × Yorkshire sows (parity 1–8, the numbers of sows from first to eighth parity were 10, 28, 34, 16, 10, 4, 2 and 6, respectively) with similar body condition (backfat thickness = 19.50 ± 0.36 mm) were used in this study. The Duroc boars were used for artificial insemination. From day 107 of gestation and throughout lactation, sows were individually housed in the farrowing pens (2.5 × 1.6 m) and were fed with commercial diets (Table S1). Each farrowing pen had a separate creep area at 32°C around farrowing for piglets. Within each parity, half of the sows were assigned to control group (CGP; $n = 55$) and the other half were assigned to treatment group (TGP; $n = 55$) to make sure that sows in two groups have the same background, and the sows in TGP received dietary supplementation of silymarin (40 g/day) from day 108 of gestation till weaning. Before the two daily meals, the TGP sows were firstly fed with a mixture of 1 kg basic diet and half the daily dose of silymarin while the CGP sows only received 1kg of basic diet. Silymarin (10.32% silybin, 15.64% silydianin plus silychristin and 6.91% isosilybin) is a standardized plant extract from milk thistle and was provided by Tianben Bio-Engineering Co., Ltd. The fatty acid composition and vitamin E content of silymarin were determined (Table S2). From day 108 of gestation till farrowing, sows were all daily fed 3.5 kg of feeds (twice daily, 0800 and 1430 hr) and received the same diets on the first 4 days of lactation (twice a day, 0800 and 1430 hr, 1.34 kg/day on the farrowing day, 2.10, 2.59, 3.13, 3.59 kg were fed from day 1 to 4 of lactation) and afterwards were fed ad libitum until weaning (thrice daily, 0800, 1430 and 2030 hr). Feed intake of each sow was recorded every day from day 108 of gestation till weaning. Within 24 hr post-farrowing, litter numbers were adjusted to 12 ± 1 by cross-fostering within each treatment. Piglets were not allowed to receive any dry feed so that they received nutrition solely from the milk. All sows had free access to water from gestation to lactation.

2.2 | Measurements

An ultrasonic device (Renco Corporation) was used to measure backfat thickness (P2) of sows at day 107 of gestation, parturition (an hour after farrowing) and day 20 of lactation. At parturition, farrowing duration (hour) of each sow was recorded. Following delivery, newborn piglets were recorded as stillborn or born alive as previously described (Mateo et al., 2007) and were weighed to record the number of pigs with low body weight (BW; <0.8 kg). They were also weighed individually at weaning day (day 20 of lactation).

The colostrum yield (CY) of sows (parity 2–4) was calculated by summing up the colostrum intake of all piglets within a litter. The colostrum intake for each piglet was estimated by using the equation below:

$$\text{Colostrum intake (g)} = -106 + 2.26 \times \text{WG}_{0-24\text{hr}} + 200 \times \text{BW}_{\text{B}} + 0.111 \times D - 1414 \times \text{WG}/D + 0.0182 \times \text{WG}/\text{BW}_{\text{B}}$$

where $\text{WG}_{0-24\ \text{hr}}$ is weight gain of piglet from birth till 24 hr following beginning of parturition (g), BW_{B} is birth weight (kg) and D is duration of colostrum suckling during the 24-hr period measured in minutes (Theil et al., 2014).

2.3 | Sample collection

At parturition (1 hr after onset of farrowing) and on day 7 and 18 of lactation before the morning feeding (between 0700 and 0900 hr), sows ($n = 10$, parity 2 to 4) were randomly selected to obtain blood samples through ear venipuncture. Serum samples were obtained by centrifuging blood at 3,000 *g* and 4°C for 15 min, and then stored at −80°C until analysis. Within an hour following farrowing, colostrum samples were obtained before suckling from three functional udders (anterior, middle and posterior) of the multiparous sows ($n = 10$, parity 2 to 4). Likewise, milk samples (20 ml) on day 18 of lactation were collected ($n = 10$) after 1.0 ml oxytocin injection (20 IU/ml; Hangzhou Animal Medicine Factory). Colostrum and milk samples were stored at −20°C until analysis.

2.4 | Chemical analysis

Automatic milk analyzer was used to analyse the composition of milk after double dilution (CombiFoss FT+, Foss, Denmark). The serum metabolites of sows (total bile acid, total cholesterol, triacylglycerol, urea, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and acute-phase protein) were determined using commercial kits (Sichuan Maker Biotechnology Inc.) and automatic biochemical analyzer (HITACH 3100, Japan). For each assay, the variation of intra assay and inter assay coefficients was less than 5%. The concentration of estradiol was determined using an radioimmunoassay kits (North Institute of Biotechnology Co., Ltd.). The variation coefficients for intra assay and inter assay for each assay were less than 10% and 15% respectively. Concentrations of PRL were determined using ELISA kits (Meimian industrial Co., Ltd.). There was less than 10% variation of intra assay and 12% variation of inter assay coefficients for each assay. Serum cytokines (IL-1β, TNFα, IL-6, IL-10) and antioxidant indices (CAT, catalase; GSH-Px, glutathione peroxidase; MDA, malondialdehyde; SOD, superoxide dismutase; T-AOC, total antioxidant capacity) were determined using commercial kits (Nanjing Jiancheng Bioengineering Institute). There was less than 10% variation of intra assay and 12% variation of inter assay coefficients for each assay. Parallel measurements were made for all colostrum, milk and serum sample.

2.5 | Statistical analysis

A randomized block design was used. The individual sow was used as the experimental unit for all response variables in the model, with diet (CGP or TGP) being the main effect. Parity (primiparous or multiparous) was used as a block for piglet and litter performance from day 108 of gestation to day 20 of lactation. Data (backfat thickness, reproductive performance of sows and performance of suckling piglets) were analysed using the MIXED procedure in SAS 9.4 (SAS Institute Inc.). The blood, colostrum, milk sample and CY were collected from multiparous sow with similar parity (parity 2 to 4). The data of colostrum intake, milk and colostrum composition and serum parameters were analysed by an independent-samples *t* test using SAS 9.4 (SAS Institute Inc.). Differences were considered as significant when $p < .05$, whereas $.05 < p < .10$ was considered a tendency.

3 | RESULTS

3.1 | Reproductive performance and litter growth

The backfat thickness of sows was similar in the two treatment groups at day 108 of gestation. The backfat thickness of sows at farrowing and weaning day (day 20 of lactation) was unaffected by silymarin supplementation (Table 1). The total number of piglets born, stillborn, born alive and the number of normal BW piglets (≥0.8 kg) were unaffected by silymarin supplementation. The mean litter weight and mean piglets' birth weight were not different between the two groups. The CY ($p < .05$) and average daily feed intake ($p < .01$) during lactation were higher in TGP sows than CGP sows. In addition, farrowing duration was shorter ($p < .05$) in TGP sows than CGP sows.

Piglets' performance during the 20-day lactation period is shown in Table 1. Litter size at weaning was similar in two groups. Notably, average piglet weight at weaning was higher ($p < .05$) in TGP than CGP. There were tendencies towards greater ($p < .10$) litter weights at weaning following silymarin treatment. No differences were found with regard to the number of weaning piglets per litter and the pre-weaning survival rate between treatments.

3.2 | Composition of colostrum and milk

As shown in Table 2, colostrum composition (dry matter, protein, fat and urea) was unaffected by silymarin ($p > .1$), but there was a tendency for the lactose to be increased ($p < .10$). The contents of protein and urea in milk on day 18 of lactation were significantly greater ($p < .05$) in TGP sows when compared with CGP sows. On day 18 of lactation, sows received the two dietary treatments had similar contents of dry matter, fat, lactose and protein, and fat and lactose.

3.3 | Serum oxidative status, cytokines, hormones and metabolites

Measurements reflecting oxidative status in serum are shown in Table 3. At parturition, day 7 and day 18 of lactation, the serum concentrations of MDA, SOD and T-AOC were unaffected by silymarin supplementation. Compared with the CGP sows, the TGP sows had higher serum concentrations of CAT on day 18 of lactation ($p < .05$) and GSH-Px on day 7 of lactation ($p < .01$). However, no differences were observed between two groups regarding serum concentrations of CAT or GSH-Px at other timepoints.

TABLE 1 Effects of silymarin supplementation during transition and lactation on performance of sows and suckling piglets

Items	CGP	TGP	*p*-value
Backfat thickness, mm			
Farrowing day	19.5 ± 0.5	19.5 ± 0.5	.99
Weaning day	16.2 ± 0.5	16.2 ± 0.5	.98
Litter size at birth, No/litter			
Total born	12.3 ± 0.4	12.6 ± 0.4	.57
Born alive	11.6 ± 0.4	11.9 ± 0.4	.51
Stillborn piglets	0.7 ± 0.1	0.6 ± 0.1	.77
Piglets ≥ 0.8 kg	11.4 ± 0.4	11.4 ± 0.4	.83
Litter size after cross-foster, No/litter	11.4 ± 0.1	11.4 ± 0.1	.62
Mean litter weight, kg	16.4 ± 0.9	15.9 ± 0.9	.23
Piglet mean BW, kg	1.5 ± 0.7	1.4 ± 0.7	.14
CY, g[1]	5,706 ± 243[a]	6,474 ± 257[b]	.04
Farrowing duration, hr	4.0 ± 0.2[a]	3.3 ± 0.2[b]	.04
ADFI during lactation, kg	4.6 ± 0.1[a]	5.0 ± 0.1[b]	<.01
Litter size at weaning, No/litter	10.9 ± 0.2	10.9 ± 0.2	.89
Pre-weaning survival[2], %	96.5 ± 0.01	96.1 ± 0.01	.69
Litter weight at weaning, kg	62.6 ± 5.6	65.9 ± 5.6	.06
Average piglet weight at weaning, kg	5.8 ± 0.4[a]	6.1 ± 0.4[b]	.03
Average piglet daily gain, g/day	216 ± 17[a]	234 ± 17[b]	.01

Note: Values are least squares means ± standard error, $n = 55$ for each group.

Abbreviations: ADFI, average daily feed intake; CGP, control group; CY, colostrum yield; TGP, treat group.

[a,b]Values within a row with different superscript letters differ ($p < .05$).

[1]The values are mean ± standard error, $n = 15$ (parity 2 to 4).

[2]Pre-weaning survival rate (%) = (number of piglets weaned/number of piglets after cross-foster) × 100.

TABLE 2 Effects of silymarin supplementation during transition and lactation on compositions of colostrum and milk from sows

Items	CGP	TGP	*p*-value
Colostrum			
Dry matter, %	28.7 ± 0.7	29.1 ± 2.2	.85
Fat, %	5.1 ± 0.2	4.5 ± 0.6	.34
Protein, %	18.2 ± 0.8	18.6 ± 1.5	.78
Lactose, %	2.5 ± 0.1	2.9 ± 0.2	.08
Urea, mg/dl	71.6 ± 2.4	74.9 ± 6.3	.63
Milk at day 18 of lactation			
Dry matter, %	19.0 ± 0.5	19.3 ± 0.4	.60
Fat, %	6.5 ± 0.4	6.6 ± 0.4	.91
Protein, %	5.2 ± 0.1[a]	5.7 ± 0.1[b]	.01
Lactose, %	5.8 ± 0.1	5.7 ± 0.1	.49
Urea, mg/dl	52.7 ± 1.2[a]	56.9 ± 1.1[b]	.046

Note: Values are mean ± standard error, $n = 10$.

Abbreviations: CGP, control group; TGP, treat group.

[a,b]Means within a row with different superscript letters differ ($p < .05$).

TABLE 3 Effects of silymarin supplementation during transition and lactation on serum oxidative indices of sows

Items	CGP	TGP	*p*-value
MDA, nmol/ml			
Parturition	11.0 ± 1.2	12.4 ± 0.8	.35
Day 7 of lactation	10.1 ± 1.3	10.9 ± 0.8	.65
Day 18 of lactation	10.4 ± 1.8	7.0 ± 1.4	.15
SOD, U/ml			
Parturition	94.6 ± 1.6	96.8 ± 1.6	.36
Day 7 of lactation	85.7 ± 1.8	88.6 ± 1.8	.28
Day 18 of lactation	85.6 ± 2.6	86.3 ± 1.9	.83
CAT, U/ml			
Parturition	4.9 ± 0.6	5.7 ± 0.5	.28
Day 7 of lactation	5.7 ± 0.6	7.7 ± 1.2	.16
Day 18 of lactation	4.2 ± 0.5[a]	6.1 ± 0.4[b]	.01
GSH-Px, U/ml			
Parturition	669 ± 56	689 ± 58	.80
Day 7 of lactation	610 ± 58[a]	839 ± 23[b]	<.01
Day 18 of lactation	879 ± 29	856 ± 25	.56
T-AOC, μmol/ ml			
Parturition	0.61 ± 0.02	0.63 ± 0.03	.54
Day 7 of lactation	0.62 ± 0.03	0.60 ± 0.01	.59
Day 18 of lactation	0.64 ± 0.01	0.62 ± 0.02	.44

Note: Values are mean ± standard error, $n = 10$.

Abbreviations: CAT, catalase; CGP, control group; GSH-Px, glutathione peroxidase; MDA, malondialdehyde; SOD, superoxide dismutase; T-AOC, total antioxidant capacity; TGP, treat group.

[a,b]Means within a row with different superscript letters differ ($p < .05$).

As shown in Table 4, lower serum concentrations of IL-1β ($p < .01$) on day 18 of lactation and TNF-α ($p < .05$) on day 7 of lactation were observed in TGP, whereas serum concentrations of IL-6 and IL-10 were similar in two groups. Circulating concentrations of hormones are shown in Table 4. There was a tendency for the serum concentration of E2 to be increased ($p < .10$) with silymarin supplementation on parturition. The concentration of PRL was significantly higher on day 7 ($p < .05$) in serum of TGP sows compared with that of CGP sows.

As shown in Table 5, Sows from the TGP had lesser serum TBA concentration ($p < .01$) on day 7 of lactation and UREA concentration ($p < .05$) on day 18 of lactation in comparison to sows from the CGP. However, on parturition, day 7 and day 18 of lactation, no differences were observed in two groups regarding serum concentrations of TC, TG, LDL-C, HDL-C and CRP.

TABLE 4 Effects of silymarin supplementation during transition and lactation on serum cytokines and hormones in sows

Items	CGP	TGP	*p*-value
IL-1β, ng/L			
Parturition	95.5 ± 19.4	101.4 ± 22.2	.84
Day 7 of lactation	79.6 ± 12.4	62.4 ± 10.7	.31
Day 18 of lactation	98.1 ± 17.2[a]	43.6 ± 7.7[b]	.01
IL-6, ng/L			
Parturition	888 ± 232	911 ± 168	.94
Day 7 of lactation	955 ± 238	769 ± 195	.55
Day 18 of lactation	1,128 ± 285	782 ± 198	.33
IL-10, ng/L			
Parturition	928 ± 150	983 ± 167	.81
Day 7 of lactation	859 ± 222	799 ± 141	.82
Day 18 of lactation	816 ± 205	720 ± 148	.71
TNF-α, ng/L			
Parturition	192 ± 40	178 ± 50	.84
Day 7 of lactation	324 ± 31[a]	155 ± 51[b]	.02
Day 18 of lactation	298 ± 80	232 ± 42	.47
E2, pg/ml			
Parturition	780 ± 142	1,189 ± 173	.09
Day 7 of lactation	6.1 ± 1.1	5.2 ± 0.6	.51
Day 18 of lactation	5.5 ± 0.4	6.0 ± 0.4	.44
PRL, ng/ml			
Parturition	44.9 ± 4.0	47.4 ± 4.7	.69
Day 7 of lactation	28.9 ± 1.7[a]	35.2 ± 2.4[b]	.04
Day 18 of lactation	27.5 ± 2.4	25.6 ± 2.2	.56

Note: Values are mean ± standard error, $n = 10$.

Abbreviations: CGP, control group; E2, 17β-estradiol; PRL, prolactin; TGP, treat group.

[a,b]Means within a row with different superscript letters differ ($p < .05$).

TABLE 5 Effects of silymarin supplementation during transition and lactation on serum metabolites in sows

Items	CGP	TGP	*p*-value
TC, m mol/L			
Parturition	1.7 ± 0.1	1.7 ± 0.1	.94
Day 7 of lactation	1.8 ± 0.1	1.7 ± 0.1	.63
Day 18 of lactation	2.5 ± 0.3	2.2 ± 0.2	.46
TG, m mol/L			
Parturition	0.40 ± 0.02	0.37 ± 0.01	.15
Day 7 of lactation	0.34 ± 0.03	0.32 ± 0.01	.38
Day 18 of lactation	0.35 ± 0.03	0.33 ± 0.01	.56
LDL-C, m mol/L			
Parturition	0.51 ± 0.02	0.55 ± 0.03	.32
Day 7 of lactation	0.52 ± 0.05	0.56 ± 0.04	.65
Day 18 of lactation	0.67 ± 0.07	0.66 ± 0.06	.90
HDL-C, m mol/L			
Parturition	0.31 ± 0.02	0.32 ± 0.02	.55
Day 7 of lactation	0.44 ± 0.05	0.39 ± 0.03	.39
Day 18 of lactation	0.63 ± 0.09	0.58 ± 0.05	.61
TBA, μ mol/L			
Parturition	49.0 ± 4.8	40.7 ± 4.5	.23
Day 7 of lactation	51.7 ± 6.2[a]	30.2 ± 2.1[b]	<.01
Day 18 of lactation	53.2 ± 6.5	44.9 ± 4.0	.29
CRP, mg/L			
Parturition	6.9 ± 0.3	7.8 ± 0.4	.12
Day 7 of lactation	6.2 ± 0.4	5.9 ± 0.3	.56
Day 18 of lactation	6.0 ± 0.4	7.3 ± 0.6	.64
UREA, m mol/L			
Parturition	4.5 ± 0.1	4.3 ± 0.2	.35
Day 7 of lactation	3.9 ± 0.2	3.6 ± 0.2	.24
Day 18 of lactation	4.7 ± 0.2[a]	4.1 ± 0.2[b]	.01

Note: Values are mean ± standard error, $n = 10$.

Abbreviations: CGP, control group; CRP, C-reactive protein.; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TBA, total bile acid; TC, total cholesterol; TG, triglyceride; TGP, treat group.

[a,b]Means within a row with different superscript letters differ ($p < .05$).

4 | DISCUSSION

In this study, consumption of silymarin could significantly increase piglets' average weaning weight and average daily gain. Sow' milk yield and composition are known as important factors influencing piglets' growth performance (Harrell et al., 1993). In line with our assumption, the colostrum yield was higher in TGP sows. In addition, increased milk protein content while decreased serum urea concentration was observed in sows from TGP. The urea in blood is the major end product of amino acid oxidation (Meijer, Lamers, & Chamuleau, 1990) and has been suggested to be a marker reflecting whole-body nitrogen utilization efficiency (Coma, Carrion, & Zimmerman, 1995). It appeared that sows consumed silymarin utilized more amino acids to synthesize milk protein. It was therefore inferred that the improved growth performance of piglets could be attributed to increased milk protein content, colostrum and milk production in sows from TGP.

Notably, milk secretion in sows can be affected by various factors such as mammary gland development, hormone level and oxidative status. Feed intake is also an important factor determining the milk yield of sows. However, insulin resistance frequently occurs during peripartum, which is also a sign of metabolic syndrome (Barbour et al., 2007). The feed intake of sows may unfortunately decrease owing to the excessive decrease in insulin sensitivity during late pregnancy and lactation (Pere & Etienne, 2007). Silymarin treatment has been shown to relieve insulin resistance and inflammation, and silybin is an effective component of silymarin that helps to improve metabolic syndrome (Sayin et al., 2016). Therefore, increased feed

intake in the treatment group may be related to improved insulin resistance of sows.

Mammary gland development is known to be one crucial basis ensuring the milk production of the sows (C. Farmer & Hurley, 2015), which is regulated by several hormones including prolactin (PRL) and 17β-estradiol (Hennighausen & Robinson, 2005). Interestingly, in the present study, the serum concentration of PRL was increased on day 7 of lactation and the serum concentration of estradiol tended to increase during delivery following silymarin supplementation. Herein, increased production of PRL and estradiol appeared to be responsible for enhanced milk secretion in sows consuming silymarin.

PRL is very important for the initiation and maintenance of milk production in sows throughout lactation (C Farmer, Robert, & Rushen, 1998). There are various factors that can alter secretion of PRL (C. Farmer, 2016). Increasing evidences suggest that a bidirectional communication exists between the immune and neuroendocrine systems (Goetzl, Adelman, & Sreedharan, 1990; Smith & Blalock, 1988), and their interactions are mediated by cytokines (Fontana, Frei, Bodmer, & Hofer, 1987). Several cytokines and growth factors affect pituitary hormone release, and some of them are expressed in the pituitary gland itself (Ray & Melmed, 1997). IL-1β has been shown to decrease PRL release in a dose-dependent fashion (Hishii, Ebato, Sato, Okumura, & Nitta, 1994), whereas TNF-α has been demonstrated to affect the release of pituitary hormones (Theas et al., 1998), which was supported by the discovery of its binding site in the anterior pituitary (Wolvers, Marquette, Berkenbosch, & Haour, 1993). Herein, the reduction of TNF-α and IL-Iβ in serum of sows fed with silymarin may be beneficial for PRL secretion.

On the other hand, silybin can bind to purified estrogen receptor (Seidlova-Wuttke, Becker, Christoffel, Jarry, & Wuttke, 2003). The liganded and un-liganded ERα can regulate the PRL receptor in a non-DNA dependent manner (Kavarthapu, Morris, & Dufau, 2014). In addition, estrogen can stimulate mitosis and secretion in PRL cells of rat anterior pituitary (Arroba, Frago, Argente, & Chowen, 2005). Estradiol can inhibit dopamine transmission acts at the hypothalamus-pituitary gland level, which stimulate PRL synthesis and secretion (Villegas-Gabutti, Pennacchio, Jahn, & Soaje, 2016). Therefore, the addition of silymarin may affect prolactin secretion through estrogen receptor or estrogen synthesis.

Oxidative stress is adverse to milk yield, health and litter performance (Kim, Weaver, Shen, & Zhao, 2013; Lipko-Przybylska & Kankofer, 2012). The gestation and lactation are always accompanied by increasing systemic oxidative stress (Berchieri-Ronchi et al., 2011). Silymarin is well known for its antioxidant effects (Bouderba, Sanchez-Martin, Villanueva, Detaille, & Koceir, 2014). Firstly, silymarin can prevent radical formation and scavenge free radical. Secondly, it can maintain optimal redox status of the cell by activating some non-enzymatic antioxidant and antioxidant enzymes via Nrf2 and NF-κB pathways. Finally, it can activate a range of vitagenes including heat shock proteins, thioredoxin and so on (Surai, 2015). It was previously reported that silymarin relieved oxidative stress by decreasing serum levels of MDA (Fallahzadeh et al., 2012). Herein, at each timepoint, the MDA level was not different between two groups. However, compared with that at parturition, the MDA level in TGP sows at day 18 of lactation decreased 43%, which could reflect the relieved oxidative stress following silymarin consumption, whereas high oxidative stress continued throughout lactation peroid in CGP sows. In the current study, the elevated concentrations of CAT on day 18 of lactation and GSH-Px on day 7 of lactation might reflect improved oxidative status in TGP sows and might thus contribute to promoted growth performance of their offsprings.

5 | CONCLUSIONS

In summary, our results indicate that silymarin supplementation during transition and lactation can increase circulating concentrations of PRL transiently, reduce oxidative stress and increase feed intake, and enhance protein metabolism, thereby significantly increasing milk yield of sows and subsequently improving growth performance of their offsprings.

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CONFLICT OF INTEREST

The authors declared no conflicts of interest in this study.

ANIMAL WELFARE STATEMENT

The study was conducted at Tianpeng Sow Farm, Zigong, China. The experiment followed the actual law of animal protection and was approved by the Animal Care and Use Committee of the Sichuan Agricultural University (Ethic Approval Code: SCAUAC201408-3), and followed the current laws of animal protection.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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