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Maternal supplementation of *Lonicera flos* and *Scutellaria Baicalensis* mixed extracts improve reproduction performance and metabolic health through modulating gut microbiota during pregnancy

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Abstract

Background This study aimed to evaluate the impacts of dietary supplementation with a combination of plant extracts on performance, metabolic health, and gut microbiota of sows. A total of 1003 crossbred pregnancy sows (DanBred Landrace × DanBred Yorkshire, mean parity 4.44 ± 1.84) were assigned to one of the two dietary treatments: a control group (CON, basal diet) and a *Lonicera flos* and *Scutellaria baicalensis* mixed extracts group (LSE, basal diet supplemented with 0.5 g/kg of mixed extracts).

Results Supplementation of LSE increased ($P < 0.05$) the numbers of total born, litter weight and average piglet weight on L21 d, average daily feed intake, and survival rate of piglets during lactation. Compared to CON, LSE group reduced ($P < 0.05$) interleukin-6 (IL-6) concentration in the feces and plasma on G109 d, while increased ($P < 0.05$) interleukin-10 (IL-10) concentration on G109 d and on L3 d. Supplementation of LSE had lower ($P < 0.05$) plasma reactive oxygen species levels on G30 d and on L3 d, and had a reducing tendency ($P = 0.07$) for thiobarbituric acid reactive substances concentrations and a trend toward increased ($P = 0.08$) value of homeostatic model assessment of insulin sensitivity of sow plasma on G109 d. In addition, supplementation of LSE increased ($P < 0.05$) the abundance of Firmicutes and Proteobacteria and decreased ($P < 0.05$) the abundance of Bacteroidetes and Spirochaetes on G109 d. The abundance of *Christensenellaceae_R_7_group*, *UCG_002*, *Clostridium_sensu_stricto_1*, *Escherichia_Shigella*, *un_f__Christensenellaceae*, *Bacteroides*, and *Terrisporobacter* were significantly increased ($P < 0.05$) in the LSE diet group. The abundance of *Christensenellaceae_R_7_group*, *UCG_002* and *un_f__Ruminococcaceae* were positively correlated with plasma IL-10 ($P < 0.01$), and negatively correlated with plasma IL-6 and TBARS levels.

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Conclusions This study demonstrates that dietary supplementation with Lonicera flos and Scutellaria baicalensis mixed extracts (LSE) at 0.5 g/kg during gestation significantly improves reproductive performance and metabolic health in sows, likely through modulating gut microbiota composition.The observed improvements in performance and health parameters coincide with microbiota-driven inflammation attenuation and redox balance restoration, suggesting a gut-immune axis regulatory role of LSE.

Keywords Plant extracts, Reproductive performance, Gut microbiota, Inflammation and stress indicators, Sow

Background

In modern intensive pig farms, sows are the foundation of the swine industry. The re productive efficiency of sows is closely related to the economic benefits of the farm [1]. Research has shown hormone secretion and immune response of maternal undergo significant changes during gestation, which may be related to alterations or disruptions in the intestinal flora [2, 3, 4]. These alterations can increase intestinal permeability and serum endotoxin levels, leading to the occurrence of metabolic disorders such as insulin resistance and systemic low-grade inflammation in sows [5, 6, 7]. Furthermore, under external environmental stress, the severity of metabolic disorders may be exacerbated [8]. A study report that when the outdoor temperature was 17 °C or higher, elevates reactive oxygen and upregulates pro-inflammatory cytokines, disruptins homeostasis and compromises reproductive performance [9]. In particular, excessive weight gain during the gestation period of sows can intensify the occurrence of periparturient metabolic syndrome, resulting in an increase in the number of weak piglets at birth, reduced feed intake during lactation, and poor lactation performance of sows [10, 11, 12].Therefore, regulating the composition of intestinal microflora of sows may be an effective strategy to alleviate the metabolic disorder syndrome of sows during pregnancy and improve the reproductive performance of sows and weaning weight of piglets.

In recent decades, researchers have been investigating a range of natural sources such as plant extracts, essential oils, and plant by-products to assess their potential positive effects on animal health and productivity [13, 14, 15]. Chinese herbal medicine, also known as Traditional Chinese Medicine (TCM), has a long history dating back thousands of years. Parham et al., and Shahrajabian and Sun, two research groups systematically summarized the role of traditional Chinese medicine, including clove, ginger, thyme, mint, anise, chamomile, lemon balm, mallow and garlic ect. in anti-microbial, anti-oxidant, anti-inflammation, enhance the immune system properties [16, 17]. And it is often used as dietary supplements to maintain good health in animals [18]. *Lonicerae Flos* (LF) is a traditional Chinese medicinal herb with the effects of clearing heat and detoxifying, and dispersing wind-heat [19]. Its extract is rich in chlorogenic acid, the content of chlorogenic acid should not be less than 1.5% in the Chinese Pharmacopeia. It has been reported that the main functions of chlorogenic acid include antibacterial, antiviral, anti-inflammatory, and antioxidant effects [8, 20]. *Scutellaria baicalensis Georgi* (SBG), a widely utilized Chinese herbal medicine, exhibits pharmacological actions including heat-clearing and dampness-resolving, fire-purging and detoxifying, as well as hemorrhage-arresting with fetal-stabilizing effects [21]. *Scutellaria baicalensis Georgi* has also been extensively studied for anti-inflammatory, antioxidant and digestive supporting properties, potentially reducing stress and improving health under pig rearing conditions [22, 23]. Baicalin is the most abundant component of SBG extracts, which also has antibacterial, anti-inflammatory, and antioxidant effects [24, 25, 26]. Recent studies have shown that chlorogenic acid has the effect of inhibiting weight gain and promoting lipid metabolism in a high-fat diet-induced obese mouse model [27]. In addition, chlorogenic acid can improve insulin sensitivity [28]. Furthermore, studies have shown that chlorogenic acid can regulate the composition of intestinal microbiota and improve obesity in a high-fat diet-induced obese mouse model [29]. Similar reports have been made about the research on baicalin, which can improve insulin sensitivity caused by obesity [30]. In addition, Traditional Chinese formulations (e.g., Shuanghuanglian oral liquid) combine LF and SBG for enhanced antimicrobial/antiviral effects [31]. Experimental studies in respiratory infections and inflammatory diseases support their synergistic efficacy [32]. In summary, LF targets gut microbiota dysbiosis and lipid metabolism, while SBG inhibits oxidative stress and inflammatory pathways. Together, they may amplify benefits through a "gut-microbiota-inflammation-metabolism" axis.

Although it has been reported that *LF* enhanced immunity and reduced diarrhea in piglets [33]. Extract of LF and SBG improved intestinal barrier function, alleviated oxidative stress, and promoted growth in broiler chickens [34]. However, the effects on reproductive performance and health of sows are still unknown. Therefore, the aim of this study was to investigate the effects of the supplementation of LF and SBG mixed extracts (LSE) in sows from gestation to lactation on reproduction performance, perinatal metabolic disorder syndrome, insulin sensitivity, and gut microbiota. This study will reveal the mechanisms by which LSE alleviate perinatal metabolic syndrome in sows, and provide technical solutions

Table 1 Sow culling data were recorded during gestation

Item	CON	LSE
Initial breeding	501	502
Pregnancy elimination statistics		
Return to estrus	55	59
Diseases	32	45
Death	3	0
Abortion	6	6
Parturition	405	392

CON, control diet; LSE, LF and SBG mixed extracts diet

Table 2 Composition and nutrient levels of the basal diets (air-dry basis)

Item	Gestation	Lactation
Ingredients, %		
Corn,7.8% CP	10.00	13.00
Soybean meal,46% CP	5.50	13.70
Soybean oil		3.30
Barley	5.00	
Wheat bran	19.00	
Wheat	27.00	27.00
Wheat flour		15.00
brown rice	18.30	
broken rice		15.00
Fish meal		2.50
Rice bran meal	7.00	2.50
Beet pulp	4.00	
Saccharose		3.00
Calcium Phosphate	1.20	1.20
Limestone	1.10	1.30
Nacl	0.40	0.40
Sodium bicarbonate	0.25	0.25
Vitamin premix	0.50	0.50
Mineral premix	0.15	0.15
L-Lysine sulfate,70%	0.20	0.60
L-Threonine	0.05	0.15
Methionine		0.15
Other	0.35	0.30
Nutrient levels		
DE, MJ/Kg	12.14	14.22
CP,%	13.10	16.60
SID-Lysine	0.55	1.00
SID-Methionine	0.19	0.38
SID-Methionine + Cystine	0.37	0.67
SID-Threonine	0.38	0.64
SID-Tryptophan	0.13	0.18
SID-Valine	0.54	0.72
Ca,%	0.82	0.90
P,%	0.72	0.68

[1]Provided per kg of complete diet: vitamin A 12000I U; vitamin D3 2250IU; vitamin E 100 mg; vitamin K3 3.0 mg; vitamin B1 3.0 mg; vitamin B2 10.0 mg; vitamin B6 5.0 mg; vitamin B12 0.04 mg; nicotinamide 45 mg; pantothenic acid 30 mg; folic acid 4.5 mg; biotin 0.75 mg; vitamin C 100 mg; choline 1200 mg

[1]Provided per kg of complete diet: Cu 12 mg; Fe 90 mg; Zn 75 mg; Mn 60 mg; I 0.90 mg; Se 0.30 mg; Co 0.45 mg; Cr 0.20 mg

for the implementation of antibiotic-free Chinese herbal additives in sow production.

Methods

Animals and management

The animal study was reviewed and approved by the Animal Care and Use Committee of Huazhong Agricultural University.

The present experiment was conducted at the Wuli Town pig farm, Xin Yang of Tecon Biology Co.Ltd. The experiment started on May 1, 2022 and ended on December 31, 2022. A total of 1,000 breeding crossbreed sows (DanBred Landrace × DanBred Yorkshire, mean parity 4.44 ± 1.84) were stratified according to parity and backfat thickness and allocated to one of the two dietary treatments: control group ($n = 501$), and treatment group ($n = 502$). All sows were individually housed in stalls (2.2 m length × 0.65 m width × 0.6 m height). As previously reported, sows were fed different amounts of gestation diet at different stages of gestation [10]. On d 109 of gestation, sows were moved to the farrowing rooms with stalls in pens. Sow culling data were recorded during gestation (Table 1).

Dietary treatments and experimental design

After artificial insemination, sows were assigned randomly to 2 treatments; Control, CON (basal diet), and LSE group (basal diet supplemented with 0.5 g/kg of LF and SBG mixed extracts with a 1:1 ratio). Prior studies in rodents and livestock demonstrated that chlorogenic acid (LF) and baicalin (SBG) at doses of 0.2–1.0 g/kg diet improved metabolic health, gut function, and inflammation [33, 34]. Consequently, a supplementation dose of 0.5 g/kg of LF and SBG mixed extracts was selected for this study. The LSE products were provided by Beijing Centre Biology Co., Ltd., (Beijing, China). The concentrationis of chlorogenic acid and baicalin shown in Figure S1.

All experimental diets were formulated to meet or exceed the NRC (2012) recommendations for gestating and lactating (Table 2). The gestation diet was provided at 2.6 kg/d, 2.2 kg/d, 2.8 kg/d from d 0 to d 30, from d 31 to d 90, and from d 91 to d 109, respectively. During gestation, sows were housed individually in gestation stalls (2.2 × 0.7 × 1.1 m) with concrete floors. Sows were moved to the farrowing rooms on day 110 of gestation after sows were washed and then housed individually (2.4 × 2.2 m) in fully slatted farrowing crates. Sows were fed 2.0 kg/d from day 110 to the day before parturition. After farrowing, sows were fed 1.0 kg of diet on the first day postpartum, which was increased by 1 kg/d in the following 7 days, and then sows had free access to feed until weaning. The farrowing room temperature was maintained at

approximately 20 ℃ to 22 ℃. Water was freely available to sows and piglets throughout the experimental period.

Recording and sampling

Data about sow performance and reproductive parameters were recorded during gestation and lactation, respectively. These include total born piglets, live born piglets, birth weight, number of stillbirths, count of mummified fetuses, number weaned, weaning weight, and return to estrous interval. The sows' backfat (BF) thickness were recorded on d 0 (G0 d), 30 (G30 d), 60 (G60 d), 90 (G90 d), and 109 (G109 d) of gestation, and at weaning. The BF thickness was measured using the P2 position (approximately 6.5 cm away from dorsal midline at the last rib curve) of the sows by ultrasonography using a Sono-Grader II (Renco Corporation, Minneapolis, MN) [11]. Individual feed intake of sows was recorded daily, from which the total feed intake and average daily feed intake (ADFI) for each sow was calculated of gestation and lactation.

The reproductive performance data were recorded, including the number of total born, born alive, healthy piglets (birth weight ≥ 0.8 kg), intrauterine growth retardation (birth weight < 0.8 kg), born dead (stillborn, mummified, crushed, and abnormal), litter birth weight, and individual birth weight. In addition, the number of each group were cross-fostered within 48 h postpartum, number weaned, weaning weight, and weaning to estrous interval (WEI) were recorded. The weaning survival rate and WEI rate within 7 days was calculated.

A subset of 40 sows were randomly selected from each group and sampled for blood using ear venipuncture method on G30 d, G109 d of gestation, and on day 3 (L3 d) of lactation. Next, blood samples were collected in 15 mL centrifuge tube, and centrifuged at at 3,500 rpm for 10 min. The plasma was harvested from all blood samples and stored at − 80 °C until analysis. Meanwhile, fresh fecal samples from sows corresponding to blood samples about 5 g were collected, and then stored at − 80 °C immediately until analysis.

Chemical analysis

Plasma interleukin-6 (IL-6), interleukin-10 (IL-10), fecal sample IL-6, IL-10, and Lipocalin-2 (LCN2) concentrations were determined with commercial ELISA kits (Bio-Camio Co. Ltd., Nanjing, China) according to instructions of their respective manufacturers, respectively. The oxidative and antioxidative parameters, including reactive oxygen species (ROS), thiobarbituric acid reactive substances (TBARS), and total superoxide dismutase (SOD) were measured with specific assay kits (Nanjing Jiancheng Bioengineering Institute, Nanjing, China). Plasma glucose was determined with a glucose dehydrogenase activity colorimetric assay kit (BioVision Inc., CA, United States).

Microbial analysis

Bacterial genomic DNA was extracted from frozen sow fecal samples with an E.Z.N.A. TM Stool DNA kit (Omega Bio-Tek, Norcross, GA, USA). Sequencing and data analysis were subsequently performed on an Illumina MiSeq PE300 platform platform (Illumina, San Diego, USA) according to the standard protocols by Majorbio Bio-Pharm Technology Co. Ltd. (Shanghai, China), as previously described in Cheng et al. [5]. Then the high-quality sequences were de-noised using DADA2 plugin in the Qiime2 platform (version 2020.2) pipeline with recommended parameters, which obtains single nucleotide resolution based on error profiles within samples. DADA2 denoised sequences are usually called amplicon sequence variants (ASVs). The alpha diversity and beta diversity were calculated for comparison of taxonomic data. The observed species, Chao 1 index, and Shannon index were used to determine differences in alpha diversity according to different diets. Unifrac weighted distance matrices were calculated, and analysis of similarities (Anosim) was used to access differences among the microbial communities. All analyses from clustering to alpha and beta diversity were performed in QIIME (V1.7.0) and displayed in R software (V2.15.3).

Statistical analysis

Data were analyzed using the GLM procedure of SAS (version 9.4; SAS Institute Inc., Cary, NC). The individual sow was as an experiment unit. We used the EVenn online tool to visualize the ASVs that overlapped between different treatments at the same time points. Differential taxa were identified by Wilcoxon non-parametric tests and corrected *P*-values using the Benjamini-Hochberg method. Correlations between reproductive performance or biochemical indicators and the relative abundance of genus from 16 S data were tested with the Spearman rank. Spearman's rank correlation coefficients were calculated using the cor.test function and visualized with a heatmap constructed by the R package pheatmap. Data are displayed as means ± SD. Significant difference was declared at $P < 0.05$, while $0.05 \le P < 0.1$ was declared a tendency.

Results

Sows and piglets performance

As shown in Table 3, the numbers of total born, white stillbirth, litter weight and average piglets' weight on L21 d, average daily feed intake during lactation, and survival rate of piglets was improved ($P < 0.05$) in LSE group compared with CON group. In Table 3, litter size after cross-fostering was increased ($P = 0.04$) in LSE group. However,

Table 3 Effects of dietary supplementation with LF and SBG mixed extracts on litter performance of sows

Item	CON	LSE	*P*-value
Number of sows, n	405	392	
Average parity of sows	1.59 ± 0.68	1.76 ± 0.82	0.56
Litter size, n			
Total born	16.55 ± 4.55	17.36 ± 4.03	< 0.01
Born alive	15.16 ± 4.02	15.46 ± 3.42	0.15
healthy piglets	13.98 ± 3.72	14.15 ± 3.04	0.26
IUGR	1.18 ± 1.68	1.27 ± 2.00	0.45
White stillbirth	1.04 ± 1.53	1.50 ± 1.53	< 0.01
Black stillbirth	0.16 ± 0.52	0.20 ± 0.57	0.63
Mummies	0.17 ± 0.77	0.17 ± 0.49	0.46
After cross-foster	13.91 ± 1.30	13.30 ± 1.17	< 0.01
21 d of lactation	12.86 ± 1.42	12.96 ± 0.81	0.22
Litter weight, kg			
Born alive	19.26 ± 4.91	19.63 ± 3.82	0.37
After cross-fostering	17.94 ± 3.67	17.31 ± 3.58	0.26
21 d of lactation	64.07 ± 13.71	66.80 ± 12.70	0.04
Average pig weight, kg			
Born alive	1.30 ± 0.21	1.28 ± 0.22	0.68
After cross-fostering	1.30 ± 0.18	1.30 ± 0.19	0.72
21 d of lactation	4.99 ± 0.97	5.15 ± 0.90	0.04
Average daily feed intake during lactation, kg/d	5.75 ± 0.44	5.98 ± 0.54	0.04
Survival rate of piglets, %	92.46	97.44	0.03
WEI, d	7.18 ± 7.41	6.93 ± 5.37	0.42
Mating rate at weaning 7d, %	86.53	82.02	0.14

CON, control diet; LSE, LF and SBG mixed extracts diet; IUGR, intrauterine growth retardation; WEI, weaning to estrous interval

the numbers of born alive, healthy piglets, IUGR, black stillbirth, mummies, litter weight at birth, average pig weight at birth, WEI, and mating rate on d 7 after weaning were not different between the CON and LSE group.

Intestinal permeability and inflammatory response in sows

Figure 1 showed a systematic evaluation of biomarker related to gut permeability, endotoxin in feces and plasma samples on G30 d, G109 d, and L3 d. There were also no differences in the feces and plasma concentrations of endotoxin ($P > 0.05$) between the CON group and LSE groups at different time of pregnancy and lactation of sows. Next, we examined biomarkers associated with inflammation including IL-6, IL-10, LCN-2 in feces and plasma samples (Fig. 2). Compared to CON, IL-6 concentration in the feces and plasma were significantly lower ($P < 0.05$) on G109 d in LSE group. In addition, plasma IL-10 concentration was higher ($P < 0.05$) on G109 d, and L3 d in LSE group than in CON group. No differences were found in IL-10 and LCN-2 levels in feces ($P > 0.05$).

Antioxidant indexes of plasma of sows

The oxidative stress parameters of sows are displayed in Fig. 3. Compared to CON, plasma ROS levels exhibited a reduction ($P < 0.05$) on G109 d and L3 d in LSE group. The TBARS concentrations of sow plasma on G109 d showed a reducing tendency ($P = 0.07$) in LSE group. No differences were found in SOD levels in plasma ($P > 0.05$).

Insulin homeostasis

Despite no difference ($P > 0.05$) in plasma concentrations of glucose, insulin, and HOMR-IR during starvation on G30 d, G109 d, and L3 d between the two groups (Fig. 4), while the LSE group sows had a trend toward increased ($P = 0.08$) value of HOMA-IS on G109 d.

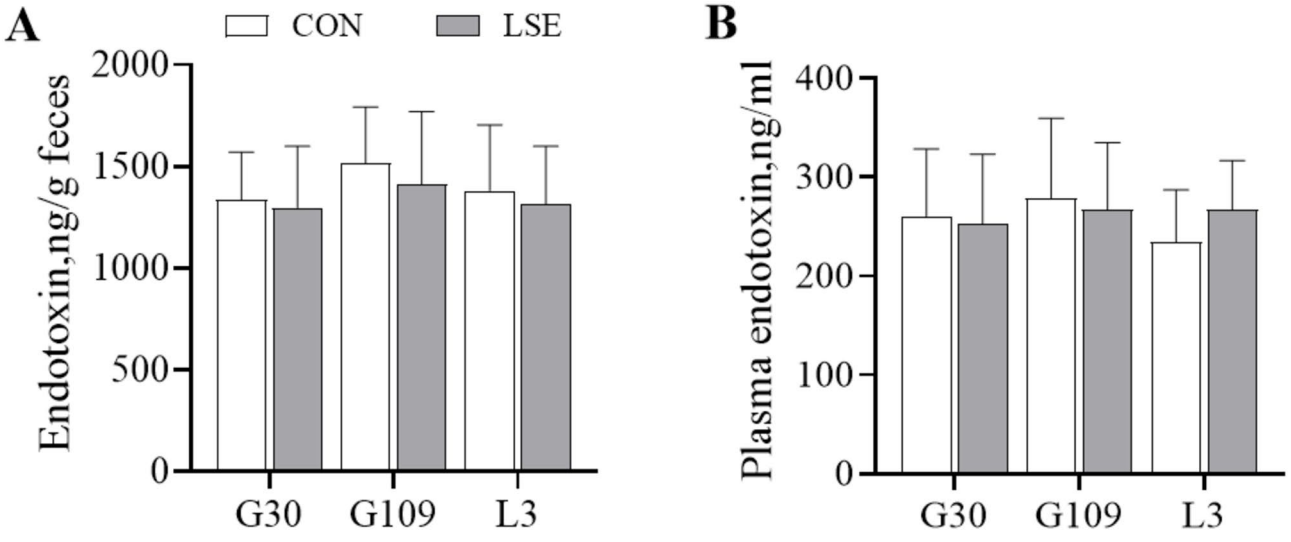

Fig. 1 Effects of *Lonicera flos* and *Scutellaria baicalensis* mixed extracts on intestinal permeability of sow. (**A**) fecal endotoxin; (**B**) plasma endotoxin. CON, control group; LSE, basal diet supplemented with 0.5 g/kg of LF and SBG mixed extracts; G30 d, d 30 of gestation; G109 d, d 109 of gestation; L3 d, d 3 of lactation. Data were means ± SD ($n = 20$)

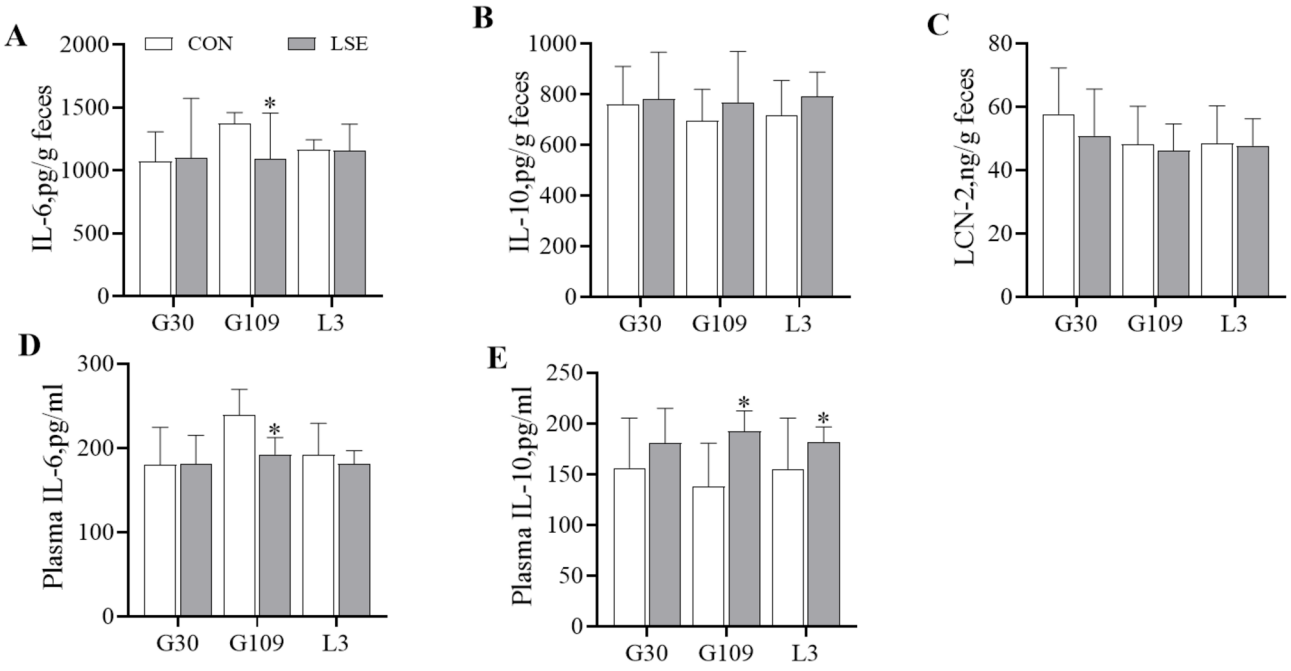

Fig. 2 Effects of *Lonicera flos* and *Scutellaria baicalensis* mixed extracts on fecal and plasma inflammatory cytokines of sows. (**A**-**C**) plasma inflammatory cytokines on G30 d, G109 d, and L3 d. (**D**-**E**) fecal inflammatory cytokines on G30 d, G109 d, and L3 d. IL-6, interleukin-6; IL-10, interleukin-10; LCN2, Lipocalin-2. CON, control group; LSE, basal diet supplemented with 0.5 g/kg of LF and SBG mixed extracts; G30 d, d 30 of gestation; G109 d, d 109 of gestation; L3 d, d 3 of lactation. Data were means ± SD ($n = 20$). *mean a significant difference ($P < 0.05$)

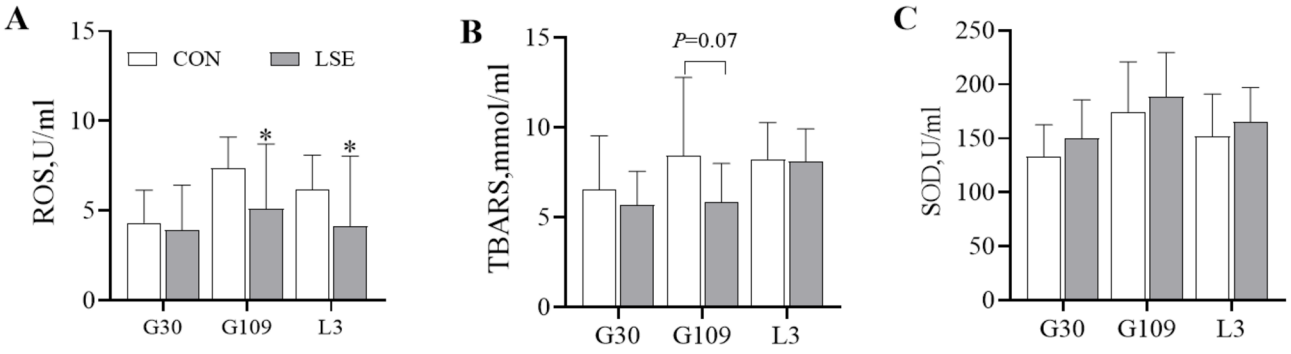

Fig. 3 Effects of *Lonicera flos* and *Scutellaria baicalensis* mixed extracts on plasma antioxidative capacity of sows. (**A**) reactive oxygen species (ROS), (**B**) thiobarbituric acid reactive substances (TBARS), (**C**) superoxide dismutase (SOD) activities on G30 d, G109 d, and L3 d in plasma of sows, respectively. CON, control group; LSE, basal diet supplemented with 0.5 g/kg of LF and SBG mixed extracts; G30 d, d 30 of gestation; G109 d, d 109 of gestation; L3 d, d 3 of lactation. Data were means ± SD ($n = 20$). *mean a significant difference ($P < 0.05$)

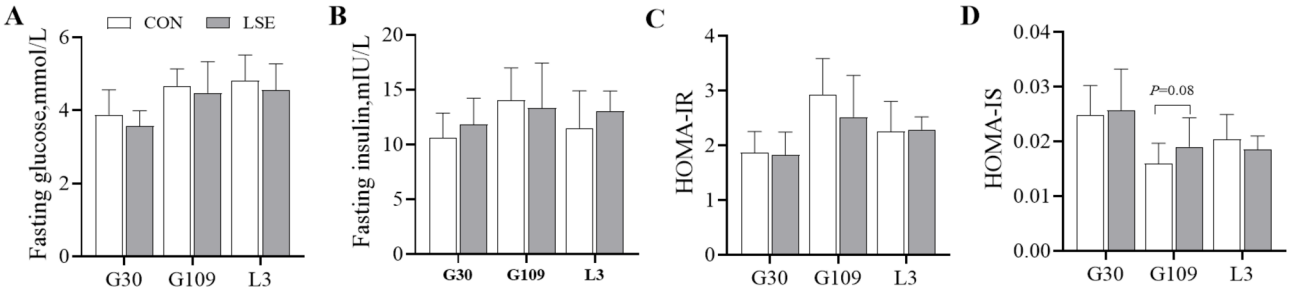

Fig. 4 Effects of *Lonicera flos* and *Scutellaria baicalensis* mixed extracts on plasma insulin homeostasis of sows. (**A**) plasma glucose, (**B**) plasma insulin (**C**) homeostasis model assessment of insulin resistance (HOMR-IR), (**D**) homeostatic model assessment of insulin sensitivity (HOMA-IS) on G30 d, G109 d, and L3 d in plasma of sows, respectively. CON, control group; LSE, basal diet supplemented with 0.5 g/kg of LF and SBG mixed extracts; G30 d, d 30 of gestation; G109 d, d 109 of gestation; L3 d, d 3 of lactation. Data were means ± SD ($n = 20$)

Fecal microbiota

To understand the effects of LSE on gut microbiota, 16 S rRNA gene sequencing of fecal samples were performed. The Venn diagram showed that there were 7311, 7880 ASVs obtained from CON and LSE group, of which 2037 were common ASVs on G30 d (Fig. 5A). There were 9943, 4514 ASVs obtained from CON and LSE group, of which 1418 were common ASVs on G109 d (Fig. 5B). On L3 d, there were 6399, 6419 ASVs obtained from CON and LSE group, of which 1547 were common ASVs (Fig. 5C). To assess fecal microbial alpha diversity, Sobs, Shannon, Chao 1, and Pielou index were calculated. LSE diet tended to increase Sobs, Shannon, Chao 1 index on d 30 of gestation (Fig. 5D). The Sobs, Shannon, Chao 1, and Pielou index were significantly decreased on G109 d (Fig. 5E), while increased on L3 d in the LSE group (Fig. 5F). Principal coordinate analysis (PCoA) exhibited a clear separation of the microbial community between two treatments on G30 d, G109 d and L3 d (Fig. 5G-I). At the phylum level, Firmicutes and Bacteroidetes were the dominant phyla at three time points, accounting for more than 90%, followed by Proteobacteria and Spirochaetes (Fig. 6A). The LSE diet groups increased the ratios of Firmicutes/Bacteroidetes on G109 d (Fig. 6B). The abundance of Firmicutes and Proteobacteria were significantly increased, while Bacteroidetes and Spirochaetes abundance were significantly decreased in the LSE group on G109 d (Fig. 6C). The relative abundances of microbiota of the top 15 differential genera were presented in Fig. 7. Sows fed LSE had greater *norank_f__Eubacterium_coprostanoligenes_group*, *NK4A214_group*, *Monoglobus*, *un_f__Erysipelotrichaceae*, *un_f__Anaerovoracaceae*, *un_f__Eggerthellaceae*, and un_f__Eggerthellaceae than CON group on G30 d.

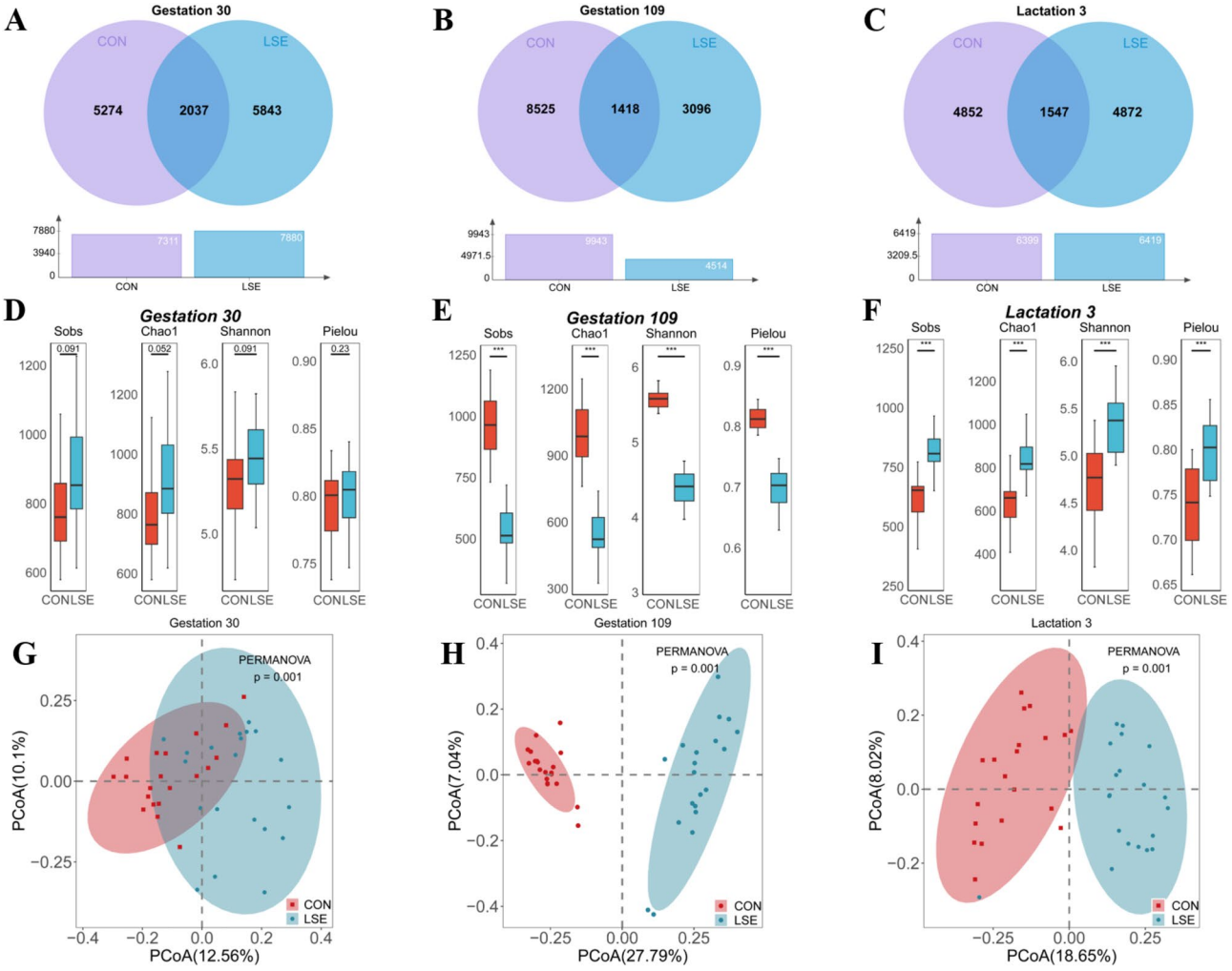

Fig. 5 Effects of *Lonicera flos* and *Scutellaria baicalensis* mixed extracts on fecal microbial composition and diversity of sows. (**A**-**C**) the amplicon sequence variants (ASVs) in sow feces on G30 d, G109 d, and L3 d, respectively. (**D**-**F**) α-diversity analysis based on indices of Sobs, Chao1, Shannon, and Pielou on G30 d, G109 d, and L3 d, respectively. (**G**-**I**) β-diversity based on principal coordinate analysis of the gut microbiota of sows on G30 d, G109 d, and L3 d, respectively. Data were means ± SD ($n = 20$). ***mean a significant difference ($P < 0.001$)

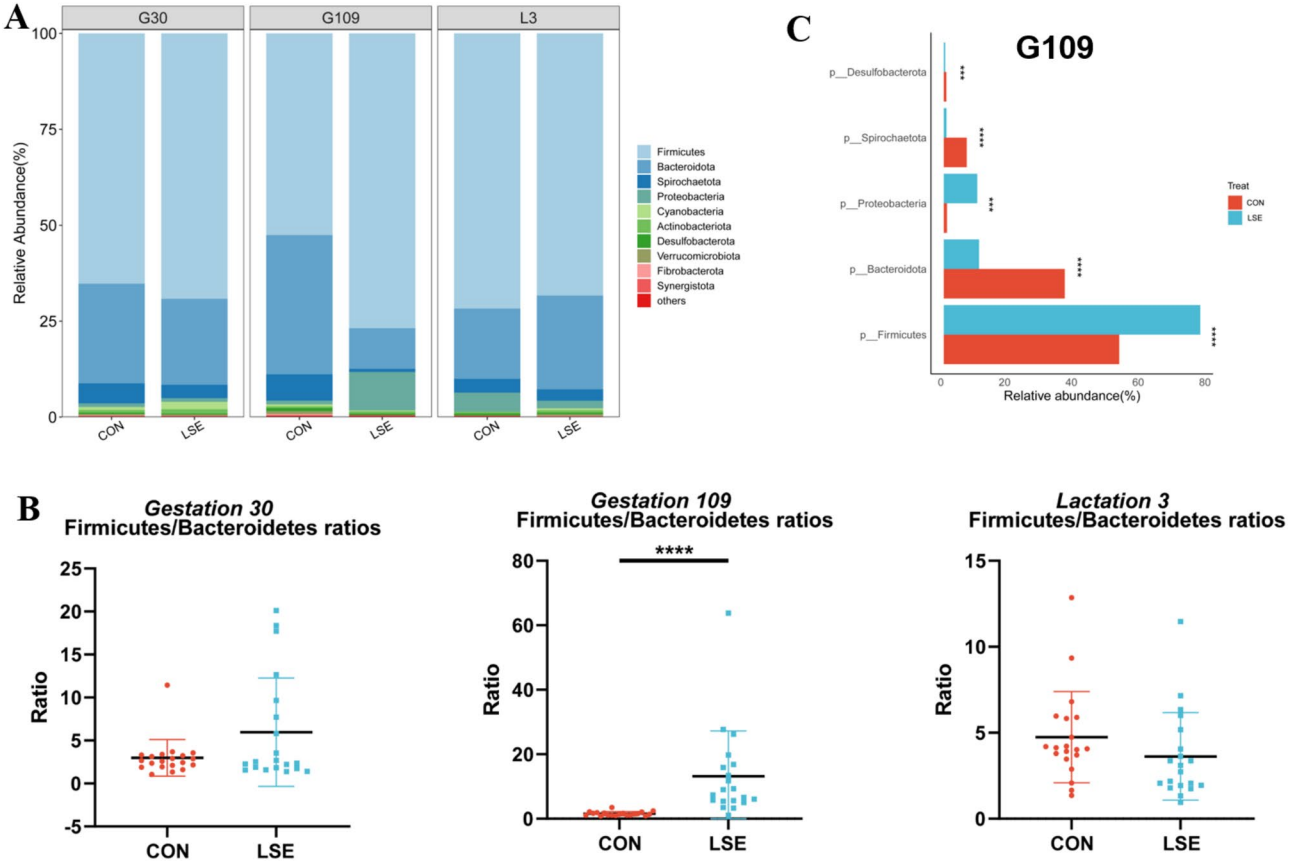

Fig. 6 Effects of *Lonicera flos* and *Scutellaria baicalensis* mixed extracts on phylum level of fecal microbiota of sows. (**A**) fecal microbial community bar plot at the genus level on G30 d, G109 d, and L3 d. (**B**) Firmicutes/Bacteroidetes ratios on G30 d, G109 d, and L3 d. (**C**) the main fecal microbial phylum level on G109 d. Data were means ± SD ($n = 20$). *mean a significant difference ($P < 0.05$), **mean a significant difference ($P < 0.01$), ****mean a significant difference ($P < 0.0001$)

On G110 d, *Christensenellaceae_R_7_group*, *UCG_002*, *Clostridium_sensu_stricto_1*, *Escherichia_Shigella*, *un_f__Christensenellaceae*, *Bacteroides*, and *Terrisporobacter* were significantly increased in the LSE diet group. On L3, sows fed LSE had greater greater abundance *norank_f__Eubacterium_coprostanoligenes_group*, *norank_f__Muribaculaceae*, *UCG_005*, *Lachnospiraceae_XPB1014_group*, *Lachnospiraceae_XPB1014_group*, *norank_f__norank_o__Clostridia_UCG_014*, *Lachnospiraceae_AC2044_group*, *Oscillospira*, *Phascolarctobacterium.*

Relationship between diet, microbiota, sow reproduction performance, and plasma and fecal parameters

A Spearman correlation analysis was performed to investigate the relationships between dietary, the microbiota in feces of sows, sow reproduction performance, and plasma and fecal parameters (Fig. 8). The *Turicibacter*, *Family_XIII_AD3011_group*, *UBA1819*, *Escherichia_Shigella*, and *Bacteroides* were positively correlated with average daily feed intake during lactation (Fig. 8A). The *Christensenellaceae_R_7_group*, *un_f__Eggerthellaceae*, and *un_f__Christensenellaceae* were positively correlated with litter weight and average pig weight on L21 d. Subsequently, the genus microbiota that were positively correlated with sow reproduction performance were further correlated with plasma and fecal parameters (Fig. 8B). The *un_f__Ruminococcaceae* was positively correlated with plasma IL-10 ($P < 0.01$), but negatively correlated with plasma fasting glucose ($P < 0.01$). The *Candidatus_Soleaferrea* was positively correlated with plasma IL-10 ($P < 0.01$), but negatively correlated with plasma TBARS ($P < 0.05$). The *un_f__Peptococcaceae* was positively correlated with plasma IL-10 ($P < 0.01$) and T-SOD ($P < 0.05$), and negatively correlated with fecal IL-6 levels($P < 0.05$). The *UCG_002* was positively correlated with plasma IL-10 ($P < 0.01$) and HOMA-IR ($P < 0.05$), but negatively correlated with plasma and fecal IL-6 levels ($P < 0.05$). Additionally, the *Christensenellaceae_R_7_group* was positively correlated with HOMA-IR ($P < 0.01$) and plasma IL-10 ($P < 0.05$), and negatively correlated with plasma IL-6($P < 0.01$) and TBARS ($P < 0.01$), and fecal IL-6 levels ($P < 0.05$). The *un_f__Eggerthellaceae* was negatively correlated with Plasma IL-6 ($P < 0.01$) and TBARS

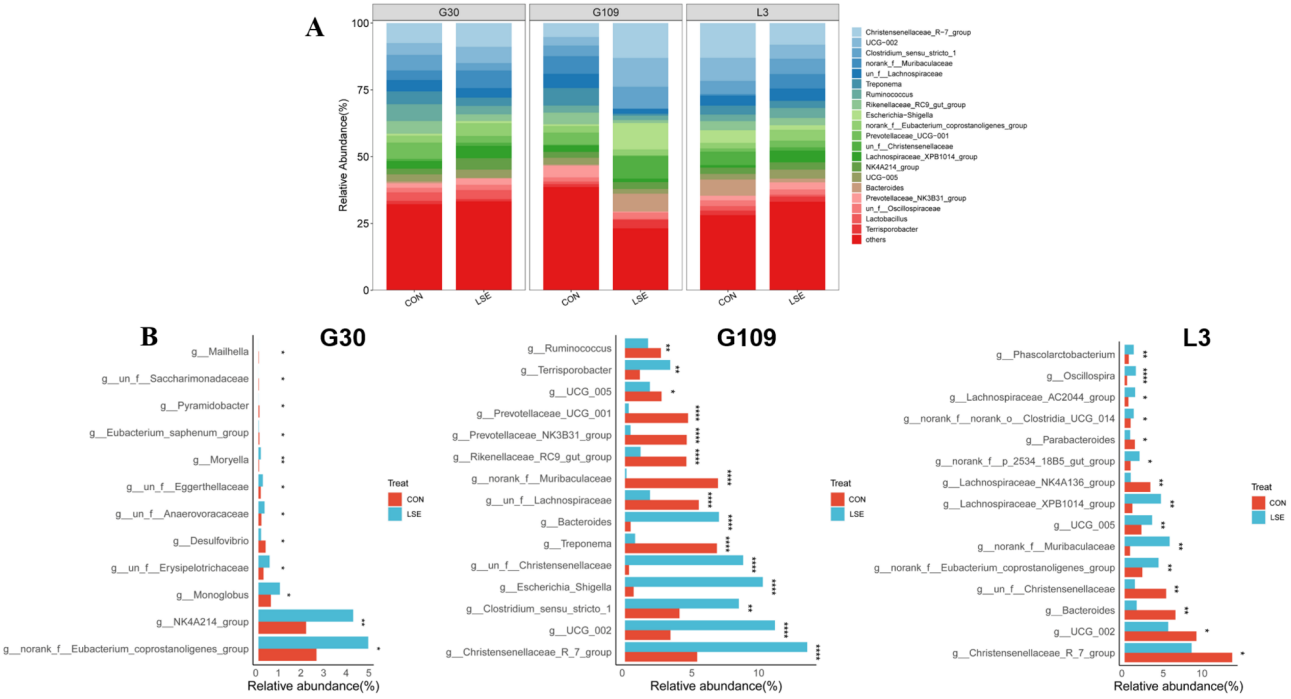

Fig. 7 Effects of *Lonicera flos* and *Scutellaria baicalensis* mixed extracts on genus level of fecal microbiota of sows. (**A**) fecal microbial community bar plot at the phylum level on G30 d, G109 d, and L3 d. (**B**) the top 15 differential genera on G30 d, G109 d, and L3 d. Data were means ± SD ($n = 20$). ***mean a significant difference ($P < 0.001$). ****mean a significant difference ($P < 0.0001$)

($P < 0.05$). Furthermore, the relative abundances of *un_f__Ruminococcaceae*, *Candidatus_Soleaferrea*, *un_f__Peptococcaceae*, *UCG_002*, *Christensenellaceae_R_7_group*, and *un_f__Eggerthellaceae* were significantly increased ($P < 0.01$) in the LSE diet group on G109 d (Fig. 8C).

Discussion

The gestation period is critical for sows' reproductive performance, directly impacting fetal development and subsequent lactation efficiency [35–36]. Physiological adjustments and environmental stressors during pregnancy often lead to progressive oxidative stress in sows [10]. Hyper-prolific sows particularly suffer from metabolic syndrome symptoms, including chronic inflammation, increased oxidative stress in late gestation/lactation, and reduced insulin sensitivity in early lactation [10, 37]. Thus, maintaining maternal health during gestation is essential for optimizing productivity in hyper-prolific sows.

Chinese herbal medicine contains bioactive compounds (e.g., organic acids, phenolic acids, flavonoids) with antimicrobial, antioxidative, anti-inflammatory, and immunomodulatory properties [16, 17]. Recent swine nutrition studies have increasingly evaluated herbal extracts as feed additives to improve animal health [18]. Dietary supplementation with herbal extracts has been shown to enhance feed intake and lactation performance in rats [38], sows [33, 39], and goats [40]. Lonicerae flos (LF) and Scutellaria baicalensis Georgi (SBG) are novel extracts rich in chlorogenic acid and baicalin, respectively. LF exhibits antimicrobial, antioxidative, and growth-promoting effects [19, 41], while SBG demonstrates broad-spectrum therapeutic properties, including anti-inflammatory, antioxidative, and immunomodulatory activities [42–43]. Despite these benefits, limited research has explored combined LF and SBG supplementation in gestating sows.

This study found that gestational Lonicerae-Scutellaria extract (LSE) supplementation improved total litter birth weight, day-21 piglet weight, lactation feed intake, and piglet survival rate. These improvements were associated with reduced maternal inflammation and oxidative stress. Specifically, LSE-fed sows showed lower fecal/plasma IL-6 and higher plasma IL-10 at G109. Additionally, LSE reduced plasma ROS and TBARS while enhancing HOMA-IS at G109. Given that oxidative stress and inflammation contribute to insulin resistance and feed intake reduction in lactating sows [10], these findings suggest LSE improves lactation performance through mitigating metabolic dysfunction.

Dietary bioactives influence gut microbiota composition, which plays a key role in host health [44]. Previous studies have shown that chlorogenic acid can selectively promote the growth of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* [45], while baicalin has been reported to inhibit pathogenic bacteria like *Escherichia*

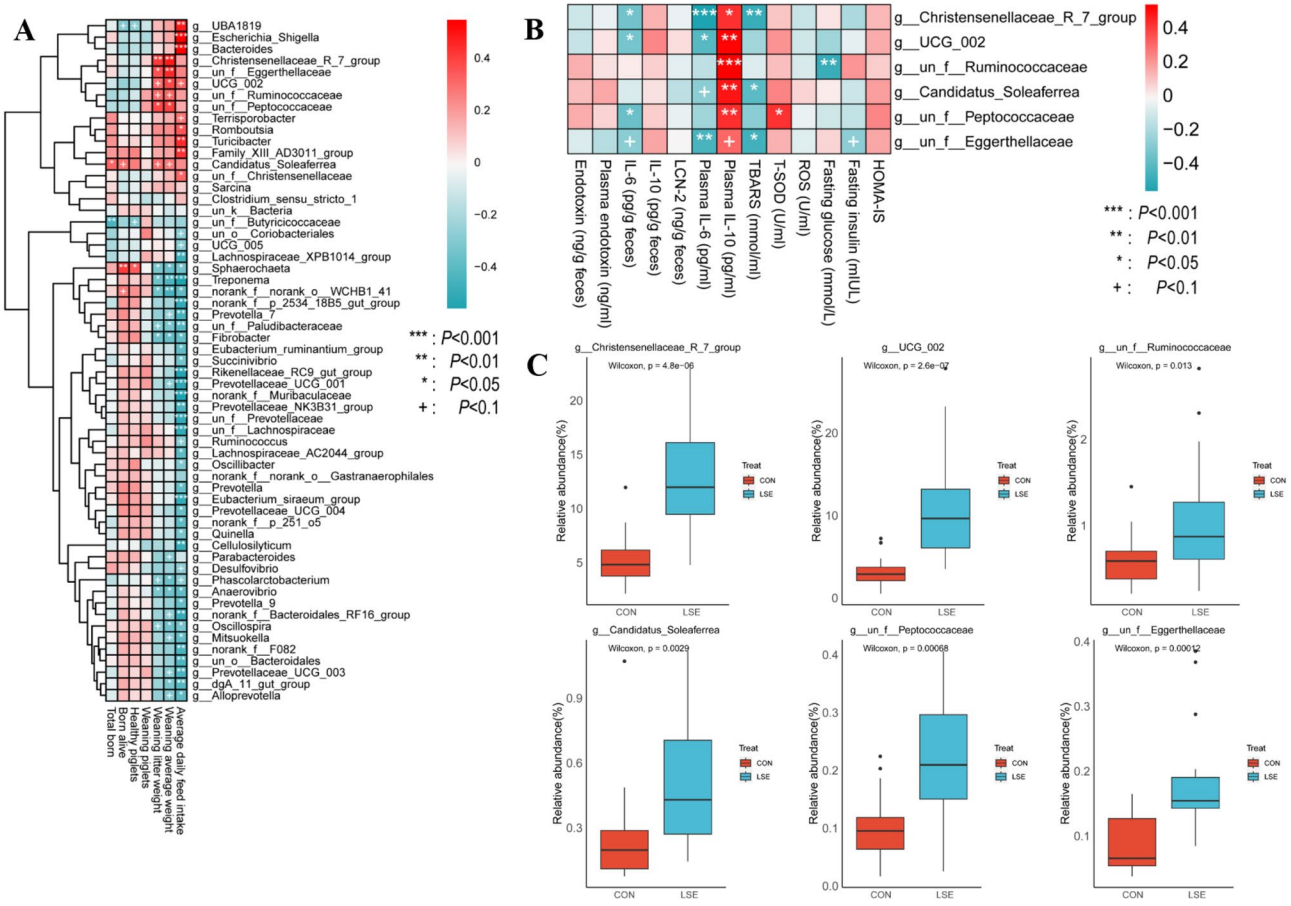

Fig. 8 Relationship between diet, microbiota, sow reproduction performance, and plasma and fecal parameters. (**A**) the relationships between feces microbiota and reproduction performance of sows. (**B**) the relationships between feces microbiota and plasma and fecal parameters of sows. (**C**) Relative abundance of significantly correlation genera on G109 d. Data were means ± SD ($n = 20$). $^{+}$mean a significant difference ($P < 0.1$), *mean a significant difference ($P < 0.05$),**mean a significant difference ($P < 0.01$), ***mean a significant difference ($P < 0.0001$)

coli and *Salmonella* through its antimicrobial properties [46]. The synergistic ratio in LSE may therefore create a balanced microbial environment, as demonstrated in our preliminary 16 S rRNA sequencing data (Fig. 5). Gut dysbiosis has been linked to metabolic disorders like insulin resistance and chronic inflammation in sows [3, 4, 5, 6]. Therefore, this study analyzed gut microbial profiles to explore microbiota-host interactions. Previous research indicates herbal extract supplementation (e.g., Lonicera japonica, Astragalus membranaceus) modulates gut microbiota by increasing beneficial bacteria and reducing pathogens in pigs [47]. The current findings were similar to previous studies that experienced significant changes in gut microbiota of sows during gestation and lactation [5, 48]. Principal coordinate analysis indicated that a significant difference in microbial composition existed in the two groups. In addition, the G109 sows exhibited a lower gut microbial richness and alpha diversity in LSE group compare to CON group, while the G109 sows had a higher alpha diversity in LSE group. This is beneficial for regulating intestinal flora structure and homeostasis of flora community at the late gestation stage. Cheng et al. (2019) reported that the microbiota diversity was greater at the late gestation stage than in early and mid-term gestation [10]. In the present study, gut microbiota revealed a significant change at different stages of gestation and lactation, either phylum or genus level between the two groups [49]. Guan et al. (2021) indicated *Scutellaria baicalensis* Georgi significantly altered Firmicutes/Bacteroidetes ratio, and increased abundance of short chain fatty acid in Rats [50]. Firmicutes and Bacteroidota were the top abundant phyla identified in late pregnancy for sows [51]. The LSE supplementation significantly increased the abundance of *Christensenellaceae_R_7_group* compared with CON in late pregnancy. *Christensenellaceae* is a recently described family in the phylum Firmicutes, plays an important role in human health [52]. It has been shown that *Christensenellaceae_R-7_group* is positively correlated with absorption and digestion of nutrients [53]. Our results indicate that the relative abundance of *UCG-002* increased in LSE group at G109 d. Although

their relative abundance was reduced at L3 d, the reason may be related to the change in the feeding environment from the gestation room to the farrowing room, and pregnancy diets changed accordingly to lactation diets. *UCG-002* is a member of the *Erysipelotrichaceae* family in the *Firmicutes* phylum and was previously reported to be involved in volatile fatty acid synthesis [54] and suppression of intestinal inflammation [55]. These finding are consistent with our results that *UCG-002* and *Christensenellaceae_R_7_group* was positively correlated with plasma IL-10, and negatively correlated with plasma and feces IL-6 and plasma TBARS. Furthermore, the *Candidatus_Soleaferrea* was positively correlated with plasma IL-10, but negatively correlated with plasma TBARS. A previous study indicated that *Candidatus Soleaferrea* has anti-inflammatory effects in pregnant women [56]. A similar research also found that sugar beet pulp supplementation could improve metabolism, immune responses and gut health in sows but by differently affecting microbial composition [57]. It has been shown that the presence of specific gut bacterial species will be involved in improving a healthy gut ecosystem and antioxidant status [58, 59, 60]. In livestock production, combination of plant extracts (*Lonicera japonica*, *Astragalus membranaceus*, *Eucommia folium*, *and Codonopsis pilosula*) have antioxidant and anti-inflammatory activities that improve performance and modify the composition of intestinal flora [47]. In the current study, combined herbs LSE diet during gestation increase the relative abundances of *un_f__Ruminococcaceae*, *Candidatus_Soleaferrea*, *un_f__Peptococcaceae*, *UCG_002*, *Christensenellaceae_R_7_group*, and *un_f__Eggerthellaceae* on G109 d. The *Candidatus_Soleaferrea* was negatively correlated with with plasma TBARS. The *un_f__Peptococcaceae* was positively correlated with plasma T-SOD. A previous study indicated that Thyme extract Georgi significantly ameliorated *Faecalibaculum* and *Roseburia* levels, both *Faecalibaculum* and *Roseburia* include systemic inflammatory response and oxidative stress state [59]. The phenolic-rich extract of *P. lobata* increased the abundance of beneficial bacteria, involving *Lactobacillaceae* and *Bacteroidetes*, and enhancing the antioxidant status [58]. These plant extracts, especially the phenols only a small part are absorbed in the small intestine, while the majority will reach the large intestine and interact with colonic bacteria [60]. It could be a key reasons plant extracts as modulators of gut microbes and regulating the body health of the key reasons.

Conclusions

Dietary supplementation with *Lonicera flos* and *Scutellaria baicalensis* mixed extracts (LSE) during gestation significantly improved reproductive performance and metabolic health in sows. Specifically, LSE supplementation increased total born piglets, litter weight, average piglet weight at 21 days post-farrowing, and lactation feed intake, while reducing plasma reactive oxygen species (ROS) and interleukin-6 (IL-6) levels. These improvements were closely associated with altered gut microbiota composition, characterized by increased abundances of beneficial taxa (e.g., *Christensenellaceae_R_7_group*, *UCG_002*, *Clostridium_sensu_stricto_1*) and reduced inflammation-related bacteria (e.g., *Bacteroidetes*, *Spirochaetes*). Correlation analyses further revealed that key microbial genera were positively linked to anti-inflammatory markers (IL-10) and negatively correlated with oxidative stress (TBARS) and insulin resistance. Collectively, these findings highlight LSE as a promising natural additive to enhance sow health and productivity by modulating gut microbiota and mitigating metabolic disorders during pregnancy.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12917-025-04753-5.

Supplementary Material 1

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Author contributions

Y. Z. and J. P. designed the experiments. M. W., J. C., Y. G. and H. L. conducted the experiments. M. W., S. Y., J. C. and Y. Z. collected and analyzed the data. Y. Z., M. W. and S. Y., wrote the manuscript. J. P., S. J. and Y. Z. revised the manuscript. All authors have read and approved the final manuscript.

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Data availability

The 16S rRNA sequencing raw data during the current study was uploaded and registered in the NCBI SRA database with accession numbers (PRJNA1171731) [https://www.ncbi.nlm.nih.gov/sra/PRJNA1171731]. Other raw datasets may also be requested from the corresponding author provided that all ethical requirements have been met.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Animal Experimentation Ethics Committee of Huazhong Agricultural University, Wuhan, China (JN. No20161025201704 11(76)). The sow owner gave an informed consent and agreed to use for this study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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