



## Review Article

## Plant-derived polyphenols in sow nutrition: An update

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## ABSTRACT

Oxidative stress is a potentially critical factor that affects productive performance in gestating and lactating sows. Polyphenols are a large class of plant secondary metabolites that possess robust antioxidant capacity. All polyphenols are structurally characterized by aromatic rings with multiple hydrogen hydroxyl groups; those make polyphenols perfect hydrogen atoms and electron donors to neutralize free radicals and other reactive oxygen species. In the past decade, increasing attention has been paid to polyphenols as functional feed additives for sows. Polyphenols have been found to alleviate inflammation and oxidative stress in sows, boost their reproductivity, and promote offspring growth and development. In this review, we provided a systematical summary of the latest research advances in plant-derived polyphenols in sow nutrition, and mainly focused on the effects of polyphenols on the (1) antioxidant and immune functions of sows, (2) placental functions and the growth and development of fetal piglets, (3) mammary gland functions and the growth and development of suckling piglets, and (4) the long-term growth and development of progeny pigs. The output of this review provides an important foundation, from more than 8,000 identified plant phenols, to screen potential polyphenols (or polyphenol-enriched plants) as functional feed additives suitable for gestating and lactating sows.

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## 1. Introduction

Oxidative stress is a potentially critical factor that affects the reproductive and lactation performance of both gestating and lactating sows (Surai and Fisinin, 2016). During pregnancy, the placenta is a place of active oxygen metabolism which incessantly produces oxidative stress (Wu et al., 2016). Lipid peroxidation and oxidative stress have been reported to be elevated in pregnant women compared with non-pregnant women (Mihu et al., 2012). The excessive generation of reactive nitrogen species and reactive oxygen species disrupts the normal physiological function of the mammalian placenta (Wu et al., 2016). Oxidative and immune

disorders are closely related to defective pregnancy outcomes such as intrauterine growth restriction, preeclampsia, and spontaneous abortion (Wu et al., 2016). During the lactation phase, sows require a large amount of energy for substantial metabolism (Chen et al., 2021b). Correspondingly, genes and transcription factors related to milk component synthesis are significantly upregulated in the mammary glands of lactating sows (Palombo et al., 2018). There were 632 genes differentially expressed in the liver of lactating sows compared to non-lactating sows; these altered genes are mainly related to amino acid metabolism, fatty acid metabolism, the citric acid cycle, and peroxisome proliferator-activated receptor (PPAR) signaling (Rosenbaum et al., 2012a). It has also been reported that lactation triggers the hepatic nuclear factor erythroid 2-related factor 2 (Nrf2) pathway in sows, which is a stress-related pathway involving oxidative stress and inflammation (Rosenbaum et al., 2012b). Energy intake and substantial metabolism result in tremendous oxygen consumption and the generation of numerous oxygen free radicals and lipid peroxides (Kim et al., 2013). Therefore, it is imperative to seek nutritional programs that increase the antioxidant capacity and reduce the oxidative stress of pregnant and lactating sows. Recent studies have

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shown that several functional bioactive substances, such as polyphenols, have beneficial effects on relieving oxidative stress in sows.

Polyphenols are a large class of plant secondary metabolites with polyphenolic structural units (Durazzo et al., 2019). Polyphenols are the fourth major ingredient in plants, and the polyphenol content is second only to those of cellulose, hemicellulose, and lignin in plants (Durazzo et al., 2019). They are widely distributed in the bark, roots, wood, leaves, and fruits of plants (Durazzo et al., 2019). To date, more than 8,000 phenolic compounds have been identified in plants (Hossen et al., 2020). Most importantly, there is a growing body of evidence that plant-derived polyphenols and related plant extracts could be developed as functional feed additives for sows. In detail, polyphenols have been reported to improve sow reproductivity and offspring growth and development, which are greatly related to their antioxidant and anti-inflammatory properties (Meng et al., 2018). The biological functions of polyphenols are primarily due to their chemical structure characterized by aromatic rings bearing multiple hydroxyl groups (Singla et al., 2019). Herein, we first briefly introduce the structural characterization and classification of polyphenols, and then systematically summarized the latest research advances in polyphenols in sow nutrition.

## 2. The structural characteristics of polyphenols

The biological properties of polyphenols, such as the robust antioxidant activity, are mainly attributed to their unique structural characteristics (Singla et al., 2019). Specifically, polyphenols are a group of phenolic systems featured with at least phenyl rings and one or more hydroxyl substituents (Singla et al., 2019). Based on this basic structure, thousands of natural polyphenols have been identified, ranging from simple phenolic acids to complex polymeric compounds such as tannins (Losada-Barreiro and Bravo-Díaz, 2017). Polyphenols are typically categorized by their chemical structures, mainly focusing on the number of phenol subunits, as well as the amount and position of substituents present in the aromatic rings (Losada-Barreiro and Bravo-Díaz, 2017).

Polyphenols are divided into flavonoids and non-flavonoids based on the number of phenolic rings with aliphatic carbon skeletons and phenols that bind these rings to one another (Ahmadifar et al., 2021). Flavonoids are the most abundant subgroup of plant polyphenols with thousands of established chemical structures (Losada-Barreiro and Bravo-Díaz, 2017; Abdel-Moneim et al., 2020). All flavonoids possess a carbon skeleton of diphenylpropane and 2 benzene rings connected by a linear three-carbon chain (backbone structure: C<sub>6</sub>–C<sub>3</sub>–C<sub>6</sub>) (Losada-Barreiro and Bravo-Díaz, 2017). In addition, a closed pyran ring with a central chain is present along with one of the benzene rings (Losada-Barreiro and Bravo-Díaz, 2017). Depending on the heterocycle type, flavonoids can be further subclassified into several subgroups, including isoflavones, flavonols, flavanols, flavones, flavanones, and anthocyanins (Losada-Barreiro and Bravo-Díaz, 2017). Currently, there are more than 4,000 kinds of flavonoids identified in plants, including genistein, silymarin, catechin, baicalin, naringenin, and cyanidin (Obaid et al., 2021).

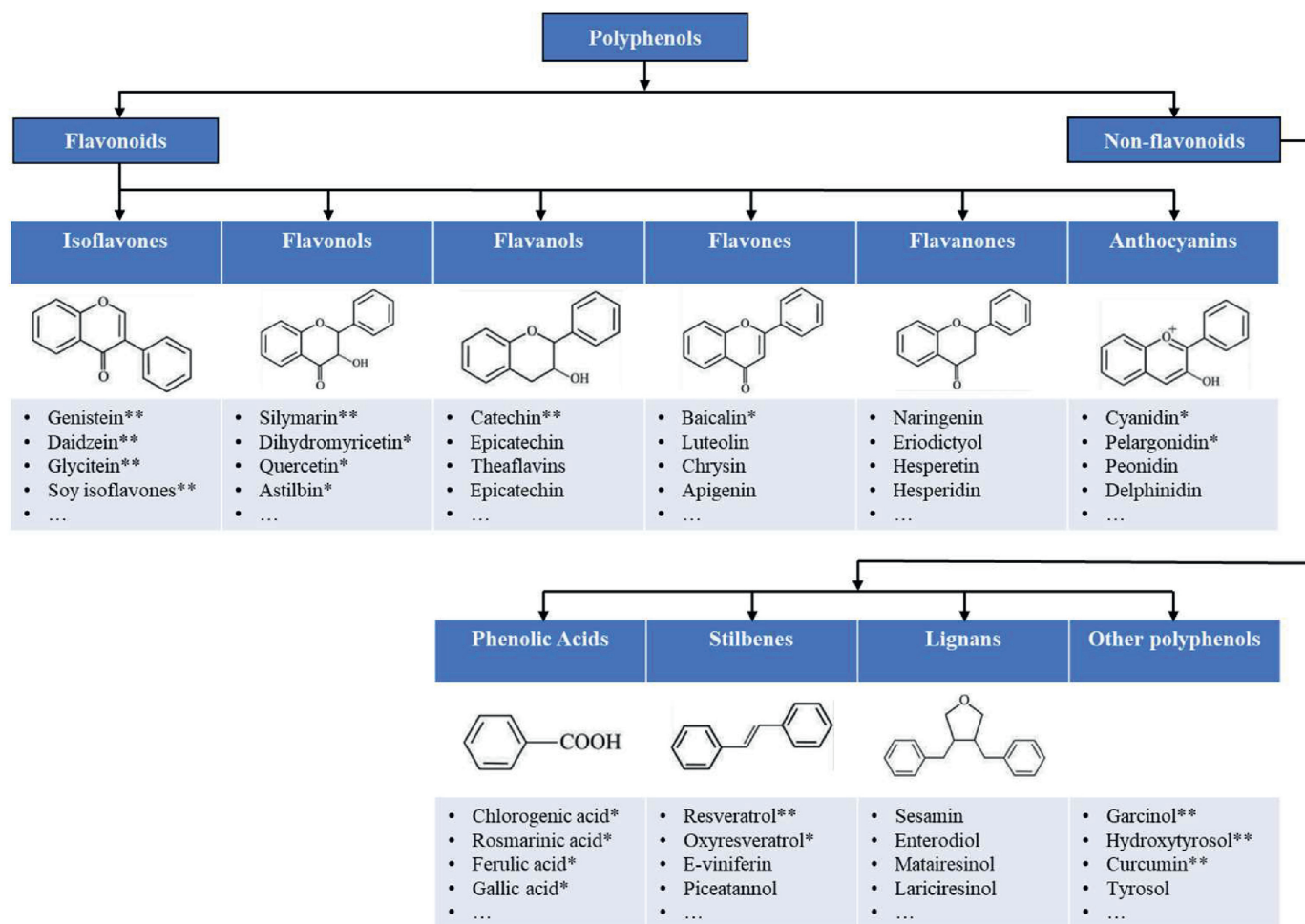
Phenolic acids, a type of non-flavonoids, have a carboxylic acid group that can be connected to an aromatic ring (benzoic acid derivatives) or an alkyl residue (hydroxycinnamic acid derivatives) (Losada-Barreiro and Bravo-Díaz, 2017). Phenolic acids mainly consist of cinnamic acids, benzoic acids, and their derivatives (Ahmadifar et al., 2021). Phenolic acids are divided into 2 categories according to their carbon skeleton, namely the C<sub>6</sub>–C<sub>3</sub> type (ferulic acid, caffeic acid, coumaric acid, and sinapic acid) and the C<sub>6</sub>–C<sub>1</sub> type (gallic acid, vanillic acid, and other benzoic acids). The location

and identity of diverse substituents in the basic backbone result in a variety of phenolic acid antioxidants (Losada-Barreiro and Bravo-Díaz, 2017). Stilbene is another type of non-flavonoid, which is characterized by a double bond joining phenolic rings (Losada-Barreiro and Bravo-Díaz, 2017). The existing forms of stilbenes are stereoisomers, and the vast majority of naturally occurring stilbenes exist in the *trans* form. Resveratrol is the most well-characterized and extensively studied stilbene (Losada-Barreiro and Bravo-Díaz, 2017). Lignans, which are also non-flavonoids, feature 2 propyl-benzene units and a four-carbon bridge (Ahmadifar et al., 2021). Lignans are biosynthesized via the phenylpropanoid pathway (Ahmadifar et al., 2021). Owing to their special structural characteristics, plant polyphenols have been reported to have robust antioxidant, anti-inflammatory, and antibacterial properties (Gessner et al., 2017). The basic structures of polyphenols are shown in Fig. 1. The next section, as the main body of this review, will provide a systematic overview of the latest advances in plant-derived polyphenols in sow nutrition. Fig. 2 exemplified the chemical structures of major polyphenols reported in sow nutrition. The summary of plant-derived polyphenols and polyphenols-enriched additives in sow nutrition is presented in Table 1.

## 3. The latest research progress on plant-derived polyphenols in sow nutrition

### 3.1. Effects on the antioxidant and immune functions of sows

Recent studies have suggested that the dietary addition of polyphenols can effectively improve the antioxidant and immune functions of sows (Fan et al., 2015; Hu et al., 2015; Meng et al., 2018; Wang et al., 2019a; Jiang et al., 2020; Sun et al., 2020; Li et al., 2021b; Long et al., 2021b; Papatsiros et al., 2022). Flavonoids are the most abundant subgroup of polyphenols, and multiple flavonoids, including daidzein (Li et al., 2021b), glycitein (Hu et al., 2015), and catechins (Fan et al., 2015), have been demonstrated to promote the antioxidant and immune functions of sows. Daidzein is an isoflavonic phytoestrogen that is abundant in soybeans and other legumes (Ren et al., 2001). Li et al. (2021b) demonstrated that the dietary addition of 200 mg/kg of daidzein in sow diets throughout the gestation period elevated the total antioxidant capacity (T-AOC) and immunoglobulin G (IgG) concentration, the activities of glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) in the serum of sows on d 35 of pregnancy, as well as the T-AOC and the activities of SOD in the serum of sows on d 85 of pregnancy. The antioxidant defense system in the animal body includes both enzymatic and non-enzymatic antioxidant systems. Among them, GSH-Px, SOD, and catalase (CAT) belong to the enzymatic antioxidant system, whereas T-AOC is an overall indicator of the total antioxidant capacity of animals (Fraga et al., 2014). Glycitein is also an isoflavone. According to Hu et al. (2015), feeding sows 15, 30, and 45 mg/kg of glycitein during late pregnancy and lactation linearly increased the plasma T-AOC and SOD activities from d 1 to 18 of lactation, the plasma CAT activity from d 7 to 18 of lactation, and the GSH-Px activity in the plasma of sows on d 110 of pregnancy and from d 7 to 18 of lactation. Additionally, the malondialdehyde (MDA) content in the plasma of sows was linearly reduced from d 110 of pregnancy to d 18 of lactation when they were fed diets supplemented with 15, 30 and 45 mg/kg of glycitein (Hu et al., 2015). Similarly, Fan et al. (2015) reported that the dietary inclusion of 200 mg/kg of catechins from breeding to d 40 of pregnancy markedly increased the activities of SOD and CAT and decreased the levels of MDA and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in the serum of sows at farrowing. As a typical representative stilbene, resveratrol



**Fig. 1.** The basic structures of subclassified polyphenols (Ahmadifar et al., 2021; Sobhani et al., 2021). \*\*Polyphenols reported in sows (Farmer et al., 2010; Norrby et al., 2011; Fan et al., 2015; Hu et al., 2015; Scott et al., 2015; Meng et al., 2018; Garcia-Contreras et al., 2019; Wang et al., 2019a; Jiang et al., 2020; Li et al., 2021a, 2021b); \*polyphenols reported in swine except for sows (Wu et al., 2004; Chen et al., 2018; Wan et al., 2018; Cai et al., 2020; Liao et al., 2020; Pomothy et al., 2020; Xu et al., 2020a, 2020b; Long et al., 2021a; Wang et al., 2021).

possesses antioxidant and anti-inflammatory potentials (Lee et al., 2018; Banez et al., 2020). In a study conducted by Meng et al. (2018), supplementing sows with 300 mg/kg of resveratrol from d 20 of pregnancy until d 21 of lactation enhanced their plasma GSH-Px and CAT activities on d 110 of gestation, the SOD and CAT activities on d 14 of lactation, and the SOD activity on d 21 of lactation. In addition, the oxidative stress of sows was mitigated by resveratrol supplementation, as reflected by the reduced MDA levels in their plasma on d 110 of gestation and d 14 and 21 of lactation, as well as the decreased H<sub>2</sub>O<sub>2</sub> levels in their plasma on d 110 of pregnancy and d 14 of lactation (Meng et al., 2018). Garcinol is characterized by its polyphenolic structure and possesses potent antioxidant properties (Chang et al., 2021). As reported by Wang et al. (2019a), the dietary supplementation of 600 mg/kg of garcinol during the perinatal period notably increased the T-AOC and the activities of GSH-Px, SOD, and CAT, and decreased the MDA content in the plasma of sows on both d 110 of gestation and d 21 of lactation. Silymarin, featuring a polyphenolic structure, has also been shown to enhance the antioxidant status of sows (Farmer et al., 2017; Jiang et al., 2020). As documented by Jiang et al. (2020), the dietary addition of 40 g/d of silymarin from d 108 of pregnancy until d 20 of lactation augmented the serum CAT activity of sows on d 18 of lactation and the serum GSH-Px activity of sows on d 7 of lactation. Silymarin supplementation also decreased the

serum IL-1 $\beta$  concentration of sows on d 18 of lactation and the serum TNF- $\alpha$  concentration of sows on d 7 of lactation.

Several phytogetic additives rich in polyphenols have also been reported in sow nutrition owing to their antioxidant capacity (Sun et al., 2020; Long et al., 2021b; Papatsiros et al., 2022). Papatsiros et al. (2022) demonstrated that the dietary addition of 5 g/d phytogetic feed additives enriched in polyphenols notably lowered the levels of thiobarbituric acid-reactive substances (TBARS) and protein carbonyls in the plasma of sows at farrowing. The TBARS and protein carbonyls are the main indicators of lipid and protein oxidation, respectively (Kim et al., 2013). Long et al. (2021b) also noticed that the dietary inclusion of 100 mg/kg of *Forsythia suspensa* extracts rich in polyphenols during late pregnancy decreased the IL-6 level and increased the IL-10 level and GSH-Px activity in the serum of sows at farrowing. *Moringa oleifera* is enriched in polyphenols, several of which have been identified by researchers (Zhu et al., 2020). In a feeding trial conducted by Sun et al. (2020), sows that were supplemented with 8% of *Moringa Oleifera* from 2 weeks pre-breeding until d 21 of lactation had markedly augmented serum T-AOC and CAT activity on d 60 of gestation; additionally, they had markedly augmented serum T-AOC on d 90 of gestation and T-AOC and GSH-Px activity on d 10 of lactation. Although more than 8,000 polyphenol compounds derived from plants have been reported (Hossen et al., 2020), there is still room

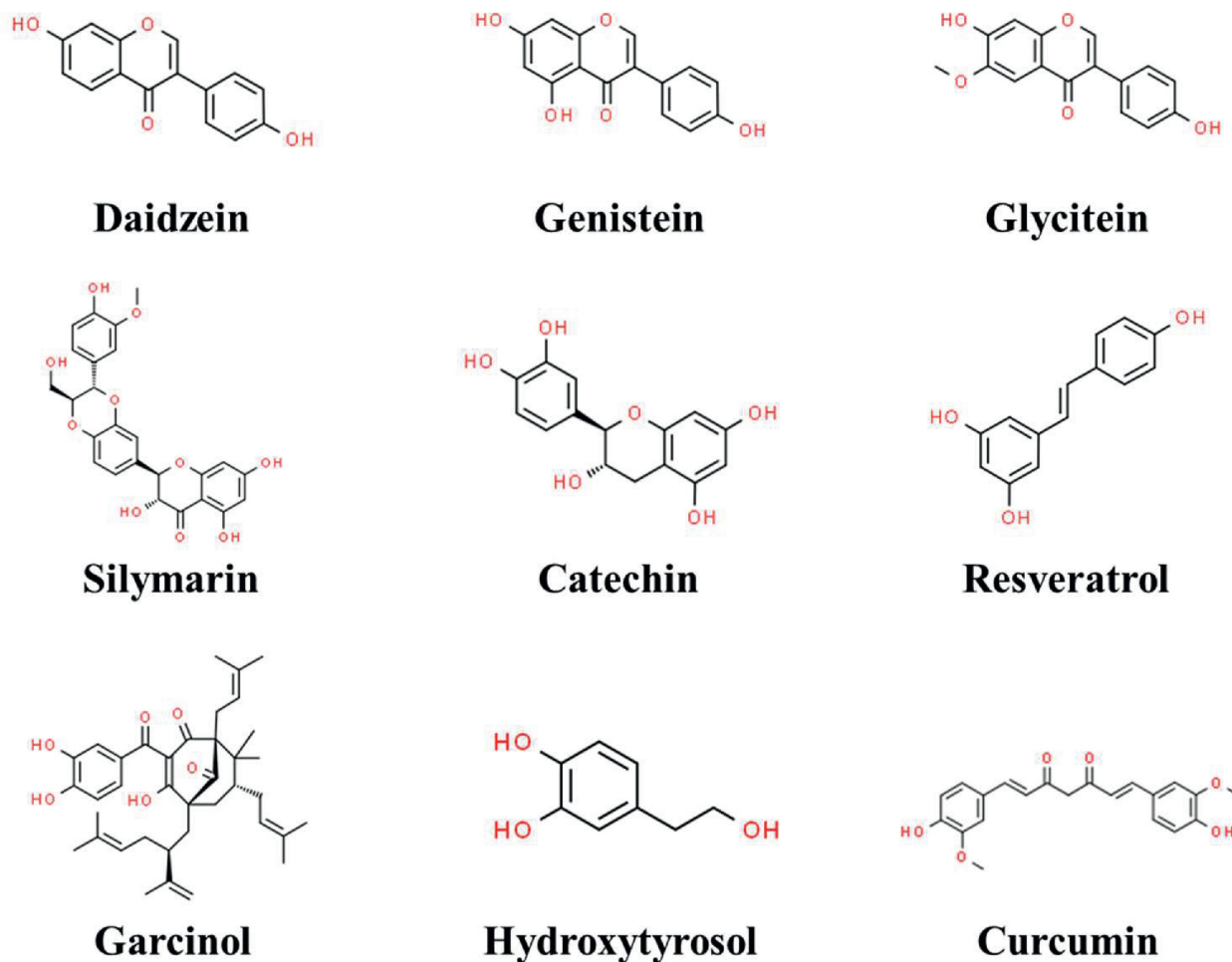


Fig. 2. The chemical structures of major polyphenols reported in sow nutrition.

to explore more polyphenols (or phytochemical extracts rich in polyphenols) for sow dietary use to improve their antioxidant capacity.

### 3.2. Effects on the placental functions of sows

The placenta is a place of active oxygen metabolism which incessantly produces oxidative stress during pregnancy (Wu et al., 2016). The excessive generation of reactive nitrogen species and reactive oxygen species disrupts the normal physiological function of the mammalian placenta (Wu et al., 2016). Oxidative and immune disorders are closely related to defective pregnancy outcomes such as intrauterine growth restriction, preeclampsia, and spontaneous abortion (Wu et al., 2016). Plant polyphenols, natural substances with robust antioxidant activity, have been reported to alleviate placental oxidative stress and improve the physiological functions of the placenta of sows. A dose of 300 mg/kg of resveratrol supplementation from d 20 of gestation until farrowing markedly elevated the GSH-Px, SOD, and CAT activities and reduced the MDA and H<sub>2</sub>O<sub>2</sub> content in the placental tissue of sows (Meng et al., 2018). In addition, research has shown that the addition of 300 mg/kg of resveratrol triggered the Sirt 1 and Keap1/Nrf2 pathways in the placenta of sows, as indicated by the upregulated protein expression of Sirt 1 and Nrf2, as well as the downregulated protein expression of Keap1 (Meng et al., 2018). Upon activating the Keap1/Nrf2 pathway, resveratrol notably upregulated the expression of downstream Nrf2-regulated genes in placental tissues,

including *CAT*, *GPX1*, *GPX4*, *SOD1*, *HO1*, *GCLM*, *MGST1*, and *UGT1A1* in the placenta of sows fed a resveratrol-supplemented diet (Meng et al., 2018). These results suggest that polyphenols, such as resveratrol, have huge potential to augment the antioxidant ability and lower oxidative stress in the placenta of gestating sows. There is an increasing body of evidence that many polyphenols have an identical pharmacological mechanism of action as Nrf2 activators, which may enlighten us that Nrf2 could be considered as a molecular target to develop other plant polyphenols as feed additives to improve the antioxidant status and immunity of sows. In terms of the placental functions, the results of another study suggested that feeding gestating sows with 200 mg/kg of daidzein from breeding until parturition, notably upregulated the mRNA expression of *SNAT1* and *IGF-1* in their placental tissue, which indicates that daidzein supplementation is beneficial for placental nutrient transport in sows (Li et al., 2021b). Consistently, another feeding trial confirmed that the dietary supplementation with 200 mg/kg of daidzein during early gestation markedly elevated citrate, arginine, and creatine concentrations in the amniotic fluid of sows (Xie et al., 2020). In addition, Supplementing the diet of prepubescent gilts with 600 mg/kg of soybean isoflavone for 21 d detoxicated zearalenone-induced reproductive organ injury, and protected gilts from reproductive hormone disorders (Wang et al., 2010, 2013). Polyphenols supplementation during pregnancy has great potential to mitigate placental oxidative stress and augment placental antioxidant capacity and nutrient transport in pregnant sows.

**Table 1**  
The summary of plant-derived polyphenols and polyphenols-enriched additives in sow nutrition.<sup>1</sup>

Polyphenols	Supplemental dosage and duration	Main findings	References
Daidzein	<ul style="list-style-type: none"> <li>Dosage: 200 mg/kg</li> <li>Duration: G<sub>0</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>Improved reproductive performance of sows (↑ the no. of piglets born and piglets born alive);</li> <li>Elevated serum antioxidant status of sows (↑ T-AOC [G<sub>35</sub> and G<sub>85</sub>], SOD [G<sub>35</sub> and G<sub>85</sub>], and GSH-Px [G<sub>35</sub>]);</li> <li>Improved serum immunity of sows (↑ IgG [G<sub>35</sub>]);</li> <li>Enhanced placental nutrient transport (↑ <i>SNAT1</i> mRNA expression).</li> </ul>	Li et al. (2021b)
Daidzein	<ul style="list-style-type: none"> <li>Dosage: 200 mg/kg</li> <li>Duration: G<sub>0</sub>–G<sub>35</sub></li> </ul>	<ul style="list-style-type: none"> <li>Improved reproductive performance of sows (↑ the no. of viable embryos [G<sub>35</sub>], ↓ mummy embryos [G<sub>35</sub>]);</li> <li>Improved antioxidant status in amniotic fluid of sows (↑ GSH-Px [G<sub>35</sub>]);</li> <li>Increased some key metabolites in amniotic fluid of sows (↑ citrate, arginine, and creatine [G<sub>35</sub>]).</li> </ul>	Xie et al. (2020)
Daidzein	<ul style="list-style-type: none"> <li>Dosage: 1 mg/kg body weight</li> <li>Period: G<sub>85</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>Increased pH of longissimus thoracis in pigs from large litters of sows (↑ pH<sub>45</sub> and pH<sub>end</sub>);</li> <li>Increased the percentage of fast-twitch glycolytic fibers in semi-tendinous muscle of offspring pigs at 180 d old (↑ fast-twitch glycolytic fibers, ↓ fast-twitch oxidative fibers).</li> </ul>	Rehfeldt et al. (2007)
Daidzein	<ul style="list-style-type: none"> <li>Dosage: 8 mg/kg</li> <li>Period: G<sub>85</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>Improved reproductive performance of sows (↑ newborn survival percentage);</li> <li>Up-regulated the mRNA expression of <i>IGF-1R</i> in skeleton muscle of offspring newborn piglets.</li> </ul>	Ren et al. (2001)
Soy isoflavones	<ul style="list-style-type: none"> <li>Dosage: 10, 20 and 40 mg/kg</li> <li>Period: G<sub>90</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>Linearly improved lactation performance of sows (↑ sow ADFI during lactation, piglet body weight [L<sub>10</sub> and L<sub>21</sub>], piglet ADG [L<sub>3</sub>–L<sub>10</sub> and L<sub>3</sub>–L<sub>21</sub>]);</li> <li>Linearly improved serum antioxidant of sows (L<sub>10</sub>: ↑ T-AOC, SOD, ↓ MDA).</li> </ul>	Li et al. (2021a)
Soybean isoflavones (and astragalus polysaccharide)	<ul style="list-style-type: none"> <li>Dosage: 100, 200 and 300 mg/kg mixture (soybean isoflavones and astragalus polysaccharide)</li> <li>Period: G<sub>107</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>Improved lactation performance of sows (↑ sow ADFI during lactation, total lactation yield);</li> <li>Improved serum antioxidant status of sows (L<sub>1</sub>: ↑ T-AOC, GSH-Px, SOD, ↓ MDA; L<sub>10</sub>: ↑ GSH-Px, SOD, ↓ MDA; L<sub>21</sub>: ↑ T-AOC, GSH-Px, SOD, CAT, ↓ MDA);</li> <li>Improved serum immunity of sows (L<sub>1</sub>: ↑ IgA; L<sub>10</sub>: ↑ IgG, IgA, IL-2, C4; L<sub>21</sub>: ↑ IgG, IgA, IL-2).</li> </ul>	Wu et al. (2021)
Glycitein	<ul style="list-style-type: none"> <li>Dosage: 15, 30, and 45 mg/kg</li> <li>Period: G<sub>85</sub>–L<sub>18</sub></li> </ul>	<ul style="list-style-type: none"> <li>Linearly improved lactation performance of sows (↑ litter weaning weight and ADG of piglets during lactation);</li> <li>Linearly improved milk composition (↑ protein [L<sub>1</sub> and L<sub>7</sub>], fat [L<sub>1</sub>, L<sub>7</sub> and L<sub>14</sub>], and lactose [L<sub>1</sub>]);</li> <li>Linearly improved plasma antioxidant status of sows (↑ T-AOC [L<sub>1</sub>, L<sub>7</sub>, L<sub>14</sub> and L<sub>18</sub>], GSH-Px [G<sub>110</sub>, L<sub>7</sub>, L<sub>14</sub> and L<sub>18</sub>], SOD [L<sub>1</sub>, L<sub>7</sub>, L<sub>14</sub> and L<sub>18</sub>], CAT [L<sub>7</sub>, L<sub>14</sub> and L<sub>18</sub>], and ↓ MDA [G<sub>110</sub>, L<sub>1</sub>, L<sub>7</sub>, L<sub>14</sub> and L<sub>18</sub>]);</li> <li>Linearly improved milk antioxidant status of sows (↑ GSH-Px [L<sub>1</sub>], SOD [L<sub>18</sub>], and ↓ MDA [L<sub>7</sub> and L<sub>18</sub>]).</li> </ul>	Hu et al. (2015)
Genistein	<ul style="list-style-type: none"> <li>Dosage: 2 g/d</li> <li>Period: G<sub>90</sub>–G<sub>100</sub></li> </ul>	<ul style="list-style-type: none"> <li>No effects on the levels of daidzein, glycitein, estradiol in plasma of sows;</li> <li>Changed genistein levels in plasma of sows (↓ G<sub>95</sub>, ↑ G<sub>110</sub>).</li> </ul>	Farmer et al. (2013)
Genistein	<ul style="list-style-type: none"> <li>Dosage: 2.3 g/d</li> <li>Period: 90- to 183-d-old</li> </ul>	<ul style="list-style-type: none"> <li>Promoted mammary development of gilts at post-puberty (mammary tissues: ↓ dry matter, ↑ protein, DNA, histological score, estrogen receptors).</li> </ul>	Farmer et al. (2010)
Catechins	<ul style="list-style-type: none"> <li>Dosage: 100, 200, 300 and 400 mg/kg</li> <li>Period: G<sub>0</sub>–G<sub>40</sub></li> </ul>	<ul style="list-style-type: none"> <li>Improved reproductive performance of sows (↑ the No. of newborn alive, healthy newborn, ↓ stillborn);</li> <li>Elevated serum antioxidant status of sows at farrowing (↑ SOD and CAT, ↓ MDA and H<sub>2</sub>O<sub>2</sub>).</li> </ul>	Fan et al. (2015)
Resveratrol	<ul style="list-style-type: none"> <li>Dosage: 300 mg/kg</li> <li>Period: G<sub>20</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>Improved lactation performance of sows (↑ individual piglet weight and litter weight at weaning [L<sub>21</sub>]);</li> <li>Improved serum antioxidant status of sows (↑ GSH-Px [G<sub>110</sub>], CAT [G<sub>110</sub> and L<sub>14</sub>] and SOD [L<sub>14</sub> and L<sub>21</sub>]), ↓ H<sub>2</sub>O<sub>2</sub> [G<sub>110</sub> and L<sub>14</sub>] and MDA [G<sub>110</sub>, L<sub>14</sub> and L<sub>21</sub>]);</li> <li>Promoted placental antioxidant functions of sows (antioxidant status: ↑ GSH-Px, SOD, CAT, ↓ H<sub>2</sub>O<sub>2</sub> and MDA; antioxidant pathway: ↑ protein expression of Sirt 1, Keap1, Nrf2, and p-NFκB-</li> </ul>	Meng et al. (2018)

Table 1 (continued)

Polyphenols	Supplemental dosage and duration	Main findings	References
Resveratrol	<ul style="list-style-type: none"> <li>• Dosage: 300 mg/kg</li> <li>• Period: G<sub>20</sub>–L<sub>21</sub></li> </ul>	<p>p65; Nrf2-regulated genes expression: ↑ <i>GPX1</i>, <i>GPX4</i>, <i>CAT</i>, <i>SOD1</i>, <i>HO1</i>, <i>GCLM</i>, <i>MGST1</i> and <i>UGT1A1</i>);</p> <ul style="list-style-type: none"> <li>• Improved milk antioxidant status of sows (↑ SOD [L<sub>0</sub> and L<sub>14</sub>] and CAT [L<sub>7</sub> and L<sub>21</sub>], ↓ H<sub>2</sub>O<sub>2</sub> [L<sub>7</sub> and L<sub>21</sub>] and MDA [L<sub>14</sub> and L<sub>21</sub>]);</li> <li>• Improved antioxidant status of offspring piglets (↑ GSH-Px [L<sub>0</sub> and L<sub>21</sub>], SOD [L<sub>21</sub>], CAT [L<sub>0</sub> and L<sub>21</sub>], ↓ H<sub>2</sub>O<sub>2</sub> [L<sub>0</sub>] and MDA [L<sub>21</sub>]).</li> <li>• Improved colostrum and milk composition (↑ Lactose [L<sub>0</sub>], total solids [L<sub>21</sub>], and fat [L<sub>21</sub>]);</li> <li>• Elevated lipid-related metabolites of suckling piglets at 21 d old (↑ lipase, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol and insulin);</li> <li>• Elevated enzyme activities in adipose tissue of suckling piglets at 21 d old (↑ hormone-sensitive lipase, lipoprotein lipase, acetyl-CoA carboxylase);</li> <li>• Up-regulated mRNA expression of lipid metabolic regulators in adipose tissue of offspring suckling piglets at 21 d old (↑ <i>LPL</i>, <i>ACCα</i>, <i>C/EBPα</i>, and <i>FATP1</i>).</li> </ul>	Sun et al. (2019)
Resveratrol	<ul style="list-style-type: none"> <li>• Dosage: 300 mg/kg</li> <li>• Period: G<sub>20</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Increased backfat thickness and intramuscular fat of offspring finishing pigs;</li> <li>• Improved meat quality of Longissimus thoracis in offspring finishing pigs (↓ drip loss, lactic acid, MDA, mRNA expression of <i>MyHC IIb</i>, ↑ pH<sub>24h</sub>, SOD, and mRNA expression of <i>SOD2</i>, mRNA and protein expression of <i>MyHC I</i>).</li> </ul>	Meng et al. (2020)
Resveratrol	<ul style="list-style-type: none"> <li>• Dosage: 300 mg/kg</li> <li>• Period: G<sub>20</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Reduced weaning-related intestinal inflammation (↓ IL-6) and diarrhea (↓ fecal score) of offspring piglets;</li> <li>• Improved intestinal morphology in offspring piglets (↑ villus height, microvillus height, villus/crypt ratio);</li> <li>• Increased the percentage of fecal butyrate-producing bacteria in weaning piglets.</li> </ul>	Meng et al. (2019)
Garcinol	<ul style="list-style-type: none"> <li>• Dosage: 200 and 600 mg/kg</li> <li>• Period: G<sub>90</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved reproductive and lactation performance of sows (↑ litter birth weight, litter weaning weight, litter weight gain, and ↓ piglet mortality during lactation);</li> <li>• Improved plasma antioxidant status of sows (G<sub>100</sub> and L<sub>21</sub>: ↑ T-AOC, GSH-Px, SOD, CAT, ↓ MDA);</li> <li>• Improved milk quality of sows (↑ L<sub>0</sub>: IgG and IgA; ↑ L<sub>17</sub>: protein, IgG and IgA);</li> <li>• Improved serum immunoglobulin levels of suckling piglets (↑ L<sub>14</sub>: IgG and IgA);</li> <li>• Improved acid-base balance in umbilical arterial (UA) and venous (UV) blood of newborns (UA and UV: ↑ pH, base excess, HCO<sub>3</sub><sup>-</sup>, ↓ P<sub>CO2</sub>%).</li> </ul>	Wang et al. (2019a)
Silymarin	<ul style="list-style-type: none"> <li>• Dosage: 40 g/d</li> <li>• Period: G<sub>108</sub>–L<sub>20</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved lactation performance of sows (↑ individual piglet weight at weaning and average daily gain of piglets during lactation);</li> <li>• Improved milk composition of sows (↑ the protein and urea of 18-d milk);</li> <li>• Improved serum antioxidant status and reduced serum inflammation of sows (↑ GSH-Px [L<sub>7</sub>] and CAT [L<sub>18</sub>], ↓ TNF-α [L<sub>7</sub>] and IL-1β [L<sub>18</sub>]).</li> </ul>	Jiang et al. (2020)
Silymarin	<ul style="list-style-type: none"> <li>• Dosage: 12 g/d</li> <li>• Period: G<sub>107</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>• No effect on reproductive performance and colostrum yield of sows;</li> <li>• Reduced offspring litter body weight gain during early postnatal period.</li> </ul>	Loisel et al. (2014)
Silymarin	<ul style="list-style-type: none"> <li>• Dosage: 1 and 8 g/d</li> <li>• Period: G<sub>114</sub>–L<sub>20</sub></li> </ul>	<ul style="list-style-type: none"> <li>• No effects on lactation performance of sows;</li> <li>• No effects on antioxidant status of sows.</li> </ul>	Farmer et al. (2017)
Silymarin	<ul style="list-style-type: none"> <li>• Dosage: 8 g/d</li> <li>• Period: G<sub>90</sub>–G<sub>110</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Reduced circulating prolactin levels of sows at d 94 of pregnancy.</li> </ul>	Farmer et al. (2014)
Hydroxytyrosol	<ul style="list-style-type: none"> <li>• Dosage: 1.5 mg/kg</li> <li>• Period: G<sub>35</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved reproductive performance of sows (↑ individual birth weight, ↓ IUGR rate).</li> </ul>	Vazquez-Gomez et al. (2017)
Hydroxytyrosol	<ul style="list-style-type: none"> <li>• Dosage: 1.5 mg/kg</li> <li>• Period: G<sub>35</sub>–G<sub>100</sub></li> </ul>	<ul style="list-style-type: none"> <li>• No effects on placental gene expression of sows (<i>HIF1A</i>, <i>NOS2</i>, <i>UCP2</i>, <i>VEGFA</i>, <i>SOD1</i>, <i>CAT</i>, and <i>IGF1</i>);</li> <li>• Increased antioxidant status of fetal piglets (↑ T-AOC);</li> <li>• Increased DNA methylation of fetal piglets.</li> </ul>	Garcia-Contreras et al. (2019)

(continued on next page)

Table 1 (continued)

Polyphenols	Supplemental dosage and duration	Main findings	References
Hydroxytyrosol	<ul style="list-style-type: none"> <li>• Dosage: 1.5 mg/kg</li> <li>• Period: G<sub>35</sub>–G<sub>100</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Promoted cell differentiation in brain neurochemistry (affected neurotransmitters profile in brain; modified the process of neuron differentiation in the hippocampal <i>Gyrus Dentatus</i> and <i>Cornu Ammonis</i> areas.</li> </ul>	Yeste et al. (2021)
Hydroxytyrosol	<ul style="list-style-type: none"> <li>• Dosage: 1.5 mg/kg</li> <li>• Period: G<sub>35</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Long-term improved growth performance of offspring pigs (↑ body weight [d 60–180 of age]);</li> <li>• Improved muscle development and adiposity of offspring pigs.</li> </ul>	Vazquez-Gomez et al. (2019)
Hydroxytyrosol (and linseed oil)	<ul style="list-style-type: none"> <li>• Dosage: 1.5 mg/kg (combined with 4% linseed oil)</li> <li>• Period: G<sub>35</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved growth performance of offspring pigs (↑ average daily weight gain);</li> <li>• Improved muscle development and better lipidemic and fatty acid profiles.</li> </ul>	Heras-Molina et al. (2020)
Polyphenols additives	<ul style="list-style-type: none"> <li>• Dosage: 50 (late gestation) and 70 mg/kg (lactation)</li> <li>• Period: G<sub>90</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved antioxidant status of sows at farrowing and weaning (↑ serum SOD, T-AOC, and blood GSH-Px);</li> <li>• Improved antioxidant status of offspring piglets at weaning (↑ serum SOD, T-AOC, retinol, α-tocopherol, and blood GSH-Px).</li> </ul>	Lipiński et al. (2019)
<i>Forsythia suspensa</i> extract	<ul style="list-style-type: none"> <li>• Dosage: 100 mg/kg</li> <li>• Period: G<sub>85</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved reproductive performance of sows (↑ litter birth weight, ↓ stillborn rate);</li> <li>• Elevated nutrients digestibility of sows (↑ gross energy, dry matter, organic matter, crude protein, and ether extracts);</li> <li>• Improved colostrum composition (↑ protein and fat);</li> <li>• Enhanced serum antioxidant status in sow serum at farrowing (↑ GSH-Px), colostrum (↑ T-AOC, SOD, and ↓ MDA), and newborn serum (↑ GSH-Px);</li> <li>• Reduced inflammation in sow serum at farrowing (↓ IL-6, ↑ IL-10), colostrum (↓ IL-6, TNF-α, ↑ IL-10), and piglet serum (↓ IL-6, IL-8).</li> </ul>	Long et al. (2021b)
<i>Moringa Oleifera</i>	<ul style="list-style-type: none"> <li>• Dosage: 4% and 8%</li> <li>• Period: G<sub>14</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved reproductive performance of sows (↓ no. of stillborn and farrowing length);</li> <li>• Improved colostrum composition of sows (↑ protein);</li> <li>• Improved serum antioxidant status of sows (G<sub>60</sub>: ↑ T-AOC, CAT; G<sub>90</sub>: ↑ T-AOC; L<sub>10</sub>: ↑ T-AOC, GSH-Px);</li> <li>• Improved antioxidant status of piglets (L<sub>21</sub>: ↑ CAT).</li> </ul>	Sun et al. (2020)
Grape seed polyphenols	<ul style="list-style-type: none"> <li>• Dosage: 200 and 300 mg/kg</li> <li>• Period: G<sub>80</sub>–L<sub>21</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved reproductive performance of sows (↓ no. of stillborn, ↑ farrowing survival rate and preweaning survival rate);</li> <li>• Improved serum antioxidant status of sows (↑ G<sub>110</sub>: GSH-Px and SOD);</li> <li>• Improved colostrum immunoglobins levels of sows (↑ IgG and IgM).</li> </ul>	Wang et al. (2019b)
Herbal antioxidant additives	<ul style="list-style-type: none"> <li>• Dosage: 580 mg/kg</li> <li>• Period: G<sub>0</sub>–G<sub>112</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved reproductive performance of sows (↑ the no. of piglets born alive, litter birth weight, ↓ low-birth-weight piglet rate);</li> <li>• Enhanced plasma antioxidant status of sows at farrowing (↓ MDA) and newborn piglets (↑ α-tocopherol, T-AOC, and ↓ MDA).</li> </ul>	Parraguez et al. (2021)
<i>Macleaya cordata</i> extracts	<ul style="list-style-type: none"> <li>• Dosage: 500 mg/kg</li> <li>• Period: G<sub>90</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved serum antioxidant status of sows at farrowing and newborn IUGR piglets (sows and piglets: ↑ GSH-Px, SOD, CAT, and ↓ MDA);</li> <li>• Improved immune function in serum of sows at farrowing and newborn IUGR piglets (sows: ↑ IgG, IL-10, IFN-γ, ↓ IL-1β, TNF-α and cortisol; piglets: ↑ IgG, IgM, IL-10, ↓ IL-6, IL-1β, TNF-α and cortisol).</li> </ul>	Li et al. (2022)
<i>Macleaya cordata</i> extracts	<ul style="list-style-type: none"> <li>• Dosage: 500 mg/kg</li> <li>• Period: G<sub>90</sub>–G<sub>114</sub></li> </ul>	<ul style="list-style-type: none"> <li>• Improved serum and hepatic antioxidant status of newborn IUGR piglets (serum and liver: ↑ GSH-Px, SOD, CAT, and ↓ MDA);</li> <li>• Improved immune function in serum and liver of newborn IUGR piglets (serum: ↑ IgG, ↓ IL-1β; Liver: ↓ IL-6, IL-1β, TNF-α).</li> </ul>	Liu et al. (2021)

Table 1 (continued)

Polyphenols	Supplemental dosage and duration	Main findings	References
Sugarcane-derived polyphenols A blend additive	<ul style="list-style-type: none"> <li>• Dosage: 0.5%</li> <li>• Period: G<sub>110±0.2</sub>–L<sub>24.6±0.1</sub></li> <li>• Dosage: not available</li> <li>• Period: G<sub>80</sub>–L<sub>28</sub></li> </ul>	<ul style="list-style-type: none"> <li>• No effects on productivity of gilts;</li> <li>• No effects on inflammation of gilts.</li> <li>• Increased relative weight of stomach of piglets (L<sub>0</sub> and L<sub>28</sub>), and decreased relative weight of small intestine (L<sub>0</sub>);</li> <li>• Increased proteolytic activity and gastric protein level of piglets (L<sub>0</sub>).</li> </ul>	<p>Wijesiriwardana et al. (2020)</p> <p>Zabielski et al. (2007)</p>

↑ = increase; ↓ = decrease; ACC $\alpha$  = acetyl coenzyme A-alpha; ADFI = average daily feed intake; ADG = average daily gain; CAT = catalase; C/EBP $\alpha$  = CCAAT-enhancer-binding proteins gene; FATP1 = fatty acid transport protein; GCLM = glutamate-cysteine ligase modifier; GPx1 = glutathione peroxidase 1; GPx4 = glutathione peroxidase 4; GSH-Px = glutathione peroxidase; HIF1A = hypoxia inducible factor 1 subunit alpha; HO1 = heme oxygenase 1; H<sub>2</sub>O<sub>2</sub> = hydrogen peroxide; IFN- $\gamma$  = interferon- $\gamma$ ; IgA = immunoglobulin A; IGF1 = insulin like growth factor 1; IGF-1R = type 1 insulin like growth factor receptor; IgG = immunoglobulin G; IgM = immunoglobulin M; IL-1 $\beta$  = interleukin-1 $\beta$ ; IL-2 = interleukin-2; IL-6 = interleukin-6; IL-8 = interleukin-8; IL-10 = interleukin-10; IUGR = intrauterine growth restriction; LPL = lipoprotein lipase gene; MDA = malondialdehyde; MGST1 = microsomal glutathione S-transferase 1; MyHC = myosin heavy chain; NF $\kappa$ B = nuclear factor kappa B; NOS2 = nitric oxide synthase 2; Nrf2 = nuclear factor E2-related factor 2; pH<sub>45</sub> = pH measured at 45 min postmortem; pH<sub>end</sub> = pH measured at 24 h postmortem; Sirt1 = sirtuin 1; SNAT1 = sodium-coupled neutral amino acid transporter 1; SOD = superoxide dismutase; SOD1 = superoxide dismutase 1; SOD2 = superoxide dismutase 2; T-AOC = total antioxidant capacity; TNF- $\alpha$  = tumor necrosis factor  $\alpha$ ; UCP2 = uncoupling protein 2; UGT1A1 = UDP glucuronosyl-transferase family 1 member A1; VEGFA = vascular endothelial growth factor A.

<sup>1</sup> G<sub>X</sub> and L<sub>Y</sub> refer to d<sub>X</sub> of gestation and d<sub>Y</sub> of lactation, respectively. For instance, G<sub>85</sub>–L<sub>21</sub> refers to the period from d 85 of pregnancy to d 21 of lactation.

Additionally, the structural similarity analysis of plant polyphenols and the capacity measurement of Nrf2 activation of polyphenols can facilitate the screening of potential polyphenol candidates for gestating sows.

### 3.3. Effects on fetal piglets of sows

#### 3.3.1. Fetal growth and development

An increasing body of evidence suggested that maternal supplementation with plant-derived polyphenols during pregnancy contributed to fetal growth and development (Ren et al., 2001; Fan et al., 2015; Rehfeldt et al., 2007; Vazquez-Gomez et al., 2017; Garcia-Contreras et al., 2019; Xie et al., 2020; Li et al., 2021b). It has been reported that the dietary addition of 200 mg/kg of daidzein during the early pregnancy period significantly augmented the levels of insulin-like growth factor-I (IGF-1) and estrogen, GSH-Px activity in the amniotic fluid, and the number of viable embryos of sows (Xie et al., 2020). More importantly, the supplementation of sow diets with 200 mg/kg of daidzein throughout gestation elevated the serum progesterone and estrogen concentrations at 35 d post-breeding (Li et al., 2021b). Researchers have also observed that the numbers of total born piglets and born alive piglets per litter were elevated owing to the maternal daidzein supplementation during the entire gestation phase (Li et al., 2021b). Additionally, it has been demonstrated that supplementing late-gestating sows with 8 mg/kg of daidzein significantly increased the birth weight of male piglets, increased the survival rate of piglets, and significantly upregulated the mRNA expression of IGF-1R (type 1 insulin-like growth factor receptor) in the skeletal muscle of newborn piglets (Ren et al., 2001). However, the dietary supplementation with 1 mg of daidzein per kg of body weight during late gestation did not affect reproductive performance, including litter size, piglets born, piglet birth weight, or litter weight (Rehfeldt et al., 2007). These results indicate that daidzein may play a key role in embryonic growth and development during early pregnancy. In a study by Fan et al. (2015), the dietary addition of either 200 or 300 mg/kg of catechins from breeding to d 40 of gestation notably augmented the number of piglets born alive, healthy born piglets, and decreased the number of stillborn piglets at farrowing compared to the control group. Garcia-Contreras et al. (2019) illustrated that supplementing sow diets with 1.5 mg/kg of hydroxytyrosol from d 35 to 100 of gestation resulted in higher DNA methylation in fetuses. Furthermore, the dietary supplementation with 1.5 mg/kg hydroxytyrosol from d 35 of gestation until parturition increased the average birth weight of piglets and reduced the number of light piglets (Vazquez-Gomez et al., 2017).

Herbs are important and medicinally valuable sources of plant polyphenols. Sow diets supplemented with plant-derived feed additives rich in polyphenols or polyphenol complexes have also been reported to aid fetal growth and development. In an experiment performed by Wang et al. (2019b), the dietary addition of 300 mg/kg of grape seed polyphenols from d 80 of gestation to d 21 of lactation, significantly lowered the number of dead fetuses and improved the farrowing survival rate. Parraguez et al. (2021) revealed that the dietary addition of 580 mg/kg of herbal antioxidants enriched in polyphenols throughout the gestation period increased the number of live piglets and litter weight at birth, reduced the rate of low-body-weight piglets, and tended to increase the weaning weight. Several plant extracts rich in polyphenols, such as *F. suspensa* extract (Long et al., 2021b) and *Macleaya cordata* extracts (Li et al., 2022), have also been utilized in sow diets. In a study by Long et al. (2021b), feeding sows 100 mg/kg of *F. suspensa* extract during the late pregnancy stage increased the litter birth weight per sow and reduced the number of stillborn piglets per sow and total stillborn rate. Li et al. (2022) fed sows 500 mg/kg of *M. cordata* extracts from d 90 of pregnancy until parturition and found that the farrowing duration of sows decreased significantly. Lipiński et al. (2019) illuminated that dietary supplementation with polyphenols during late pregnancy and lactation increased litter weight at birth and weaning as compared to the control group. As observed by Sun et al. (2020), supplementing sows with either 4% or 8% of *M. oleifera* from 2 weeks pre-breeding until d 21 of lactation significantly decreased the number of stillborn piglets and the farrowing duration. Additionally, Papatsiros et al. (2022) confirmed that dietary supplementation with 5 g/d feed additives enriched in polyphenols notably decreased the number of stillborn piglets, and increased the number of piglets born alive and piglets at weaning. In contrast, Wijesiriwardana et al. (2020) documented that dietary supplementation with 0.5% of sugarcane-derived polyphenols in late gestation/lactation and weaner diets did not improve the reproductive performance of gilts. These discrepancy results may be due to the diverse sources and structural characteristics of plant polyphenols. Although not all polyphenols act as litter growth promoters in maternal diets, they have great potential to be developed into feed for pregnant sows to enhance fetal growth and development.

#### 3.3.2. Effects on the physiological functions of fetal piglets

The maintenance of normal physiological functions in developing embryos and newborn piglets is primarily dependent on maternal nutrition during gestation (Zhang et al., 2019). Recent

studies have shown that the addition of plant polyphenols to the diets of gestating sows can regulate multiple physiological functions of developing embryos and newborn piglets, such as the antioxidant (García-Contreras et al., 2019; Parraguez et al., 2021) and gastrointestinal functions (Zabielski et al., 2007), body composition (García-Contreras et al., 2019), and acid-base balance (Wang et al., 2019a). In terms of antioxidant function, García-Contreras et al. (2019) noted that the dietary addition of 1.5 mg/kg of hydroxytyrosol from d 35 to 100 of gestation augmented the total antioxidant capacity in fetal piglets at d 100 of pregnancy. Similarly, in a study by Parraguez et al. (2021), the dietary inclusion of 580 mg/kg of herbal additives enriched in polyphenols throughout the gestation phase increased the T-AOC and  $\alpha$ -tocopherol contents and lowered the MDA content in the plasma of neonatal piglets. Liu et al. (2021) also observed that the dietary addition of 500 mg/kg of *M. cordata* extracts from d 90 of pregnancy until parturition increased the GSH-Px, CAT, and SOD activities, and reduced the MDA content in both serum and liver of offspring piglets with intrauterine growth retardation (IUGR). Supplementing the maternal diet with polyphenols has also been demonstrated to regulate the gastrointestinal function of neonatal piglets. It has been reported that the dietary addition of a blend additive including linden inflorescence (a source of flavonoids and other antioxidants such as phenolic acids) from d 80 of gestation until lactation increased the relative weight of the stomach at birth and 28 d old and decreased the relative weight of the small intestine of piglets at birth (Zabielski et al., 2007). In addition, the proteolytic activity and gastric protein levels were elevated in newborn piglets owing to the maternal supplementation of bioactive ingredients including linden inflorescence and other phenolic acids (Zabielski et al., 2007). Maternal polyphenol supplementation has been reported to affect the body composition of piglets. García-Contreras et al. (2019) illustrated that feeding sows with 1.5 mg/kg of hydroxytyrosol from d 35 to d 100 of gestation did not affect the length and width of the head, body, and muscle fibers, but reduced the organ weight of the total viscera, pancreas, lungs, liver, and intestines of fetal piglets at d 100 of gestation. In addition, the authors found that supplementing maternal diets with hydroxytyrosol did not affect the lipid metabolism parameters (total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol), but reduced the glycemic parameters including glucose and fructosamine in fetal piglets (García-Contreras et al., 2019). Wang et al. (2019a) demonstrated that the dietary supplementation of 600 mg/kg of garcinol from d 90 of gestation until d 21 of lactation significantly increased the pH, base excess, and  $\text{HCO}_3^-$  values, and decreased the  $\text{PCO}_2\%$  value and lactate levels in both the umbilical venous and arterial blood of newborn piglets. Thus, the supplementation of sow diets with polyphenols can regulate multiple physiological functions of fetal pigs, which may indirectly reflect the beneficial effects of polyphenols on the placenta and partly explain the fetal growth and development improvement.

#### 3.4. Effects on the mammary gland function of sows

The mammary gland is where the sow synthesizes and secretes milk components, including milk fat, lactose, and protein (Chen et al., 2020, 2021a). According to Farmer et al. (2013), 2 g/d of genistein supplementation for 10 d at d 90 of pregnancy significantly elevated the serum genistein concentration on d 95 and 100 of pregnancy but did not influence the concentrations of estradiol and IGF-I in the serum of sows. While supplementing gilts with 2.3 g/d of genistein from 90 d of age until 183 d of age, notably decreased the content of dry matter and estrogen receptors, and increased the protein and DNA content, as well as the histological

score of gilt mammary glands (Farmer et al., 2010). These results suggest that genistein supplementation contributes to the hyperplasia of the mammary parenchymal tissue as well as to mammary gland development (Farmer et al., 2010).

Lactation is an energy-intensive process that generates large amounts of free radicals, and the production of excess free radicals leads to oxidative stress in sows (Kim et al., 2013). It has been reported that oxidative stress is inversely related to the lactation performance of sows (Kim et al., 2013). Polyphenols were shown to enhance the antioxidant function of the mammary glands of sows, as reflected by the antioxidant status of sow colostrum and milk (Meng et al., 2018). In an experiment conducted by Meng et al. (2018), sows that were supplemented with 300 mg/kg of resveratrol from d 20 of gestation until d 21 of lactation, had significantly improved colostrum and milk antioxidant status, as indicated by the increased SOD activity in the colostrum and 14-d milk, the elevated CAT activity in 7- and 21-d milk, the decreased MDA content in 14-d and 21 d milk, and the decreased  $\text{H}_2\text{O}_2$  content in 7- and 21-d milk. Another feeding trial demonstrated that a dosage of 15, 30, and 45 mg/kg of glycitein linearly augmented the GSH-Px activity in the colostrum and the SOD activity in 18-d milk, and lowered the MDA content in 7- and 18-d milk (Hu et al., 2015). Long et al. (2021b) clarified that the dietary addition of 100 mg/kg of *F. suspensa* extract during late pregnancy elevated the T-AOC and SOD activities, and reduced the MDA content in the colostrum of sows.

Polyphenols are beneficial to improving the immune function of the mammary glands of sows, as indicated by the immune status in colostrum and milk, which are important body fluids. Wang et al. (2019a) elucidated that the dietary inclusion of either 200 or 600 mg/kg of garcinol during late pregnancy and lactation elevated the concentration of IgA and IgG in the colostrum and 17-d milk, thereby resulting in higher IgA and IgG concentrations in 14-d-old piglets. Wang et al. (2019b) also found that dietary supplementation with either 200 or 300 mg/kg of grape seed polyphenols from d 80 of gestation until d 21 of lactation increased the IgG and IgM levels in the colostrum of sows. Plant extracts, important sources of polyphenols, have also been shown to improve the immunity status of colostrum and milk in sows. Li et al. (2022) exemplified that dietary addition of 500 mg/kg of *M. cordata* extracts during late pregnancy, increased the colostrum IgG concentration and tended to increase the colostrum IgM concentration. Long et al. (2021b) revealed that supplementing sows with 100 mg/kg of *F. suspensa* extract during late pregnancy tended to increase the IL-10 concentration and decreased IL-6 and TNF- $\alpha$  contents in their colostrum.

Numerous studies have confirmed that the addition of polyphenols to sow diets can affect the nutrient composition of colostrum and milk. Li et al. (2021a) reported that the dietary addition of 10, 20, or 40 mg/kg of soy isoflavones from d 90 of pregnancy until d 21 of lactation tended to linearly increase the protein content in colostrum, and the lactose content in 10-day milk of sows. Hu et al. (2015) also found that supplementing perinatal sows with 15, 30, and 45 mg/kg of glycitein linearly increased the protein content in the colostrum and 7-d milk, the fat content in the colostrum, 7-d milk, and 14-d milk, as well as the lactose content in the colostrum of sows. Similarly, Sun et al. (2019) found that dietary supplementation with 300 mg/kg of resveratrol during gestation and lactation notably elevated the lactose content in the colostrum, the total solid and fat content in 21-d milk. In a study by Jiang et al. (2020), the dietary supplementation with 40 g/day of silymarin from d 108 of pregnancy until d 20 of lactation tended to increase the lactose content in the colostrum, and increased the protein and urea contents in 18-d milk of sows. Furthermore, Long et al. (2021b) confirmed that the dietary supplementation with 100 mg/kg of

*F. suspensa* extract during late pregnancy markedly increased fat and protein contents in the colostrum of sows. Therefore, the addition of polyphenols to sow diets has great potential to promote the antioxidant and immune functions of mammary glands, and ultimately improve the composition of colostrum and milk of sows.

### 3.5. Effects on suckling piglets of sows

#### 3.5.1. Growth performance and development of suckling piglets

Suckling piglets mainly rely on mammary secretions for the nutrients, antioxidants, and immune substances for growth and development. It has been reported that the addition of polyphenols to the diet of gestating and/or lactating sows can significantly improve the growth performance of suckling piglets (Hu et al., 2015; Meng et al., 2018; Wang et al., 2019a; Heras-Molina et al., 2020; Jiang et al., 2020; Li et al., 2021a; Wu et al., 2021). For instance, soy isoflavones have been reported to enhance the growth of suckling piglets in three feeding trials. Li et al. (2021a) exemplified that feeding sows with 10, 20, or 40 mg/kg of soy isoflavones from d 90 of pregnancy until d 21 of lactation linearly increased the body weight of piglets on d 10 and 21 as well as their average daily weight gain during the suckling period, and decreased the estrus interval of sows. In a study conducted by Hu et al. (2015), the dietary supplementation with 15, 30, and 45 mg/kg of glycetein during late gestation and lactation linearly increased the average daily weight gain of suckling piglets and litter weight at weaning. According to Wu et al. (2021), supplementing sows with astragalus polysaccharides and 200 mg/kg of soybean isoflavones during lactation increased their average daily feed intake and total milk yield. As reported by Meng et al. (2018), supplementing sows with 300 mg/kg of resveratrol from d 20 of gestation until d 21 of lactation enhanced the litter weight and individual weight of piglets at weaning. Similarly, Heras-Molina et al. (2020) clarified that the dietary addition of 1.5 mg/kg of hydroxytyrosol and 4% linseed oil from d 35 of gestation until parturition notably elevated the average daily weight gain and feed conversion rate of 15- to 30-d-old piglets. In an experiment performed by Wang et al. (2019a), the dietary inclusion of 600 mg/kg of garcinol from d 90 of gestation until d 21 of lactation increased the litter birth and litter weaning weights, as well as the litter gain during lactation, and decreased piglet mortality. In addition, Jiang et al. (2020) documented that the dietary addition of 40 g/day of silymarin from d 108 of pregnancy to d 20 of lactation notably increased the colostrum yield and average daily feed intake during lactation, decreased the farrowing duration, and increased the individual piglet weight at weaning and average daily weight gain of piglets during lactation. In general, the supplementation of sow diets with polyphenols can improve the growth performance of suckling piglets, which may be related to modifications in the sow colostrum and milk owing to the addition of polyphenols.

#### 3.5.2. Effects on the physiological functions of suckling piglets

Recent studies have reported that supplementing sow diets with polyphenols can have a beneficial effect on the antioxidant function of offspring suckling piglets. Supplementing sows with 300 mg/kg of resveratrol from d 20 of gestation to d 21 of lactation increased the activities of GSH-Px, SOD, and CAT and decreased the MDA content in 21-d-old suckling piglets (Meng et al., 2018). In addition, Lipiński et al. (2019) reported that supplementing sows with polyphenols increased the levels of retinol,  $\alpha$ -tocopherol, T-AOC, and the activities of GSH-Px and SOD in the blood of 21-d-old piglets as compared to the control group. In an experiment by Sun et al. (2020), the dietary inclusion of either 4% or 8% of *M. oleifera* from 2 weeks pre-breeding until d 21 of lactation significantly increased CAT activity in piglets at weaning.

The intestinal morphology and gut microbiota of suckling piglets have also been reported to be positively affected by the addition of polyphenols to sow diets. Most recently, it was shown that supplementing sow diets with 300 mg/kg of resveratrol from d 20 of gestation to d 21 of lactation increased the jejunal villus height and microvillus height as well as the villus height to crypt depth ratio in weaning and post-weaning piglets, thereby resulting in a better average daily weight gain in piglet one week before or after weaning (Meng et al., 2019). In addition, the supplementation of sow diets with 300 mg/kg of resveratrol from d 20 of gestation to d 21 of lactation increased the abundance of *Flavonifactor* and *Escherichia* at the genus level. The supplementation of maternal diets with resveratrol increased the abundance of *Lachnobacterium*, *Oscillibacter*, and *Odoribacter* in the feces of weaning piglets; however, the abundance of these genera decreased in the post-weaning phase (Meng et al., 2019). *Flavonifactor*, *Oscillibacter*, and *Odoribacter* are butyrate-producing bacteria (Meng et al., 2019). However, further studies about the effects of maternal supplementation with polyphenols on suckling piglet intestinal barrier and skeleton functions are warranted in the future, thereby providing a practical guide and a theoretical basis for the application of polyphenols in lactating sow diets.

### 3.6. Effects on long-term growth and development of progeny of sows

Supplementing maternal diets with polyphenols during gestation and/or lactation has been reported to have long-term effects on the growth and development of piglets and finishing pigs (Vazquez-Gomez et al., 2019; Yeste et al., 2021). Rehfeldt et al. (2007) pointed out that the dietary addition of 1 mg of daidzein per kg of body weight from d 85 of gestation to farrowing decreased the proportions of muscle tissue and increased the percentage of the skin of piglets from litters with at least 15 litter sizes in sows. Although the growth and carcass composition of 180-d-old pigs were unaffected by maternal daidzein supplementation, the pH<sub>45</sub> and pH<sub>end</sub> in pigs from large litters increased. Moreover, the percentage of fast-twitch glycolytic fibers in the semi-tendinous muscle was elevated due to the maternal daidzein supplementation (Rehfeldt et al., 2007). Ren et al. (2001) revealed that supplementing late-gestating sows with 8 mg/kg of daidzein markedly upregulated the mRNA expression of *IGF-1R*. Maternal supplementation with 300 mg/kg resveratrol from d 20 of gestation to d 21 of lactation elevated the backfat thickness and intramuscular fat of offspring finishing pigs (Meng et al., 2020). Additionally, the inclusion of resveratrol in maternal diets increased the pH<sub>24h</sub> and SOD activity of the longissimus thoracis and decreased the lactic acid and drip loss, and MDA content in the longissimus thoracis of finishing pigs (Meng et al., 2020). The maternal supplementation with resveratrol upregulated the protein expression of MyHC I and the mRNA expression of *MyHC I* and *PGC1 $\alpha$* , and downregulated the mRNA expression of *MyHC IIX* in the longissimus thoracis of pigs at the market weight (Meng et al., 2020). In a study performed by Vazquez-Gomez et al. (2019), the dietary supplementation with 1.5 mg/kg of hydroxytyrosol from d 35 of gestation until parturition markedly increased the average daily weight gain and body weight of 60-d-old or older pigs. According to Heras-Molina et al. (2020), the combined supplementation with 1.5 mg/kg of hydroxytyrosol and 4% of linseed oil from d 35 of gestation until parturition increased the absolute and relative organ weights of the adrenal glands and spleen as well as the intramuscular fat content in the longissimus dorsi of 180-d-old pigs. Heras-Molina et al. (2020) reported that the dietary inclusion of 1.5 mg/kg of hydroxytyrosol and 4% of linseed oil from d 35 of gestation until parturition decreased the concentrations of LDL-

cholesterol and HDL-cholesterol in the plasma of 120-, 150-, and 180-d-old pigs. Heras-Molina et al. (2020) also found that maternal supplementation with 1.5 mg/kg of hydroxytyrosol and 4% of linseed oil from d 35 of gestation until parturition affected the fatty acid composition of the liver, subcutaneous fat, and longissimus dorsi muscle of 60- and 180-d-old pigs. Therefore, the addition of polyphenols to sow diets is an effective way to improve the growth performance and meat quality of finishing pigs. However, there is still a lot of research needed to be conducted to investigate the long-term effects of maternal nutrition on the growth and development of offspring pigs, especially for offspring during the growing and finishing phases.

#### 4. Conclusions

The chemical structure of polyphenols is characterized by the presence of phenyl rings and two or more hydroxyl substituents, which make polyphenols perfect radical scavengers. Plant-derived polyphenols and feed additives rich in polyphenols are natural robust antioxidants that can serve as potential functional additives suitable for gestating and lactating sows. Several researchers have confirmed that polyphenols have great potential to improve the antioxidant capacity and alleviate oxidative stress in sows. Furthermore, polyphenols can beneficially regulate the placenta and mammary glands of sows, thus resulting in better growth, development, and physiological functions of offspring pigs. In light of current findings, the development and application of polyphenols is an emerging and promising direction for future research in sow nutrition.

#### Author contributions

**Wutai Guan** and **Jinming You**: Conceptualization; **Tiande Zou**: Validation; **Jun Chen**: Writing-original draft preparation; **Zhouyin Huang** and **Xuehai Cao**: Writing-review and editing; **Jun Chen**: Funding acquisition.

#### Declaration of competing interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, and there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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