Animal Nutrition 20 (2025) 239–248

Contents lists available at ScienceDirect

Animal Nutrition

journal homepage: http://www.keaipublishing.com/en/journals/aninu/

Review Article

Research advances in *Pimpinella thellungiana*: Nutrients, bioactive compounds, and functional properties benefitting livestock

Shuxian Zhang [a], Minglu Yang [b], Tao Xu [a], Qiongxian Yan [c], Allan Degen [d], Xiaoling Zhou [a, *]

[a] College of Animal Science and Technology, Tarim University, Key Laboratory of Livestock and Forage Resources Utilization Around Tarim in Ministry of Agriculture and Rural Affairs, Alaer 843300, China
[b] College of Agriculture, Tarim University, Alaer 843300, China
[c] Institute of Subtropical Agriculture, The Chinese Academy of Sciences, Changsha 410125, China
[d] Desert Animal Adaptations and Husbandry, Wyler Department of Dryland Agriculture, Blaustein Institutes for Desert Research, Ben-Gurion University of the Negev, Beer Sheva 8410500, Israel

ARTICLE INFO

Article history:
Received 17 July 2023
Received in revised form
7 November 2024
Accepted 17 November 2024
Available online 28 November 2024

Keywords:
Pimpinella thellungiana H. Wolff
Nutrition and metabolism
Bioactive compound and function
Pharmacological value
Growth retardation
Overexertion

ABSTRACT

Growth retardation affects the health and production of livestock, while overexertion can cause sudden cardiac arrest. Both cases are considered to be metabolic disorders and are detrimental to livestock production. Effective measures for relieving or treating these disorders are scarce. However, *Pimpinella thellungiana* H. Wolff (*P. thellungiana*), a medicinal herb, has been reported to relieve growth retardation and overexertion in ethnopharmacological clinical trials. This paper summarizes and classifies a total of 106 bioactive compounds that were isolated and identified from *P. thellungiana*, including flavonoids, simple phenylpropanoids, coumarins, volatile compounds, and simple polyphenols, and discusses its pharmaceutical benefits, including its growth-promoting, antioxidant, anti-inflammatory, anti-atherosclerotic, and hepatoprotective properties. The nutrition, metabolism, biological activities, and pharmacological effects of the principal compounds of *P. thellungiana* in livestock are reviewed, as well as their potential molecular targets and metabolic signaling pathways in which these compounds are involved. However, the pharmacological and toxicological effects of some compounds have not been well documented, and further investigations of the bioactive compounds are needed. Such studies are crucial for the development of natural drugs or feed additives from *P. thellungiana* to alleviate growth retardation and mitigate injuries from overexertion in livestock.

1. Introduction

With the increasing demand for high production in livestock, growth retardation and overexertion are occurring more frequently. Growth retardation is defined as delayed or arrested growth during early life due to malnutrition or diseases (Kyle et al., 2015; Tang and Xiong, 2022). Overexertion is a sub-health state triggered by prolonged working hours and excessive work intensity, which leads to obstinate or persistent metabolic disorders in various organs, and is considered the primary cause of sudden cardiac arrest (Kyle et al., 2015). These two pathological conditions are characterized by metabolic disorders (Kobayashi et al., 2012; Rachakatla and Kalashikam, 2022), a weakened immune system (Ervasti et al., 2021), wasting, inflammation, oxidative stress, and gastrointestinal microbiota imbalance (Lee et al., 2021, 2022). Most stress-induced metabolic changes are short term and can be cured by reducing stress or by temporary pharmacological intervention, but metabolic abnormalities caused by growth retardation and overwork persist after the stress fades (Kyle et al., 2015; Tang and Xiong, 2022). With increasing concerns for growth retardation

* Corresponding author.
E-mail address: zxldky@126.com (X. Zhou).
Peer review under the responsibility of Chinese Association of Animal Science and Veterinary Medicine.

Production and Hosting by Elsevier on behalf of KeAi

https://doi.org/10.1016/j.aninu.2024.11.005

and overexertion, there is an urgent need to address these complex metabolic disorders, as effective intervention measures for these disorders are currently lacking.

Pimpinella thellungiana H. Wolff (*P. thellungiana*) belongs to the family Umbelliferae. The genus *Pimpinella* encompasses approximately 150 species that are distributed worldwide (Fernández Prieto et al., 2018). These plants have been used as medicines for more than 1700 years to treat gastrointestinal dysfunction, respiratory diseases and kidney ailments, as well as for deworming livestock (Fernández Prieto et al., 2018; Sun et al., 2019; Tepe and Tepe, 2015; Wu et al., 2023). In China, *P. thellungiana*, known as "Yang Hong Shan" and "Liu Yue Han", is used for treating sexual dysfunction, and improving the cardiovascular system, lipid metabolism, immunity system, growth, and development. In addition, *P. thellungiana* can effectively alleviate growth retardation and injuries due to overexertion in livestock. In recent years, *P. thellungiana* has attracted increasing interest from researchers and pharmacologists. However, the bioactive ingredients, efficacy, and application of *P. thellungiana* in livestock have not been fully analyzed or widely reported (Hui et al., 2023).

Based on databases including Web of Science (1900 to July 2024), PubMed, Europe PMC, CNKI (1972 to July 2024), Ovid (1970 to July 2024), Agricola (from 1970 to July 2024), ProQuest (1946 to now), ScienceDirect, Springer Link, Worldlib, and Google Scholar, the keywords of "*Pimpinella*" and "*thellungiana*" were used to search the literature. After duplicates were removed, a total of 62 publications were accepted as appropriate. This paper reviews the botanical properties, medicinal values, progress in pharmacological research, key bioactive compounds and functions, and action mechanisms of *P. thellungiana*.

2. Botanical properties

P. thellungiana is widespread in Asia, predominantly in northern China, the Russian Far East, Mongolia, and Japan, and thrives at elevations ranging from 600 to 1700 m. It is a perennial herbaceous plant that grows to a height of 30 to 80 cm, and occurs commonly along rivers, on grassy slopes in forests, and among shrubs. This plant features a red-colored stem and oblong-ovate leaves with one pinnate and three to eight pairs of pinnae. The common name of *P. thellungiana* in Chinese, Yang Hong Shan, originated from the red color of its stem and the distinct pungent aroma resembling the smell of mutton when the root bark is torn (Hong, 2010). The umbels are 4 to 6 cm wide; the petals are white, ovate or obovate, with an incurved lobule at the apex; and the fruits are oblong-ovoid and measure approximately 3 mm × 2 mm (Fig. 1). The root or the whole plant of *P. thellungiana* is used as medicine.

3. Medicinal properties

The herb of *P. thellungiana* is harvested at two times of the year: most commonly during late spring and early summer for roots and/or shoots; and late autumn for roots, stems, leaves, flowers, and/or seeds (Yuan, 1979). This herb is either ground into powder and administered orally or distilled and extracted with water to form a 1:1 solution and is injected intramuscularly or intravenously (Yuan, 1979). Occasionally, it is prepared as a compound preparation, or the total flavonoids are extracted from the whole plant and injected intramuscularly or intravenously as a 3% flavonoid solution.

P. thellungiana has been used as a Chinese medicine for many decades, mainly for heart, kidney, lung, and spleen disorders (Liu et al., 2014). In animal husbandry, livestock wasting, growth retardation, and sexual dysfunction caused by malnutrition and overexertion are of high incidence. In Northern China, *P. thellungiana* is used commonly by farmers and veterinarians for fattening and treatment of growth retardation in cattle, sheep, and pigs (Yuan, 1979). Ten horses with weak spleen functions and diarrhea were cured with root powder of *P. thellungiana* at 0.75 g/kg BW (Yuan, 1979). In pigs (6–13 months old, 9.5–27.3 kg) suffering from prolonged growth retardation caused by malnutrition, a supplement of 30 to 50 g/d whole plant powder of *P. thellungiana* every two days for 10 days in two courses increased weight gain by up to 62% and weight-to-feed ratio by 40%, and, concomitantly, decreased white blood cell count and death rate (Animal Husbandry and Veterinary Science and Technology Cooperation Group in Shaanxi Weinan Area, 1976). *P. thellungiana* can alleviate injury due to overexertion and weight loss in livestock, and improve appetite and digestibility. For example, 34 of 35 pigs (97.1%) were cured of dyspepsia when treated daily with a *P. thellungiana* injection of 0.35 to 0.40 mL/kg body weight (BW) for 5 days (extracted and distilled with water to form a 1:1 injection liquid) (Yuan, 1979). In 41 sows with poor appetite after farrowing, 37 (90.2%) were cured or improved with the same dosage of *P. thellungiana* (Yuan, 1979). In 35 piglets with white dysentery symptoms caused by *Escherichia coli*, 33 (94.3%) were cured by an intramuscular injection of 3 to 5 mL solution (extracted from *P. thellungiana* and distilled with water to form a 1:1 injection liquid) twice daily for three days (Livestock Veterinary Work Station of Baishui County in Shaanxi Province, 1977). In addition, in a larger study of 642 piglets with white dysentery symptoms, 633 (98.5%) were cured with the above 1:1 liquid injection of *P. thellungiana* at 0.35 to 0.40 mL/kg BW (Yuan, 1979).

P. thellungiana also promotes gonadotropin secretion and improves reproductive performance in livestock. A dosage of 0.75 g/kg BW of *P. thellungiana* whole plant administered every two day for

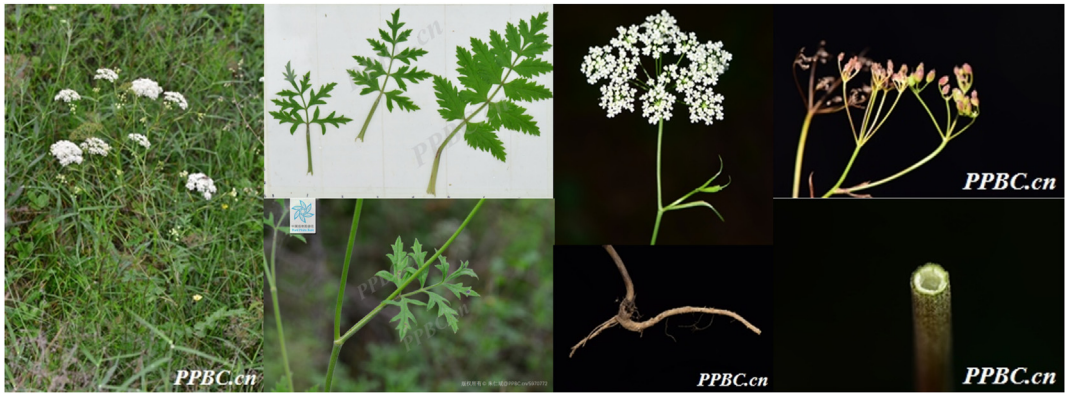

Fig. 1. Morphological characteristics of *P. thellungiana* (photo credit: Plant Photo Bank of China, http://ppbc.iplant.cn/).

10 days cured ovarian diseases in 146 mares and jennies (cure rate 87.0%), and the same dosage daily for 5 days induced reproductive behavior in 61 mares, jennies, and cows (cure rate 91.8%) (Yuan et al., 1979). A cure rate of 76.9% was reported in mares and jennies with ovarian diseases treated with 0.75 g/kg BW plant powder of *P. thellungiana* every other day for 10 days (Animal Husbandry and Veterinary Science and Technology Cooperation Group in Shaanxi Weinan Area, 1977). An intravenous injection of 0.35 to 0.40 mL/kg BW (extracted from *P. thellungiana* and distilled with water to form a 1:1 injection liquid) once daily for 5 days was effective in treating ovarian quiescence and atrophy in 15 cows (Yuan et al., 1981).

P. thellungiana is used widely in China in the treatment of injuries due to overexertion, weight loss, and growth retardation in livestock, and it strengthens the spleen and stomach and improves appetite and digestion. These effects are closely related to the chemical composition, especially of flavonoids. The effective dosage administered ranges between 0.3 and 0.5 g/kg BW of air-dried whole plant of *P. thellungiana*.

4. Progress in pharmacological research

P.thellungiana is distributed widely in China and has been used extensively in clinical trials. According to pharmacological studies by the Shaanxi Academy of Traditional Chinese Medicine, the alcoholic extract of *P. thellungiana* dilates coronary arteries, lowers coronary resistance, and reduces myocardial oxygen consumption (Miao et al., 1982). This hypotensive effect was attributed to histamine release and vasodilatation, irrelevant to sympathetic ganglion, M-cholinergic system, adrenergic system, and intravascular receptors (Chen et al., 1982). The flavonoid glycosides isolated from *P. thellungiana* enhances the activities of succinic acid dehydrogenase in the myocardium and brain tissues, reduces myocardial oxygen consumption, and improves hypoxia tolerance (Xu et al., 1994). *P. thellungiana* also reduces the elevation of blood triglycerides and the incidence of liver steatosis (Shen et al., 1982).

P. thellungiana increases physical strength, hypoxia tolerance, and endurance during exercise in animals (Shen et al., 1982). Moreover, it alleviates dexamethasone-induced DNA synthesis inhibition in muscle tissue, and, therefore, promotes muscle protein renewal, growth and development (Wei et al., 1986)In addition, *P. thellungiana* protects against *p*-aminophenol-induced liver injury in mice (Wang and Wen, 2022), which is attributed to its potent antioxidant, anti-inflammatory, and hepatoprotective properties.

Studies have concluded that the whole plant of *P. thellungiana* lowers blood pressure and blood lipids, dilates coronary arteries, provides antioxidant protection, and improves immune function, which benefits mainly striated muscles (cardiac and skeletal muscles), liver, spleen, female reproductive organs, and blood vessels. No side effect has been detected with the administration of *P. thellungiana*, but future studies on long-term safety, residues, and toxicity risks are required.

5. Nutrients, bioactive compounds, and function

5.1. Nutritional composition

Nutrient contents of *P. thellungiana* and their effects on digestion and metabolism have not been reported. We measured that the whole plant of *P. thellungiana* contained 12.4% crude protein (CP), 65.0% neutral detergent fiber (NDF) and 42.1% acid detergent fiber (ADF) on a dry matter (DM) basis (Table 1). Therefore, it could be classified as roughage. In addition, the in vivo digestibility measured in donkeys using the nylon bag technique was 52.2% (unpublished data).

Table 1
Composition of the whole plant of *P. thellungiana* (DM basis).

Item	DM	CP	NDF	ADF	EE	CA
Content, %	90.7	12.4	65.0	42.1	3.49	14.6
SD	0.02	0.06	0.73	0.86	0.26	0.09

DM = dry matter; CP = crude protein; NDF = neutral detergent fiber; ADF = acid detergent fiber; EE = ether extract; CA = crude ash; SD = standard deviation.

5.2. Composition of bioactive compounds

Pimpinella plants contain mainly bioactive constituents of terpenoids, flavonoids, coumarins, sterols, and fatty acids. At present, 106 bioactive compounds have been identified in *P. thellungiana* (Table S1), including 20 volatile components (six sesquiterpenes and 14 low-molecular-weight volatile organic compounds [VOCs]), 34 simple phenylpropanoids (including 27 phenylpropanoic acids and their esters), 13 simple phenols and organic acids, 24 flavonoids, 10 coumarins, and five lipids and phytosterols. Among these, nine chemicals listed in Table 2 have been selected as the characteristic compounds of *P. thellungiana* (Cui et al., 2022).

The concentrations of major bioactive components in *P. thellungiana* are summarized in Table 3. Luteolin-7-O-β-D-glucuronide (L7GD), apigenin-7-O-β-D-glucuronide (A7GD) and chlorogenic acid (CGA) are most abundant in the whole plant, followed by isochlorogenic acid A, schaftoside, isochlorogenic acid C, quercetin-3-O-β-D-glucuronide (Q3GD) (Cui et al., 2020; Liu et al., 2017b, 2020d). The concentrations of these compounds vary greatly among plant parts. For example, the concentrations of L7GD, A7GD, and CGA were highest in the leaves, followed by the stems, and lowest in the roots (Cui et al., 2019). Generally, the concentrations of L7GD and A7GD range between 3.73 and 5.64 mg/g (air-dry basis) (Cui et al., 2019; Liu et al., 2017b, 2020d), but their concentrations also differ greatly among studies (Cui et al., 2020; Liu et al., 2020d). The different methods of measurements could explain, at least in part, these differences (such as, test wavelength 325 nm vs. 345 nm). Thus, a standard harvesting and analytical procedure is strongly recommended.

In addition, 28 compounds were isolated from volatile oil, accounting for 0.36% of the total root weight, and these compounds were dominated by 2,6-dimethyl-6-allylphenol (>37%) and 2-methyl butyric acid (>10%) (Wang et al., 1988). A unique group of compounds was identified in the volatile oil extracted from the roots of *P. thellungiana*, including the llungianin A to H (Li et al., 1998; Qiao et al., 1997, 1998a,b, 1999, 2000), 1-butyl-3,4,5-trihydroxy-cyclohexanol (Xue et al., 1998), and 3-methoxy-5-(1′-ethoxy-2′-hydroxypropyl)-phenic acid (Wang et al., 1983). These compounds have not been reported in other plant species. Thellungianin A, B, E, F, and G are derivatives of pseudo-isoeugenol, which was identified exclusively in the *Pimpinella* genus (Reichling et al., 1995). These bioactive compounds may be responsible for the distinct effects of *P. thellungiana*.

Overall, *P. thellungiana* contains high levels of A7GD, L7GD, CGA and isochlorogenic acid A, followed by schaftoside, isochlorogenic acid C, and Q3GD, which are discussed below.

5.3. Functions of principle bioactive compounds

5.3.1. Apigenin and A7GD

The bioactive component A7GD, also known as scutellarin A or apigenin-7-glucuronide, is a natural derivative of apigenin (4′,5,7-trihydroxyflavone) (Wang et al., 2019). In addition to A7GD, the apigenin glycosides identified in *P. thellungiana* include apigenin-7-O-glucoside, apigenin-7-O-glucuronide-6″methyl ester, and

Table 2
List of 9 main compounds in *P. thellungiana*.

No.	Common name	Chemical name	CAS no.	Formula
1	Protocatechuic acid	3,4-Dihydroxybenzoic acid	99-50-3	$C_7H_6O_4$
2	Neochlorogenic acid	5-Caffeoylquinicacid	906-33-2	$C_{16}H_{18}O_9$
3	Chlorogenic acid	3-Caffeoylquinicacid	327-97-9	$C_{16}H_{18}O_9$
4	Cryptochlorogenic acid	4-O-Caffeoylquinic acid	905-99-7	$C_{16}H_{18}O_9$
5	Luteoloside	Luteolin-7-O-glucoside	1268798	$C_{21}H_{20}O_{11}$
6	3,5-Dicaffeoylquinic acid	3,5-O-Dicaffeoylquinic acid	89919-62-0	$C_{25}H_{24}O_{12}$
7	Isochlorogenic acid C	4,5-Di-O-Caffeoylquinic acid	57378-72-0	$C_{25}H_{24}O_{12}$
8	Cosmosiin	Apigenin-7-O-β-D-glucopyranoside, apigenin-7-O-β-D-glucoside, apigenin-7-O-glucoside	578-74-5	$C_{21}H_{20}O_{10}$
9	Isochlorogenic acid A	3,5-Di-O-Caffeoylquinic acid	2450-53-5	$C_{25}H_{24}O_{12}$

Table 3
The concentrations of the main compounds in *P. thellungiana*.

Item	Concentration, mg/g (air-dry basis)					
Luteolin-7-O-β-D-glucuronide	3.73–4.69	3.88–4.62	0.13–0.78	3.80–4.82	0.04–0.13	0.23–1.79
Apigenin-7-O-β-D-glucuronide	4.42–5.64	3.81–4.01	0.07–0.78	3.62–4.92	0.02–0.11	0.59–1.45
Chlorogenic acid	3.28–6.02	–	0.06–0.40	2.14–2.78	0.42–0.72	0.75–1.22
Isochlorogenic acid A	3.67–5.38	–	0.07–0.45	2.06–3.64	0.12–0.28	0.79–1.33
Isochlorogenic acid C	1.35–1.72	–	0.04–0.19	1.58–2.25	0.10–0.20	0.13–0.67
Quercetin-3-O-β-D-glucuronide	1.02–1.29	–	–	–	–	–
Neochlorogenic acid	0.51–0.88	–	0.01–0.04	0.28–0.37	0.02–0.06	0.07–0.15
Cryptochlorogenic acid	0.44–1.02	–	0.01–0.05	0.35–0.52	0.04–0.06	0.11–0.20
Isochlorogenic acid B	0.21–0.37	–	0.05–0.14	–	–	–
Schaftoside	–	–	0.19–0.85	–	–	–
Protocatechuic acid	–	–	0.01–0.32	0.13–1.10	0.06–0.13	0.15–1.29
Gallic acid	–	–	–	0.06–0.31	0.04–0.07	0.03–0.14
Sample type	Whole plant	Whole plant	Whole plant	Leaf	Root	Stem
Reference	Liu et al. (2020d)	Liu et al. (2017b)	Cui et al. (2020)	Cui et al. (2019)	Cui et al. (2019)	Cui et al. (2019)

" - " indicates that it was measured.

apigenin-7-O-butylglucuronide. Their chemical structures are presented in Fig. 2.

Flavonoid aglycones such as apigenin, luteolin, are typically insoluble or poorly soluble in water, but their water solubility increases upon glycosylation. Flavonoid glycosides undergo hydrolysis by brush border hydrolases in the small intestine (e.g., epithelial β-glucosidase) or by ruminal and colonic microorganisms in livestock (Hostetler et al., 2017). Alternatively, they can be transported into enterocytes via sodium-dependent glucose transporters, where the glycosyl moiety is hydrolyzed by β-glucosidase. Following the cleavage of the glycosyl moiety, flavonoid aglycones undergo various coupling reactions, such as glucuronidation, sulfonation, or methylation, in intestinal cells and the liver. As a result, most flavonoids in plasma and urine exist in conjugated forms rather than as aglycones (Hostetler et al., 2017).

Apigenin and its glycosides possess antioxidant (Kashyap et al., 2022), anti-inflammatory (Ha et al., 2022), anti-apoptotic, and anti-autophagy effects (Liu et al., 2020b). Apigenin-7-O-β-D-glucuronide exhibits anti-tumor, blood pressure-lowering, and matrix metalloproteinase-inhibiting activities (Liu et al., 2020b), and was reported to inhibit the uptake of oxidized low-density lipoprotein by macrophages and the intracellular accumulation of triglycerides (Ma et al., 2017). Of note, in skeletal muscle cells, apigenin promotes glucose uptake and protein synthesis through the mechanistic target of rapamycin (mTOR) complex 1 pathway (Xu et al., 2022), and stimulates skeletal muscle hypertrophy and myogenic differentiation via the protein arginine methyltransferase 7 (Prmt7)/peroxisome proliferator-activated receptor-gamma coactivator -1 alpha (PGC-1α)/G-protein-coupled receptor 56 (GPR56) and Prmt7/p38 mitogen-activated protein kinases (p38)/myogenic differentiation 1 (MyoD) pathways (Jang et al., 2017). Additionally, it mitigates age-related skeletal muscle atrophy by reducing oxidative stress and inhibiting hyperactive autophagy and apoptosis (Wang et al., 2020).

Among bioactive compounds of *P. thellungiana*, the concentrations of apigenin glycosides are relatively high, especially of A7GD which ranges between 3.62 and 5.6 mg/g. This serves as the biochemical basis of *P. thellungiana* in alleviating atherosclerosis and promoting muscle growth in individuals with growth restriction. However, reports on the effects of apigenin or its glycosides on nutrient digestion, production, or quality of animal products in pigs, cattle and/or equine are lacking.

5.3.2. Luteolin and L7GD

Luteolin and its glycosides identified in *P. thellungiana* include luteolin, luteolin-7-O-glucoside, L7GD, L7GD-6″-methyl ester, and luteolin-7-O-rutinoside (Fig. 2). The digestion, metabolism and absorption of luteolin glycosides are similar to those of apigenin glycosides. Luteolin and its glycosides exhibit mainly antioxidant, anti-inflammatory, antitussive and expectorant properties, and protect from acute liver injury (Muruganathan et al., 2022), and reduce hypertension (Gao et al., 2023). The mechanisms of luteolin are related closely to proto-oncogene C-Src (Src)/nuclear factor-κB (NF-κB) pathway, mitogen-activated protein kinase (MAPK)/activator protein-1 (AP-1) pathway, suppressor of cytokine signaling 3 (SOCS3)/ signal transducer and transcription activator (STAT) 3 pathway (Aziz et al., 2018), and the signaling pathways mediated by Janus kinase (JAK)/STAT, Notch, mTOR, and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) (Farooqi et al., 2020). In livestock, luteolin inhibits replication of the African swine fever virus by regulating the NF-κB/STAT3/activating transcription factor 6 (ATF6) (Chen et al., 2022b). Few reports on the effects of luteolin and its glycosides on nutrient digestion and performance in livestock have been published. Recently, it was reported that luteolin displays inhibitory and bactericidal activities against multidrug-resistant *Staphylococcus aureus* isolated from dairy goats (Liu et al., 2023).

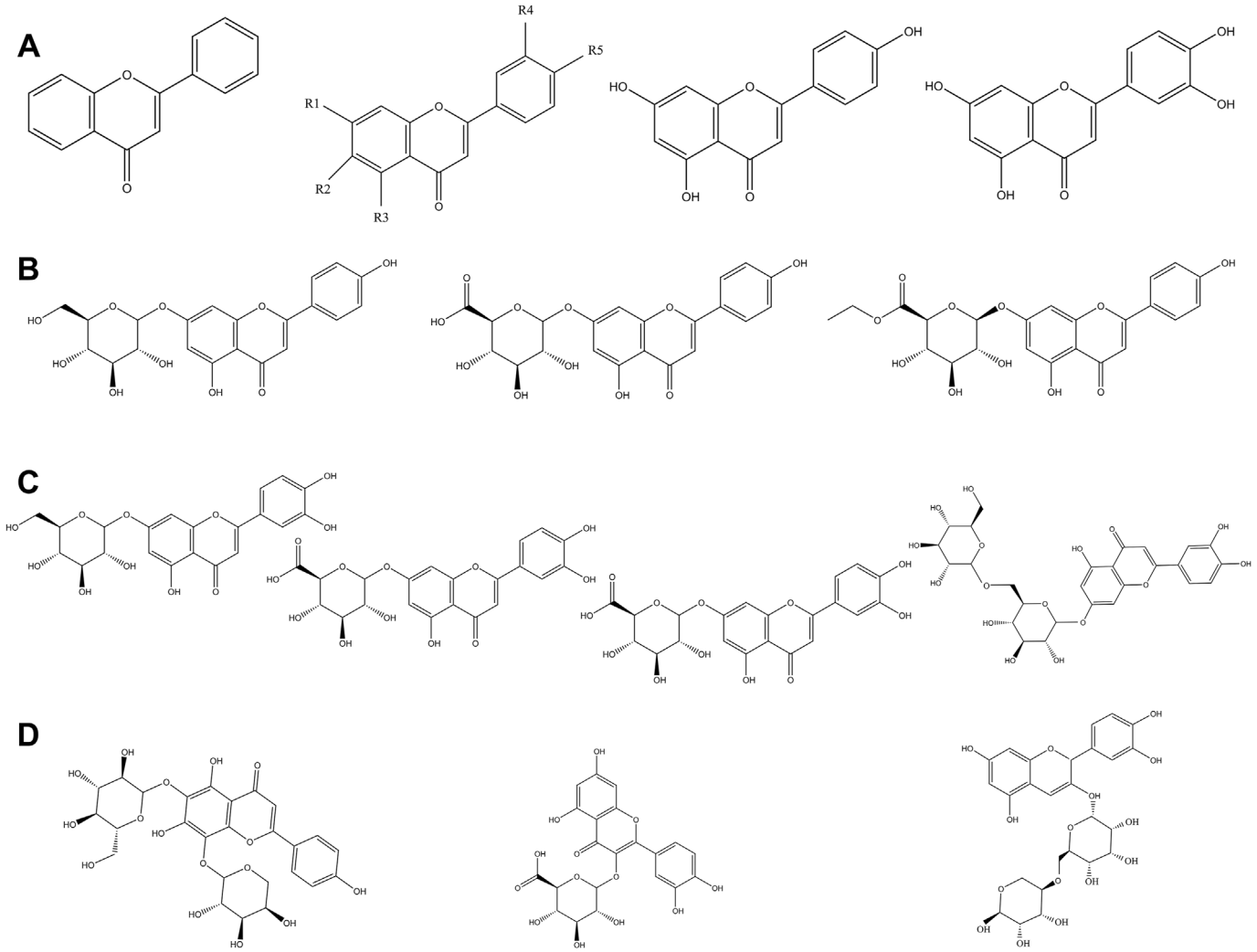

Fig. 2. Chemical structures of flavonoids and their glycosides in *P. thellungiana*. (A) From left to right: flavonoid, flavone, apigenin, and luteolin. (B) From left to right: apigenin-7-O-glucoside, apigenin-7-O-glucuronide, and apigenin-7-O-glucuronide-6″-methyl ester. (C) From left to right: luteolin-7-O-glucoside, luteolin-7-O-glucuronide, luteolin-7-O-glucuronide-6″-methyl ester, and luteolin-7-O-rutinoside. (D) From left to right: quercetin 3-O-glucuronide, and quercetin 3-O-rutinoside.

L7GD, known as luteolin-7-O-glucuronide or luteolin 7-O-β-D-glucosiduronic acid, is the most abundant luteolin glycoside in *P. thellungiana*, with concentrations ranging from 3.7 to 4.8 mg/g (Table 3). Its antioxidative activity is greater than that of luteolin (Min et al., 2006). Its antioxidant and anti-inflammatory activities are exerted by inhibiting the production of NO and pro-inflammatory cytokines (Ma et al., 2018), while its role in inhibiting matrix metalloproteinase activity (Ende and Gebhardt, 2004) is associated with the O atom at position 4 of the carbonyl group in the luteolin molecule (Zhang et al., 2012). Furthermore, L7GD displays therapeutic potential for alleviating stress due to sleep deprivation by activating the brain derived neurotrophic factor (BDNF) signaling pathway (Ryu et al., 2022). The high concentrations of luteolin and its glycosides in *P. thellungiana* are suggested to be the main reason for the beneficial properties of *P. thellungiana*.

5.3.3. Schaftoside

Schaftoside, known as apigenin-6-glucoside-8-arabinoside, is a trihydroxyflavone derived from apigenin (Fig. 2). It exhibits anti-nematodal, antioxidant, and anti-inflammatory activities (Yi et al., 2022), and enhances autophagy, and reduces apoptosis and inflammation. In addition, Schaftoside mitigates cerebral ischemia–reperfusion injury through the AMP-activated protein kinase/mTOR signaling pathway (Zhang et al., 2022), and acetaminophen-induced hepatotoxicity by activating farnesol X receptors (Liu et al., 2020a). Schaftoside also prevents cholesterol gallstone formation, at least in mice, by activating ileal liver X receptor α and hepatic farnesoid X receptor (Liu et al., 2017a), and treats calcium oxalate stones in kidneys (Liu et al., 2020c). However, the effects of schaftoside on nutrient digestion, performance, and product quality of livestock are unknown.

5.3.4. Quercetin glycosides

Two quercetin glycosides have been identified in *P. thellungiana*: Q3GD and quercetin 3-O-rutinoside (also called rutin or vitamin P). The digestion and absorption of Q3GD are similar to apigenin or luteolin glycosides, and it is eventually excreted in urine (Li et al., 2016). Quercetin-3-O-β-D-glucuronide is more readily absorbed than rutin (Li et al., 2016). The bioactivities of quercetin have been reviewed comprehensively (Li et al., 2016; Yang et al., 2020). Quercetin-3-O-β-D-glucuronide is the main active form in plasma and tissues following the oral administration of quercetin (Yang et al., 2016), while rutin is derived from quercetin through the replacement of the hydroxyl group at the C-3 position with glucose

and rhamnose. Thus, their bioactive functions are similar to that of quercetin, which are exerted mainly through the Wnt−β-catenin pathway, the tumor suppressor p53 (p53)-independent pathway, and the phosphoinositide 3-kinase (PI3K)/Akt, JAK/STAT, MAPK, p53, and NF-κB signaling pathways (Imani et al., 2021).

Quercetin or rutin was studied extensively in livestock, and approved as a safe and natural antioxidant in feed (Yang et al., 2020). In ruminants, quercetin is degraded rapidly into 3,4-dihydroxyphenylacetic acid and 4-methylcatechol in the rumen (Berger et al., 2015; Guo et al., 2021), but the absolute bioavailabilities of quercetin aglycone and rutin after intraruminal or oral application were only 0.1% and 0.5%, respectively (Berger et al., 2012; Wein et al., 2018). Supplementation with quercetin or rutin does not affect the ruminal microbes or fermentation (Berger et al., 2015). In cattle and goats, quercetin alleviates oxidative stress and inflammation of rumen epithelial cells induced by lipopolysaccharide or high-grain feed (Jiang et al., 2023; Zhan et al., 2024). Quercetin treats bacterial bovine mastitis (Disbanchong et al., 2021), prevents bovine viral diarrhea (Chen et al., 2022a), reduces liver damage in periparturient dairy cows (Stoldt et al., 2015), and exhibits anti-apoptotic effects in sheep (Ding et al., 2022).

Rutin regulates energy metabolism (Stoldt et al., 2016), increases milk yield, and enhances rumen fermentation and nitrogen metabolism in dairy cows (Cui et al., 2015), and improves meat quality in sheep (Zhan et al., 2023). In addition, rutin and isoquercetin from mulberry leaves improve growth performance, inhibit fat synthesis, and improve fatty acid distribution and nutritional quality in finishing pigs (Liu et al., 2024). Quercetin improves reproduction by enhancing the quality of bovine oocytes (Davoodian et al., 2022), alleviates H_2O_2-induced impairment in goat luteinized granulosa cells (Li et al., 2020) and promotes maturation of goat oocytes in vitro (Silva et al., 2018). It also protects goat sperm and pre-implanted embryos from Cd^{2+}-induced oxidative stress (Bhardwaj and Panchal, 2021; Mao et al., 2018), and maintains the integrity of frozen goat semen (Borges et al., 2020). Generally, supplementation with quercetin or rutin improves production performance of livestock and relieves oxidative stress and inflammatory responses in the rumen, mammary glands, and reproductive organs.

5.3.5. Chlorogenic acid

A total of 34 simple phenylpropanoids have been identified in *P. thellungiana*, with caffeoylquinic acid and isochlorogenic acid A the most abundant. Chlorogenic acid (CGA) improves antioxidant capacity, growth performance, muscle protein biosynthesis, meat quality traits, reproductive performance, intestinal health, and disease resistance in pigs through the mTOR/ribosomal protein S6 kinase 1 (S6K1)/eukaryotic initiation factor 4E - binding protein 1 (4EBP1), toll like receptor 4 (TLR4)/NF-κB, and nuclear factor erythroid 2-related factor 2 (NRF2)/heme oxygenase-1 (HO-1) (Dai et al., 2023). It is being considered as a replacement for antibiotics in feed for pigs. In ruminants, CGA could potentially replace antibiotics for the treatment of mastitis in dairy cows through the NF-κB signaling pathway and by directly targeting bacterial cell walls and membranes (Feng et al., 2023; Xu et al., 2023). Chlorogenic acid alleviates *S. aureus*-induced milk protein synthesis inhibition in bovine mammary epithelial cells (Ji et al., 2022), and inflammation induced by *E. coli* in sheep by inhibiting the TLR4/NF-κB signaling pathway of endometrial epithelium cells (Hu et al., 2020).

Isochlorogenic acid A (3,5-di-O-caffeoylquinic acid) exhibits fungistatic effects against *Alternaria alternata* (Harrison et al., 2008; Kodoma et al., 1998) and specifically inhibits the proliferation of respiratory syncytial viruses (Li et al., 2005). In addition to the antioxidant and metabolism-regulating activities, CGA and its derivatives possess potent anti-bacterial, anti-fungal, and anti-viral activities, which contribute to the treatment of pathogenic diarrhea.

5.3.6. Other compounds

Ten coumarin compounds have been identified in *P. thellungiana*, including scopoletin, scoparone, esculin, marmesin, bergapten, and isofraxidin (Table S1). Coumarin and its derivatives have anti-cancer (Al-Warhi et al., 2020), antioxidant, anti-bacterial, anti-inflammatory, anti-coagulant, neuroprotective, anti-diabetic, and anti-convulsant properties (Hassanein et al., 2020), but they also inhibit appetite (Ahmed et al., 2023) and the synthesis of vitamin K, and exert hepatotoxic effects (Pitaro et al., 2022). No report on the effect of coumarins in *P. thellungiana* on digestion, metabolism, or utilization of nutrients in livestock is available. Although the concentrations of coumarins in *P. thellungiana* are relatively low, they should be tested as a risk factor for their use as a feed additive or medicine.

The VOCs identified in the volatile oil of *P. thellungiana* can be classified into low-molecular-weight compounds and terpenes. Fifteen low-molecular-weight VOCs in *P. thellungiana* roots include alkanes, acids, aldehydes, esters, and ketones (C_5−C_{11}), while 19 terpenes in the whole plant and roots belong to the sesquiterpenes, with β-bisabolene (17.3% to 19.4%), caryophyllene oxide (12.9% to 15.7%) and β-pinene (5.31% to 6.62%) the main ingredients (Cheng et al., 2024). Terpenes differ in composition among *Pimpinella* species and possess anti-tumor, anti-inflammatory, antioxidant, anti-bacterial, and insecticidal properties (Wu et al., 2023). The VOCs profile in animal products is considered a chemical fingerprint that characterizes the food source and in livestock diets affects the flavor of milk and meat (Basdagianni et al., 2019; Borge et al., 2016; O'Callaghan et al., 2017). Few reports on the VOCs in *P. thellungiana* ae available, and the concentrations of VOCs have not been determined. Although low in content, VOCs can be used to distinguish the origin of *P. thellungiana*.

Twelve simple phenols were identified in *P. thellungiana*, including gentianic, salicylic, shikimic, and gallic acids. Simple phenols are known for their anti-bacterial, anti-cancer, anti-inflammatory, and antimutagenic properties (Kumar and Goel, 2019). Dietary supplementation with phenol extract did not affect the fatty acid composition of muscles in pigs, but reduced the thiobarbituric acid reactive substance (TBARS) values in pork chops (González and Tejeda, 2007). Supplementary gallic acid decreased the incidence of diarrhea and maintained intestinal integrity in weaning piglets (Cai et al., 2022). Gallic acid is also inhibited the proliferation and adipogenesis of bovine subcutaneous adipocytes in vitro (Jin et al., 2022).

P. thellungiana contains fatty acids (mainly oleic acid and palmitic acid) and phytosterols (β-sitosterol and γ-sitosterol). β-sitosterol has antioxidant, anti-cancer, anti-diabetic, anti-bacterial, and immunomodulatory activities (Babu and Jayaraman, 2020), and γ-sitosterol shows potential as a hypolipidemic agent (Balamurugan et al., 2015). Furthermore, pseudo-isoeugenol compounds identified in *P. thellungiana* (thellungianin A, B, E, F, and G) belong to eugenol and isoeugenol, which have antioxidant, antibacterial, anesthetic, anti-inflammatory, analgesic, neuroprotective, anti-diabetic, and anti-cancer properties (Taleuzzaman et al., 2021). However, high concentrations of isoeugenol can have carcinogenic effects on the liver and cause damage to the stomach, nose, and kidneys (National Toxicology Program, 2010). The

concentration and safety of pseudo-isoeugenol compounds in *P. thellungiana* have not been established and warrant further investigation.

6. Conclusions

P. thellungiana is a medicinal herb that has been used as an ethnobotanical feed additive for decades to treat growth retardation, overexertion, reproductive disorders and diarrhea in livestock in northeastern Asia. It also reduces blood pressure and liver tissue damage, enhances immunity, and possesses anti-hyperlipidemic, antioxidant, and antibacterial properties. These properties are attributed mainly to the bioactive compounds of L7GD, A7GD, CGA, isochlorogenic acid A, schaftoside, and Q3GD. However, the optimum dosages and methods of delivery of *P. thellungiana* still need to be established. In addition, identification of all bioactive substances in *P. thellungiana*, their pharmacological effects and their risk factors require further research.

CRediT authorship contribution statement

Shuxian Zhang: Writing – original draft. **Minglu Yang:** Writing – review & editing, Visualization. **Tao Xu:** Formal analysis, Data curation. **Qiongxian Yan:** Writing – review & editing. **Allan Degen:** Writing – review & editing, Data curation. **Xiaoling Zhou:** Funding acquisition, Conceptualization.

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.

Acknowledgments

This work was supported by the National Natural Science Foundation of China [32260844], Tianshan Talent Project of Xinjiang [2024], Bingtuan Science and Technology Program [2023AB078], and International Partnership Program of the Chinese Academy of Sciences [092GJHZ2023062GC].

Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aninu.2024.11.005.

References

Ahmed MG, Mehmood MH, Mehdi S, Farrukh M. Caryopteris odorata and its metabolite coumarin attenuate characteristic features of cardiometabolic syndrome in high-refined carbohydrate-high fat-cholesterol-loaded feed-fed diet rats. Front Pharmacol 2023;14:1097407. https://doi.org/10.3389/fphar.2023.1097407.

Al-Warhi T, Sabt A, Elkaeed EB, Eldehna WM. Recent advancements of coumarin-based anticancer agents: an up-to-date review. Bioorg Chem 2020;103:104163. https://doi.org/10.1016/j.bioorg.2020.104163.

Animal Husbandry and Veterinary Science and Technology Cooperation Group in Shaanxi Weinan Area. Experimental report on using herbal medicine of *Pimpinella thellungiana* for treating growth-retardation pig. Chin J Zool 1976;11:13–4. https://doi.org/10.13859/j.cjz.1976.03.004.

Animal Husbandry and Veterinary Science and Technology Cooperation Group in Shaanxi Weinan Area. Treatment of ovarian disease with *Pimpinella thellungiana* in horse and donkey. Chin J Zool 1977;12:45–6. https://doi.org/10.13859/j.cjz.1977.03.024.

Aziz N, Kim MY, Cho JY. Anti-inflammatory effects of luteolin: a review of *in vitro*, *in vivo*, and in silico studies. J Ethnopharmacol 2018;225:342–58. https://doi.org/10.1016/j.jep.2018.05.019.

Babu S, Jayaraman S. An update on β-sitosterol: a potential herbal nutraceutical for diabetic management. Biomed Pharmacother 2020;131:110702. https://doi.org/10.1016/j.biopha.2020.110702.

Balamurugan R, Stalin A, Aravinthan A, Kim JH. γ-sitosterol a potent hypolipidemic agent: in silico docking analysis. Med Chem Res 2015;24:124–30. https://doi.org/10.1007/s00044-014-1075-0.

Basdagianni Z, Papaloukas L, Kyriakou G, Karaiskou C, Parissi Z, Sinapis E, Kasapidou E. A comparative study of the fatty acid and terpene profiles of ovine and caprine milk from Greek mountain sheep breeds and a local goat breed raised under a semi-extensive production system. Food Chem 2019;278:625–9. https://doi.org/10.1016/j.foodchem.2018.11.093.

Berger LM, Wein S, Blank R, Metges CC, Wolffram S. Bioavailability of the flavonol quercetin in cows after intraruminal application of quercetin aglycone and rutin. J Dairy Sci 2012;95:5047–55. https://doi.org/10.3168/jds.2012-5439.

Berger LM, Blank R, Zorn F, Wein S, Metges CC, Wolffram S. Ruminal degradation of quercetin and its influence on fermentation in ruminants. J Dairy Sci 2015;98:5688–98. https://doi.org/10.3168/jds.2015-9633.

Bhardwaj JK, Panchal H. Quercetin mediated attenuation of cadmium-induced oxidative toxicity and apoptosis of spermatogenic cells in caprine testes *in vitro*. Environ Mol Mutagen 2021;62:374–84. https://doi.org/10.1002/em.22450.

Borge GI, Sandberg E, Øyaas J, Abrahamsen RK. Variation of terpenes in milk and cultured cream from Norwegian alpine rangeland-fed and in-door fed cows. Food Chem 2016;199:195–202. https://doi.org/10.1016/j.foodchem.2015.11.098.

Borges MS, Born JLB, Conti LM, Segabinazzi LG, Nichi M, Kawai GKV, Leite RF, Peixoto Jr KC, Dell'aqua Jr JA, Papa FO, Crespilho AM. Paradoxical effect of quercetin antioxidant on goat sperm parameters after cryopreservation. Cryo Lett 2020;41:128–34. www.ingentaconnect.com/content/cryo/cryo/2020/00000041/00000003/art00002.

Cai L, Wei Z, Zhao X, Li Y, Li X, Jiang X. Gallic acid mitigates LPS-induced inflammatory response via suppressing NF-κB signalling pathway in IPEC-J2 cells. J Anim Physiol Anim Nutr 2022;106:1000–8. https://doi.org/10.1111/jpn.13612.

Chen G, Xie R, Shen Y, Miao A, Wang D, Xu Q, Ma S. Pharmacological study of *Pimpinella thellungiana* (I). Preliminary analysis of antihypertensive action and mechanism. Shaanxi Med J 1982;11:48–9. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchozGZYJjtZbJV3DEaaGL_7d1yv6obvBCytxuyj6Dv6KiI4SiKdKQbUIKFw4CpzIcOUGFUXNDkTCd1h-Q4L4fCL0ZG1eVLyRgri07bhbiV31skup5GEsWd7F6nm71Ant2sRKdNRAYwWT_eJUdkQm0n8In4_GMM92ahadHP9xY8RlWhq0_OthaHHz8&uniplatform=NZKPT&language=CHS.

Chen N, Liu Y, Bai T, Chen J, Zhao Z, Li J, Shao B, Zhang Z, Zhou Y, Wang X, Zhu Z. Quercetin inhibits Hsp70 blocking of bovine viral diarrhea virus infection and replication in the early stage of virus infection. Viruses 2022a;14:2365. https://doi.org/10.3390/v14112365.

Chen Y, Guo Y, Song Z, Chang H, Kuang Q, Zheng Z, Wang H, Zhang G. Luteolin restricts ASFV replication by regulating the NF-κB/STAT3/ATF6 signaling pathway. Vet Microbiol 2022b;273:109527. https://doi.org/10.1016/j.vetmic.2022.109527.

Cheng ML, Sun Y, Liu R, Wang YL, Hao YP, Qin XM, Pei MR. Analysis of the volatile oil composition of *Pimpinella thellungiana* extracted with different methods by GC-MS combining with retention index. Chin J Pharmaceut Analy 2024;44:921–8. http://qikan.cqvip.com/Qikan/Article/Detail?id=7112549366.

Cui K, Guo XD, Tu Y, Zhang NF, Ma T, Diao QY. Effect of dietary supplementation of rutin on lactation performance, ruminal fermentation and metabolism in dairy cows. J Anim Physiol Anim Nutr 2015;99:1065–73. https://doi.org/10.1111/jpn.12334.

Cui X, Shi H, Ren H, Hu J, Meng M, Chen J, Meng X, Chen Z. Content determination of nine constituents in different medicinal parts of *Pimpinella thellungiana*. Chin J Exp Tradit Med Formulae 2019;25:97–103. https://doi.org/10.13422/j.cnki.syfjx.20191918.

Cui X, Ren H, Hu J, Chen J, Meng X, Mao Z, Chen Z. Study on HPLC fingerprint and determination of 10 components in *Pimpinella thellungiana*. Lishizhen Med Mater Med Res 2020;31:2313–6. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchoyNL4rzCExjH2uNSWHXxXTOq4Zrwnarl1sYpNvRrnO26N1pmhDo9V_ePF71qbVo1lErkP3niNK4UOu0jbaihiEtQI2xD93ja7kz5qHER753WsyTO5OlistRFK8i1_qI5wKmszCmQ7fMku5WSFglGszW77JcINMU-SFkGiAoTwfBYP8rI8Lk4BET&uniplatform=NZKPT&language=CHS.

Cui X, Hu J, Chen Z, Ren H. Qualitative analysis and quality evaluation of *Pimpinella thellungiana* by serum pharmacochemistry, network pharmacology, and QAMS. J AOAC Int 2022;106:179–91. https://doi.org/10.1093/jaoacint/qsac091.

Dai C, Li H, Zhao W, Fu Y, Cheng J. Bioactive functions of chlorogenic acid and its research progress in pig industry. J Anim Physiol Anim Nutr 2023;108:439–50. https://doi.org/10.1111/jpn.13905.

Davoodian N, Kadivar A, Davoodian N, Ahmadi E, Nazari H, Mehrban H. The effect of quercetin in the maturation media on cumulus-granulosa cells and the developmental competence of bovine oocytes. Theriogenology 2022;189:262–9. https://doi.org/10.1016/j.theriogenology.2022.06.026.

Ding H, Li Y, Zhao C, Yang Y, Xiong C, Zhang D, Feng S, Wu J, Wang X. Rutin supplementation reduces oxidative stress, inflammation and apoptosis of mammary gland in sheep during the transition period. Front Vet Sci 2022;9:907299. https://doi.org/10.3389/fvets.2022.907299.

Disbanchong P, Punmanee W, Srithanasuwan A, Pangprasit N, Wongsawan K, Suriyasathaporn W, Chuammitri P. Immunomodulatory effects of herbal compounds quercetin and curcumin on cellular and molecular functions of bovine-

milk-isolated neutrophils toward *Streptococcus agalactiae* infection. Animals 2021;11:3286. https://doi.org/10.3390/ani11113286.
Ende C, Gebhardt R. Inhibition of matrix metalloproteinase-2 and -9 activities by selected flavonoids. Planta Med 2004;70:1006–8. https://doi.org/10.1055/s-2004-832630.
Ervasti J, Pentti J, Nyberg ST, Shipley MJ, Leineweber C, Sørensen JK, Alfredsson L, Bjorner JB, Borritz M, Burr H, Knutsson A, Madsen IEH, Magnusson Hanson LL, Oksanen T, Pejtersen JH, Rugulies R, Suominen S, Theorell T, Westerlund H, Vahtera J, Virtanen M, Batty GD, Kivimäki M. Long working hours and risk of 50 health conditions and mortality outcomes: a multicohort study in four European countries. Lancet Reg Health Eur 2021;11:100212. https://doi.org/10.1016/j.lanepe.2021.100212.
Farooqi AA, Butt G, El-Zahaby SA, Attar R, Sabitaliyevich UY, Jovic JJ, Tang K-F, Naureen H, Xu B. Luteolin mediated targeting of protein network and microRNAs in different cancers: focus on JAK-STAT, NOTCH, mTOR and TRAIL-mediated signaling pathways. Pharmacol Res 2020;160:105188. https://doi.org/10.1016/j.phrs.2020.105188.
Feng S, Zhang Y, Fu S, Li Z, Zhang J, Xu Y, Han X, Miao J. Application of chlorogenic acid as a substitute for antibiotics in multidrug-resistant *Escherichia coli*-induced mastitis. Int Immunopharm 2023;114:109536. https://doi.org/10.1016/j.intimp.2022.109536.
Fernández Prieto JA, Sanna M, Bueno Sánchez Á, Molero-Mesa J, Llorens García L, Cires E. Polyphyletic origin in *Pimpinella* (Apiaceae): evidence in Western Europe. J Plant Res 2018;131:747–58. https://doi.org/10.1007/s10265-018-1046-5.
Gao HL, Yu XJ, Feng YQ, Yang Y, Hu HB, Zhao YY, Zhang JH, Liu KL, Zhang Y, Fu LY, Li Y, Qi J, Qiao JA, Kang YM. Luteolin attenuates hypertension via inhibiting NF-κB-mediated inflammation and PI3K/Akt signaling pathway in the hypothalamic paraventricular nucleus. Nutrients 2023;15:502. https://doi.org/10.3390/nu15030502.
González E, Tejeda JF. Effects of dietary incorporation of different antioxidant extracts and free-range rearing on fatty acid composition and lipid oxidation of Iberian pig meat. Animal 2007;1:1060–7. https://doi.org/10.1017/s1751731107000195.
Guo Y, Weber WJ, Yao D, Caixeta L, Zimmerman NP, Thompson J, Block E, Rehberger TG, Crooker BA, Chen C. Forming 4-methylcatechol as the dominant bioavailable metabolite of intraruminal rutin inhibits *p*-cresol production in dairy cows. Metabolites 2021;12:16. https://doi.org/10.3390/metabo12010016.
Ha SE, Bhagwan Bhosale P, Kim HH, Park MY, Abusaliya A, Kim GS, Kim JA. Apigetrin abrogates lipopolysaccharide-induced inflammation in L6 skeletal muscle cells through NF-κB/MAPK signaling pathways. Curr Issues Mol Biol 2022;44:2635–45. https://doi.org/10.3390/cimb44060180.
Harrison HF, Mitchell TR, Peterson JK, Wechter WP, Majetich GF, Snook ME. Contents of caffeoylquinic acid compounds in the storage roots of sixteen sweetpotato genotypes and their potential biological activity. J Am Soc Hortic Sci 2008;133:492–500. https://doi.org/10.21273/JASHS.133.4.492.
Hassanein EHM, Sayed AM, Hussein OE, Mahmoud AM. Coumarins as modulators of the Keap1/Nrf2/ARE signaling pathway. Oxid Med Cell Longev 2020;2020:1675957. https://doi.org/10.1155/2020/1675957.
Hong W. Four hundred kinds of natural medicine. Beijing, China: Ancient Chinese Medical Book Press; 2010.
Hostetler GL, Ralston RA, Schwartz SJ. Flavones: food sources, bioavailability, metabolism, and bioactivity. Adv Nutr 2017;8:423–35. https://doi.org/10.3945/an.116.012948.
Hu X, Wang M, Pan Y, Xie Y, Han J, Zhang X, Niayale R, He H, Li Q, Zhao T, Cui Y, Yu S. Anti-inflammatory effect of astragalin and chlorogenic acid on *Escherichia coli*-induced inflammation of sheep endometrial epithelium cells. Front Vet Sci 2020;7:201. https://doi.org/10.3389/fvets.2020.00201.
Hui K, Ma Y, Tian J, Hu J, Zhu X, Liang G. Research and application of *Pimpinella thellungiana* in livestock breeding. China Cattle Sci 2023;49:67–70. https://kns.cnki.net/kcms2/article/abstract?v=VoBN4ANGQ4c68DM_PNi-BW8g8IKXuAV5W2qMAt2eKXcMr8EsJ59XhK-IMSRMTs9zzZtWHvAAfjNsNIylYikMacMhnDTeJXjhf0v8SzKxkI-pLYLluw-UbBcfJhDWdFkoHHOZ9DivQktqlX3qhN00TA==&uniplatform=NZKPT&language=CHS.
Imani A, Maleki N, Bohlouli S, Kouhsoltani M, Sharifi S, Maleki Dizaj S. Molecular mechanisms of anticancer effect of rutin. Phytother Res 2021;35:2500–13. https://doi.org/10.1002/ptr.6977.
Jang YJ, Son HJ, Choi YM, Ahn J, Jung CH, Ha TY. Apigenin enhances skeletal muscle hypertrophy and myoblast differentiation by regulating Prmt7. Oncotarget 2017;8:78300–11. https://www.oncotarget.com/article/20962/text/.
Ji Q, Zhang M, Wang Y, Chen Y, Wang L, Lu X, Bai L, Wang M, Bao L, Hao H, Wang Z. Protective effects of chlorogenic acid on inflammatory responses induced by Staphylococcus aureus and milk protein synthesis in bovine mammary epithelial cells. Microb Pathog 2022;171:105726. https://doi.org/10.1016/j.micpath.2022.105726.
Jiang M, Wang K, Huang Y, Zhang X, Yang T, Zhan K, Zhao G. Quercetin alleviates lipopolysaccharide-induced cell oxidative stress and inflammatory responses via regulation of the TLR4-NF-κB signaling pathway in Bovine rumen epithelial cells. Toxins 2023;15:512. https://doi.org/10.3390/toxins15080512.
Jin Q, Liu G, Tan X, Zhang X, Liu X, Wei C. Gallic acid as a key substance to inhibit proliferation and adipogenesis in bovine subcutaneous adipocyte. Anim Biotechnol 2022;33:657–63. https://doi.org/10.1080/10495398.2020.1822370.
Kashyap P, Shikha D, Thakur M, Aneja A. Functionality of apigenin as a potent antioxidant with emphasis on bioavailability, metabolism, action mechanism and *in vitro* and *in vivo* studies: a review. J Food Biochem 2022;46:e13950. https://doi.org/10.1111/jfbc.13950.
Kobayashi T, Suzuki E, Takao S, Doi H. Long working hours and metabolic syndrome among Japanese men: a cross-sectional study. BMC Publ Health 2012;12:395. https://doi.org/10.1186/1471-2458-12-395.
Kodoma M, Wada H, Otani H, Kohmoto K, Kimura Y. 3,5-Di-O-caffeoylquinic acid, an infection-inhibiting factor from *Pyrus pyrifolia* induced by infection with *Alternaria alternata*. Phytochemistry 1998;47:371–3. https://doi.org/10.1016/S0031-9422(97)00621-3.
Kumar N, Goel N. Phenolic acids: natural versatile molecules with promising therapeutic applications. Biotechnol Rep (Amst) 2019;24:e00370. https://doi.org/10.1016/j.btre.2019.e00370.
Kyle UG, Shekerdemian LS, Coss-Bu JA. Growth failure and nutrition considerations in chronic childhood wasting diseases. Nutr Clin Pract 2015;30:227–38. https://doi.org/10.1177/0884533614555234.
Lee W, Kang SK, Choi WJ. Effect of long work hours and shift work on high-sensitivity C-reactive protein levels among Korean workers. Scand J Work Environ Health 2021;47:200–7. https://doi.org/10.5271/sjweh.3933.
Lee W, Yim HW, Lee Y. Cohort study of long working hours and increase in blood high-sensitivity C-reactive protein (hsCRP) concentration: mechanisms of overwork and cardiovascular disease. J Occup Health 2022;64:e12359. https://doi.org/10.1002/1348-9585.12359.
Li F, Wang C, Mi C, Shi H, Qiao B. Chemical constituents of the root of *Pimpinella thellungiana*. Acta Bot Sin 1998;40:88–90. https://kns.cnki.net/kcms2/article/abstract?v=WStw-Pbchow1mwB76EJTa4fVDPlmRf1jnK0hhkm5ThH72QG3VTt3C149HzxcBm6sCe1lMgsl5JgKOdlAg3vX4qOe-KqWLj5z7vmSD29gwlQ3LdqbRN4Po4NO31bsgBseV9-M93YD4cwECv9o61q7pdN4Nvt9tTlvOROLCmHBJfn1jm8Ri0v8LHVjW5PsnDU5&uniplatform=NZKPT&language=CHS.
Li M, Xue Y, Yu H, Mao D. Quercetin alleviated H_2O_2-induced apoptosis and steroidogenic impairment in goat luteinized granulosa cells. J Biochem Mol Toxicol 2020;34:e22527. https://doi.org/10.1002/jbt.22527.
Li Y, But PP, Ooi VE. Antiviral activity and mode of action of caffeoylquinic acids from *Schefflera heptaphylla* (L.) Frodin. Antivir Res 2005;68:1–9. https://doi.org/10.1016/j.antiviral.2005.06.004.
Li Y, Yao J, Han C, Yang J, Chaudhry MT, Wang S, Liu H, Yin Y. Quercetin, inflammation and immunity. Nutrients 2016;8:167. https://doi.org/10.3390/nu8030167.
Liu M, Liu C, Chen H, Huang X, Zeng X, Zhou J, Mi S. Prevention of cholesterol gallstone disease by schaftoside in lithogenic diet-induced C57BL/6 mouse model. Eur J Pharmacol 2017a;815:1–9. https://doi.org/10.1016/j.ejphar.2017.10.003.
Liu M, Zhang G, Song M, Wang J, Shen C, Chen Z, Huang X, Gao Y, Zhu C, Lin C, Mi S, Liu C. Activation of Farnesoid X Receptor by schaftoside ameliorates ccetaminophen-induced hepatotoxicity by modulating oxidative stress and inflammation. Antioxidants Redox Signal 2020a;33:87–116. https://doi.org/10.1089/ars.2019.7791.
Liu MM, Ma RH, Ni ZJ, Thakur K, Cespedes-Acuña CL, Jiang L, Wei ZJ. Apigenin 7-O-glucoside promotes cell apoptosis through the PTEN/PI3K/AKT pathway and inhibits cell migration in cervical cancer HeLa cells. Food Chem Toxicol 2020b;146:111843. https://doi.org/10.1016/j.fct.2020.111843.
Liu R, Wang Z, Zhang D, Pei M. UPLC determination of two flavonoid glycosides in Yanghongshan (*Pimpinella thellungiana*). Chin J Pharmaceut Analy 2017b;37:1509–12. https://doi.org/10.16155/j.0254-1793.2017.08.22.
Liu R, Meng C, Zhang Z, Ma H, Lv T, Xie S, Liu Y, Wang C. Comparative metabolism of schaftoside in healthy and calcium oxalate kidney stone rats by UHPLC-Q-TOF-MS/MS method. Anal Biochem 2020c;597:113673. https://doi.org/10.1016/j.ab.2020.113673.
Liu R, Tai G, Pei X, Wang R, Zhang S, Pei M. Determination of nine components in Yanghongshan (*Pimpinella thellungiana*) by UPLC. Chin J Pharmaceut Analy 2020d;40:1097–103. https://doi.org/10.16155/j.0254-1793.2020.06.19.
Liu X, Lin R, Huang Z. Quick reference manual of commonly used Chinese medicine. Wuhan: Hubei Science & Technology Press; 2014.
Liu X, Zuo J, Teng J, Yang L, Guo J, Liu L, Li P. Antibiofilm potential of luteolin against multidrug-resistant *Staphylococcus aureus* isolated from dairy goats and farm environments. Environ Pollut 2023;335:122274. https://doi.org/10.1016/j.envpol.2023.122274.
Liu Y, Peng Y, Chen C, Ren H, Zhu J, Deng Y, Cui Q, Hu X, He J, Li H, Zhu X, Yin Y, He J, Xiao Y. Flavonoids from mulberry leaves inhibit fat production and improve fatty acid distribution in adipose tissue in finishing pigs. Anim Nutr 2024;16:147–57. https://doi.org/10.1016/j.aninu.2023.11.003.
Livestock Veterinary Work Station of Baishui County in Shaanxi Province. Observation on the curative effect of treating white dysentery with *Pimpinella thellungiana* in piglet. Chin Qinghai J Anim Veter Sci 1977;11:1–4. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchowixU48zVhIrqhTwxz4lQ88bTPJmGTeAQXHgSWaIyAiqCDrIe8CQb_ktozOTGptFk2oHv52KZhwq9Y13CuNwy1Sk-WKViqUAxRhjoXJ44F5L1apTtLlMQDiySxtrC3pIceBqScCilc4Xnr5PUmxI3rpSJjYqkiLi6FnuU3midoNP3ldqCPb4vXc&uniplatform=NZKPT&language=CHS.
Ma Q, Zhang XM, Jiang JG, Zhu W. Apigenin-7-O-β-D-glucuronide inhibits modified low-density lipoprotein uptake and foam cell formation in macrophages. J Funct Foods 2017;35:615–21. https://doi.org/10.1016/j.jff.2017.06.026.
Ma Q, Jiang JG, Zhang XM, Zhu W. Identification of luteolin 7-O-β-D-glucuronide from *Cirsium japonicum* and its anti-inflammatory mechanism. J Funct Foods 2018;46:521–8. https://doi.org/10.1016/j.jff.2018.05.014.

Mao T, Han C, Wei B, Zhao L, Zhang Q, Deng R, Liu J, Luo Y, Zhang Y. Protective effects of quercetin against cadmium chloride-induced oxidative injury in goat sperm and zygotes. Biol Trace Elem Res 2018;185:344–55. https://doi.org/10.1007/s12011-018-1255-8.

Miao A, Chen G, Shen Y, Xie R, Tong C, Xu Q, Ma S. Pharmacological study of Yanghongshan (*Pimpinella thellungiana*) II. Effect on cardiovascular system. Shaanxi Med J 1982;11:48–9. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchowIGQQB42GBJ-1GiQw8mHNBBEC9iEw1tyUQ07f-VTaW5fRQVOpg6l6FeW6UlKKZUMjPMvTOufB0z05NiVnTe4Kv60RnBPsfRmkWdHhhcamWaAOUTHKcHMF0t2zj6jrzxwtBI6QJvdeUHZcJstTSIIjojeXeuRYT0U2c7pOy3R_h2k_u0EMn5S6O&uniplatform=NZKPT&language=CHS.

Min YS, Bai KL, Yim SH, Lee YJ, Song HJ, Kim JH, Ham I, Whang WK, Sohn UD. The effect of luteolin-7-O-beta-D-glucuronopyranoside on gastritis and esophagitis in rats. Arch Pharm Res (Seoul) 2006;29:484–9. https://doi.org/10.1007/bf02969421.

Muruganathan N, Dhanapal AR, Baskar V, Muthuramalingam P, Selvaraj D, Aara H, Shiek Abdullah MZ, Sivanesan I. Recent updates on source, biosynthesis, and therapeutic potential of natural flavonoid luteolin: a review. Metabolites 2022;12:1145. https://doi.org/10.3390/metabo12111145.

National Toxicology Program. Toxicology and carcinogenesis studies of isoeugenol (CAS No. 97-54-1) in F344/N rats and B6C3F1 mice (Gavage studies). North Carolina, USA: National Institutes of Health Public Health Service; 2010.

O'callaghan TF, Mannion DT, Hennessy D, Mcauliffe S, O'sullivan MG, Leeuwendaal N, Beresford TP, Dillon P, Kilcawley KN, Sheehan JJ, Ross RP, Stanton C. Effect of pasture versus indoor feeding systems on quality characteristics, nutritional composition, and sensory and volatile properties of full-fat Cheddar cheese. J Dairy Sci 2017;100:6053–73. https://doi.org/10.3168/jds.2016-12508.

Pitaro M, Croce N, Gallo V, Arienzo A, Salvatore G, Antonini G. Coumarin-induced hepatotoxicity: a narrative review. Molecules 2022;27:9063. https://doi.org/10.3390/molecules27249063.

Qiao B, Wang C, Mi C, Li F, Shi H, Takashima J. Separation and identification of thellungianin A and B from the root of *Pimpinella thellungiana*. Acta Pharm Sin 1997;32:56–8. https://doi.org/10.16438/j.0513-4870.1997.01.012.

Qiao B, Wang C, Li F, Mi C, Shi H, Takayama J. Studies on the chemical constituents of the root in *Pimpinella thellungiana* (III): separation and identification of thellungianin F. Chin Tradit Herb Drugs 1998a;29:3–5. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchoxTW8DWQhlI-SnZEkjbpsTmPV_0J_CdqDh7IzeoEi34gLvR51eEkZTYPeMxr08jE0XSLuGV5eU-hq6AXwUnPmYHWmcVa8so8AW5Qvgzi7eDy_AbD5DOgcCM6OFU_XQBkSoTOjUZ2e8wJSnIvB-4FuH7UakbJwofeyPerGxHo7Kg90ik6bxhszJ&uniplatform=NZKPT&language=CHS.

Qiao B, Wang C, Li F, Shi H, Mi C, Takashima J. Isolation and identification of thellungianin C and D from the root of *Pimpinella thellungiana*. Chin Tradit Herb Drugs 1998b;29:580–2. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchozdGuDe5YHv4Vbg3jSN-jSnVnXT7MGzt3x0RS4FD3fftVq_zDJbkdSBmUfR4M4aqgDycFmgKJfRl4KLuJ2Ms2FO8Muj60KoyIJ7uPKsxtNWpA1t7yoWsZhXCl8XB0pj37TGLX05SWNnwDkjaxhWmEKf5h55CL-Cyi8ynuEVCfxSvshML8oWVb63&uniplatform=NZKPT&language=CHS.

Qiao B, Wang C, Li F, Mi C, Shi H, Takashima J. Separation and identification of thellungianin G from the root of *Pimpinella thellungiana*. China J Chin Mater Med 1999;24:39–40+63. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchozdGuDe5YHv4Vbg3jSN-jSnVnXT7MGzt3yid6Q96o5mXaizgAbx2m2Hlb2WSO58MDNVr1rs3UWH5gtJvCSitvYi4dg1Fa28f03GfQydpdUGkDq_wigETV-2j9myUX04M6D8BjvqfkZOzA7IUmPHlqGO4z0-0J_dpVk2tKQgMxhxJW9gMl7R4a1L&uniplatform=NZKPT&language=CHS.

Qiao B, Wang C, Li F, Shi H, Mi C, Takashima J. Separation and identification of thellungianin H from root of *Pimpinella thellungiana*. Chin Tradit Herb Drugs 2000;31:161–2. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchoxDRrSu0j5SdsOfLOeJGkHV28VAoLzA47ncNXLFpHs36TDAwIi_KjsmQQRfHwbSnMkdSkwppoBlDt3N94pk3jufSTObSWTOOudNs9Qkfbr3yMJi7OpnClsh3DnBzbLH0F6Yies2j580xVeYBNFr8AZwOo_1ozySdOo2kaCReP_-d9KvaoQEizws&uniplatform=NZKPT&language=CHS.

Rachakatla A, Kalashikam RR. Calorie restriction-regulated molecular pathways and its impact on various age groups: an overview. DNA Cell Biol 2022;41:459–68. https://doi.org/10.1089/dna.2021.0922.

Reichling J, Kemmerer B, Sauer-Gürth H. Biosynthesis of pseudoisoeugenols in tissue cultures of *Pimpinella anisum*. Phenylalanine ammonia lyase and cinnamic acid 4-hydroxylase activities. Pharm World Sci 1995;17:113–9. https://doi.org/10.1007/BF01872387.

Ryu D, Jee HJ, Kim SY, Hwang SH, Pil GB, Jung YS. Luteolin-7-O-glucuronide improves depression-like and stress coping behaviors in sleep deprivation stress model by activation of the BDNF signaling. Nutrients 2022;14:3314. https://doi.org/10.3390/nu14163314.

Shen Y, Xie R, Miao A, Chen G, Xu Q, Ma S. Pharmacological study of *Pimpinella thellungiana* (III). Toxicity and general pharmacological study. Shaanxi Med J 1982;11:60–1. https://kns.cnki.net/kcms2/article/abstract?v=WStw-Pbchox2dlihn41Pdqf7QxD9zVm6hBsYyImF-EhgYIbVvrkEzGLwRxet10DDtsisdL6jsZePUHlS2qynzLhXZAbzYyFWgQxj2q5EixlRXhflRZm32DgTnL-lXDnqMHzrOQn60bHGkJ0GUzavt8QTbUnjYmlZH0mhp_wlZbGEHhbkD0tqcncchOY5im8N&uniplatform=NZKPT&language=CHS.

Silva AaA, Silva MNP, Figueiredo LBF, Gonçalves JD, Silva MJS, Loiola MLG, Bastos BDM, Oliveira RA, Ribeiro LGM, Barberino RS, Gouveia BB, Monte APO, Nogueira DM, Cordeiro MF, Matos MHT, Lopes Júnior ES. Quercetin influences *in vitro* maturation, apoptosis and metabolically active mitochondria of goat oocytes. Zygote 2018;26:465–70. https://doi.org/10.1017/s0967199418000485.

Stoldt AK, Derno M, Nürnberg G, Weitzel JM, Otten W, Starke A, Wolffram S, Metges CC. Effects of a 6-wk intraduodenal supplementation with quercetin on energy metabolism and indicators of liver damage in periparturient dairy cows. J Dairy Sci 2015;98:4509–20. https://doi.org/10.3168/jds.2014-9053.

Stoldt AK, Derno M, Das G, Weitzel JM, Wolffram S, Metges CC. Effects of rutin and buckwheat seeds on energy metabolism and methane production in dairy cows. J Dairy Sci 2016;99:2161–8. https://doi.org/10.3168/jds.2015-10143.

Sun W, Shahrajabian MH, Cheng Q. Anise (*Pimpinella anisum* L.), a dominant spice and traditional medicinal herb for both food and medicinal purposes. Cogent Biol 2019;5:1673688. https://doi.org/10.1080/23312025.2019.1673688.

Taleuzzaman M, Jain P, Verma R, Iqbal Z, Mirza MA. Eugenol as a potential drug candidate: a review. Curr Top Med Chem 2021;21:1804–15. https://doi.org/10.2174/1568026621666210701141433.

Tang X, Xiong K. Intrauterine growth retardation affects intestinal health of suckling piglets via altering intestinal antioxidant capacity, glucose uptake, tight junction, and immune responses. Oxid Med Cell Longev 2022;2022:2644205. https://doi.org/10.1155/2022/2644205.

Tepe AS, Tepe B. Traditional use, biological activity potential and toxicity of *Pimpinella* species. Ind Crops Prod 2015;69:153–66. https://doi.org/10.1016/j.indcrop.2015.01.069.

Wang C, Ding K, Wu Y, Guo W, Chen J, Yuan Z. Studies on the chemical constituents in the root of *Pimpinella thellungiana*. Acta Pharm Sin 1983;18:522–4. https://doi.org/10.16438/j.0513-4870.1983.07.008.

Wang C, Mi C, Qiao B, Fang H. Chemical composition of *Pimpinella thellungiana* IV: volatile oil in root. Northwest Pharmaceut J 1988;3:24–6. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchowB31CFBpIE4q69yPwzvg2RJxmb0CVKRNCRwwtzMh1GyGUIsQEVgSGQtFDuiE-74tBDjltvYleiHZrg4XZZPLArK1IrvTYn85CKEfEwUUD1Qe63UfmTSc8g8c4QIl2E8E4ntixgJQcrVxK_kfpCCuRxqeKkX9aIe8uJiXxN6GDsdSJHjxtSmaLc&uniplatform=NZKPT&language=CHS.

Wang D, Yang Y, Zou X, Zhang J, Zheng Z, Wang Z. Antioxidant apigenin relieves age-related muscle atrophy by inhibiting oxidative stress and hyperactive mitophagy and apoptosis in skeletal muscle of mice. J Gerontol A Biol Sci Med Sci 2020;75:2081–8. https://doi.org/10.1093/gerona/glaa214.

Wang H, Wen J. Protective effect of Yanghongshan (*Pimpinella thellungiana*) on liver injury induced by acetaminophen in mice. Guangdong Feed 2022;31:28–30. https://kns.cnki.net/kcms2/article/abstract?v=WStw-Pbchox2DLL2F56KLKonPNEKlNfQg9Ch8upXp0uz5tuudjPWCTFoO6w3ijHRRfShGGeGZ5EzBgFw5GUJ7-4RHViQ-9W3c5ioAgEmvo3Qrptm6VVtjUSvONAvvwce4HHhZOJVQ8W2l_wuxJqJL5nv0g8DBxPBPHGPupHRvEAes-Uc7RgGsLG3FnY2HJ_y&uniplatform=NZKPT&language=CHS.

Wang M, Firrman J, Liu L, Yam K. A review on flavonoid apigenin: dietary intake, ADME, antimicrobial effects, and interactions with human gut microbiota. BioMed Res Int 2019;2019:7010467. https://doi.org/10.1155/2019/7010467.

Wei D, Miao A, Long Z. Effect of *Pimpinella thellungiana* on animal protein metabolism. China J Chin Mater Med 1986;11:53–4. https://kns.cnki.net/kcms2/article/abstract?v=WStw-PbchozfY_rHY_e6Gp365kUuu_t-cEcwjqvuCEB5EUHjDx7_-mVbc_FteZ8sXGACh HDsUiKPGcHfYHFE0EUmWwKn6k-P4_QnKyxtqLE0ls8oqMN_BejKTy-nVD4BGvuAbtD92c9z15Gt2mLbAlw5RhVOUdYqDPsIw4PD3xdIB3uf-Zy3ubqdHwLCuRLV&uniplatform=NZKPT&language=CHS.

Wein S, Beyer B, Zimmermann BF, Blank RH, Wolffram S. Bioavailability of quercetin from onion extracts after intraruminal application in cows. J Agric Food Chem 2018;66:10188–92. https://doi.org/10.1021/acs.jafc.8b03049.

Wu J, Cao Z, Hassan SSU, Zhang H, Ishaq M, Yu X, Yan S, Xiao X, Jin H-Z. Emerging biopharmaceuticals from *Pimpinella* genus. Molecules 2023;28:1571. https://doi.org/10.3390/molecules28041571.

Xu P, Xu X, Fotina H, Fotina T. Anti-inflammatory effects of chlorogenic acid from *Taraxacum officinale* on LTA-stimulated bovine mammary epithelial cells via the TLR2/NF-κB pathway. PLoS One 2023;18:e0282343. https://doi.org/10.1371/journal.pone.0282343.

Xu Q, Shen Y, Wang D. Pharmacological study of flavonoid in *Pimpinella thellungiana*. Chin Tradit Herb Drugs 1994;25:51. https://kns.cnki.net/kcms2/article/abstract?v=WStw-Pbchoy4ZKEzTptMWdiv29Cm7RBkXvOtWkKkFUQga2YX6d8-MJFiQG7aqaUcx32leS_IqWhc71EBb0aWuoXl-eZmXm_7jeFK38-p0TTjvr-yITI3fTS9qkKDKirnKTpICPXPhiFIZonCT3M1jugT_TD8LdW5uQNyzbMaJbFXR7y-Wiyp6VSM1RTTyNwB-&uniplatform=NZKPT&language=CHS.

Xu Y, Li X, Wang H. Protective roles of apigenin against cardiometabolic diseases: a systematic review. Front Nutr 2022;9:875826. https://doi.org/10.3389/fnut.2022.875826.

Xue K, Ma B, Wang J, Wang L. Separation and identification of thellungianol from *Pimpinella thellungiana*. Chin Tradit Herb Drugs 1998;29:1–3. https://kns.cnki.net/kcms2/article/abstract?v=WStw-Pbchoy_IyXkj_U9S23W3q9NXz-bNUsmChbpsxBK2u2WusqXLR2gF2wwvgv4oop8NgaHIwVSuB8U6wA-t-bej-Vdt5Aq62oMMoYA7fNPmaq5qwtIEvPhEaF2iPTUt7UYRi3zZCiuJrp2JDAC_FheYaKtmxRf_dnMT3yTBqm4zxUARZcXfqRFgUhxKIgi&uniplatform=NZKPT&language=CHS.

Yang D, Wang T, Long M, Li P. Quercetin: its main pharmacological activity and potential application in clinical medicine. Oxid Med Cell Longev 2020;2020:8825387. https://doi.org/10.1155/2020/8825387.

Yang LL, Xiao N, Li XW, Fan Y, Alolga RN, Sun XY, Wang SL, Li P, Qi LW. Pharmacokinetic comparison between quercetin and quercetin 3-O-β-glucuronide in rats by UHPLC-MS/MS. Sci Rep 2016;6:35460. https://doi.org/10.1038/srep35460.

Yi Y, Zhang M, Xue H, Yu R, Bao YO, Kuang Y, Chai Y, Ma W, Wang J, Shi X, Li W, Hong W, Li J, Muturi E, Wei H, Wlodarz J, Roszak S, Qiao X, Yang H, Ye M. Schaftoside inhibits $3CL^{pro}$ and PL^{pro} of SARS-CoV-2 virus and regulates immune response and inflammation of host cells for the treatment of COVID-19. Acta Pharm Sin B 2022;12:4154–64. https://doi.org/10.1016/j.apsb.2022.07.017.

Yuan F. Preliminary understanding of Chinese herbal medicine of *Pimpinella thellungiana*. Chin J Veterin Med 1979;15:20–3. https://kns.cnki.net/kcms2/article/abstract?v=VoBN4ANGQ4dF7KP13si8NBkcMa0LCGs4D4PR0YbptYTuqD6OPnPhCOxkylw0L2-G_88x3-M7XrdcQNMoxI4tcdl74U-oXk2SazzgcSJdDDKgA-wJltbjqcpypAp7rGvqXuuaYLilCXw=&uniplatform=NZKPT&language=CHS.

Yuan F, Liu Y, Li S, Zhang H, Xiao L, Dong Y. Preliminary study on the aphrodisiacal effect of Yanghongshan (*Pimpinella thellungiana*) on horse and donkey. Acta Vet Zootech Sin 1979;10:105–10. https://kns.cnki.net/kcms2/article/abstract?v=WStw-Pbchoy033LWStCPe6pZyLBBUG4xtev_cgY6T7xzrGiwx44PFBoBbePy0r_u2EETJJoNex9uHnMyR_fNkByfSlnSdSDXy0vIyFZMfkjtgQBQKmgF6WgCoxXFxAEbftn6Cz7O7cPgplBDDVHKHo6Wohvy7t5t6uskr53srrnKFqYkf571SKEQO7Zp2BLs&uniplatform=NZKPT&language=CHS.

Yuan F, Liu J, Yuan S, Kang X, Xiao L. Experimental report of injection from *Pimpinella thellungiana* on the aphrodisiasis of dairy cows. Chin Veterin Sci 1981;11:46–8. https://doi.org/10.16656/j.issn.1673-4696.1981.09.013.

Zhan J, Gu Z, Wang H, Liu Y, Wang L, Huang L, Huo J, Wu Y. Effects of rutin supplementation on growth performance, slaughter performance, serum parameters, and meat quality of Nubian goats. Anim Sci J 2023;94:e13819. https://doi.org/10.1111/asj.13819.

Zhan J, Gu Z, Wang H, Liu Y, Wu Y, Huo J. Rutin alleviated lipopolysaccharide-induced damage in goat rumen epithelial cells. Anim Biosci 2024;37:303–14. https://doi.org/10.5713/ab.23.0028.

Zhang J, Li H, Fan YR, Zhou X. Mechanisms of interaction between luteolin and the catalytic zinc ion in matrix metalloproteinases: a computational study. J Phys Org Chem 2012;25:1306–14. https://doi.org/10.1002/poc.3025.

Zhang L, Wu M, Chen Z. Schaftoside improves cerebral ischemia-reperfusion injury by enhancing autophagy and reducing apoptosis and inflammation through the AMPK/mTOR pathway. Adv Clin Exp Med 2022;31:1343–54. https://doi.org/10.17219/acem/152207.