



## Review

# New insights into bee pollen: Nutrients, phytochemicals, functions and wall-disruption

Jiangtao Qiao<sup>a,b</sup>, Yu Zhang<sup>a</sup>, Eric Haubruge<sup>b</sup>, Kai Wang<sup>a,b</sup>, Hesham R. El-Seedi<sup>d,e,f</sup>, Jie Dong<sup>c</sup>, Xiang Xu<sup>a,\*</sup>, Hongcheng Zhang<sup>c,\*</sup>

<sup>a</sup> State Key Laboratory of Resource Insects, Institute of Apicultural Research, Chinese Academy of Agricultural Sciences, Beijing 100093, China

<sup>b</sup> Terra Research Center, Gembloux Agro-Bio Tech, University of Liege, Gembloux 5030, Belgium

<sup>c</sup> Key Laboratory of Bee Products for Quality and Safety Control, Ministry of Agriculture and Rural Affairs, Beijing 100093, China

<sup>d</sup> Pharmacognosy Group, Department of Pharmaceutical Biosciences, BMC, Uppsala University, Box 591, SE 751 24 Uppsala, Sweden

<sup>e</sup> International Research Center for Food Nutrition and Safety, Jiangsu University, Zhenjiang 212013, China

<sup>f</sup> Department of Chemistry, Faculty of Science, Islamic University of Madinah, Madinah 42351, Saudi Arabia



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## ABSTRACT

Bee pollen is hailed as a treasure trove of human nutrition and has progressively emerged as the source of functional food and medicine. This review conducts a compilation of nutrients and phytochemicals in bee pollen, with particular emphasis on some ubiquitous and unique phenolamides and flavonoid glycosides. Additionally, it provides a concise overview of the diverse health benefits and therapeutic properties of bee pollen, particularly anti-prostatitis and anti-tyrosinase effects. Furthermore, based on the distinctive structural characteristics of pollen walls, a substantial debate has persisted in the past concerning the necessity of wall-disruption. This review provides a comprehensive survey on the necessity of wall-disruption, the impact of wall-disruption on the release and digestion of nutrients, and wall-disruption techniques in industrial production. Wall-disruption appears effective in releasing and digesting nutrients and exploiting bee pollen's bioactivities. Finally, the review underscores the need for future studies to elucidate the mechanisms of beneficial effects. This paper will likely help us gain better insight into bee pollen to develop further functional foods, personalized nutraceuticals, cosmetics products, and medicine.

## 1. Introduction

Pollen represents the male reproductive cells produced by the anthers of flowering plants, serving the crucial purpose of transferring gametes to the stigma of receptive female flowers (Dong, Gao, et al., 2015). From a bee's perspective, pollen is a pivotal and highly valued product within the hive ecosystem, and supplies almost all nutrients for brood rearing and adult growth and development (Aylanc, Falcão, et al., 2021). During foraging visits to flowers, worker honeybees attract and collect copious amounts of pollen using a weak electrostatic field generated between the negatively charged flower and the positively charged honeybee's body (Fig. 1) (Clarke et al., 2017). After collection, pollens are moistened with salivary secretions and nectar to aggregate into granular form and compacted into a 1.4–4 mm pellet enriched with pollen, nectar, enzymes, and saliva (Saavedra et al., 2013). These distinctive products are commonly referred to as bee pollen. Beekeepers

use specialized pollen traps (Fig. 1), meticulously positioned at the entrance of beehives, as the most common approach for collecting bee pollen.

Bee pollen is recognized as a significant dietary supplement because of its abundant nutritional constituents, and finds widespread application in cosmetics, health food products, and modern medicine (Aylanc, Falcão, et al., 2021; Wu et al., 2019). Its therapeutic properties are being extensively studied and admired, including its anti-inflammatory, antioxidant, antimicrobial, and immune-enhancing attributes, helping recovery from chronic illness, slowing aging, lowering cholesterol levels, and regulating intestinal functions (Li et al., 2018; Thakur & Nanda, 2020b). The various health benefits of bee pollen are primarily attributed to its rich nutrients and functional compounds, especially phytochemicals, such as phenolic acids, phenolamides, and flavonoids (Aylanc, Falcão, et al., 2021; Wu et al., 2019). In recent years, studies have revealed dozens of new phytochemicals in bee pollen (Qiao, Feng,

\* Corresponding authors.

E-mail addresses: [xuxiang@caas.cn](mailto:xuxiang@caas.cn) (X. Xu), [460414874@qq.com](mailto:460414874@qq.com) (H. Zhang).

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et al., 2023; H. Zhang et al., 2023; X. Zhang et al., 2023; X. Zhang et al., 2022); therefore, it is necessary to summarize and provide a new insight into the functional phytochemicals in bee pollen. Moreover, the intricate wall structure of bee pollen can hinder the release of its bioactive compounds, leading to suboptimal utilization of the nutritional content of bee pollen (Wu et al., 2021). The inquiry into the necessity of wall disruption in bee pollen and its consequential impact on the augmented liberation of nutritional constituents, as well as the ensuing enhancement in digestion and absorption rates, has consistently constituted a focal point of scholarly discourse within the scientific community.

Therefore, this review aims to provide a comprehensive overview

regarding the nutrient and functional compounds of bee pollen, and human health benefits. Furthermore, this review delves into the necessity of wall disruption, the techniques employed for wall disruption in bee pollen, and the impact on its nutritional and functional attributes. Additionally, it provides concise perspective challenges and future prospects that could foster industrial advancement and diverse applications.

## 2. Nutrients and phytochemicals

According to established standards, the human diet should provide



**Fig. 1.** The bee pollen production process, encompassing stages such as pollen collection by bees, formation of bee bread, pollen grain interception via pollen traps, the acquisition of four distinct monofloral bee pollen types from China, the drying of bee pollen, and the microstructural analysis of bee pollen grains utilizing a Scanning Electron Microscope (SEM).

adequate energy and essential nutrients for physical and mental growth. Bee pollen is acclaimed as a superfood due to its comprehensive profile of essential nutrients required for human sustenance (Wu et al., 2021). Therefore, bee pollen can supplement the daily nutrient diet. The average content of various nutrients in bee pollen from previous research (Bogdanov, 2012; Thakur & Nanda, 2020a) and the nutritional requirements of adults is shown in Table 1. The proportion of primary nutritional constituents, notably carbohydrates and fats, is relatively modest in bee pollen. Nevertheless, crude fiber and protein content can contribute substantially, with 100 g of bee pollen constituting up to 60 % and 70 % of the Recommended Dietary Allowance (RDA), respectively. Certain vitamins and minerals present in bee pollen can fulfill the entirety of the required daily intake. The only deficiency in the nutritional composition of bee pollen lies in the absence of vitamins D and K, and the presence of some indigestible substances, such as sporopollenin.

### 2.1. Carbohydrates

Carbohydrates are the principal constituent of bee pollen, accounting for about 70 % of dry pollen weight (Li et al., 2018; Thakur & Nanda, 2020a). Bee pollen is mainly composed of monosaccharides and

disaccharides, with fructose being the highest in content, followed by glucose and sucrose (Li et al., 2018; Thakur & Nanda, 2020a). In addition, bee pollen also contains dietary fiber and oligosaccharides. Dietary fiber in bee pollen originates from components like sporopollenin, cellulose, hemicellulose, and pectin found in the outer covering. The total dietary fiber contents in bee pollen have been reported to range from 17.60 % to 31.26 % (Yang et al., 2013). For instance, the total dietary fiber content identified in bee pollen sourced from Switzerland, France, and Colombian manifests within the range of 9.9 to 15 g/ 100 g (Thakur & Nanda, 2020a). Oligosaccharides are mainly sporopollenin, present in the pollen wall. Cellulose and pectin have been reported to exist in the inner wall of pollen (Dong, Gao, et al., 2015). These oligosaccharides seem to have little nutritional value and cannot be digested or absorbed, but they are essential in regulating several biological functions (Aylanc, Falcão, et al., 2021; Kieliszek et al., 2018).

### 2.2. Protein and amino acids

Protein was the second most abundant component in bee pollen and exhibits significant variation depending on plant sources. Upon drying, the protein contents in bee pollen may range from 2.5 % to 62 %

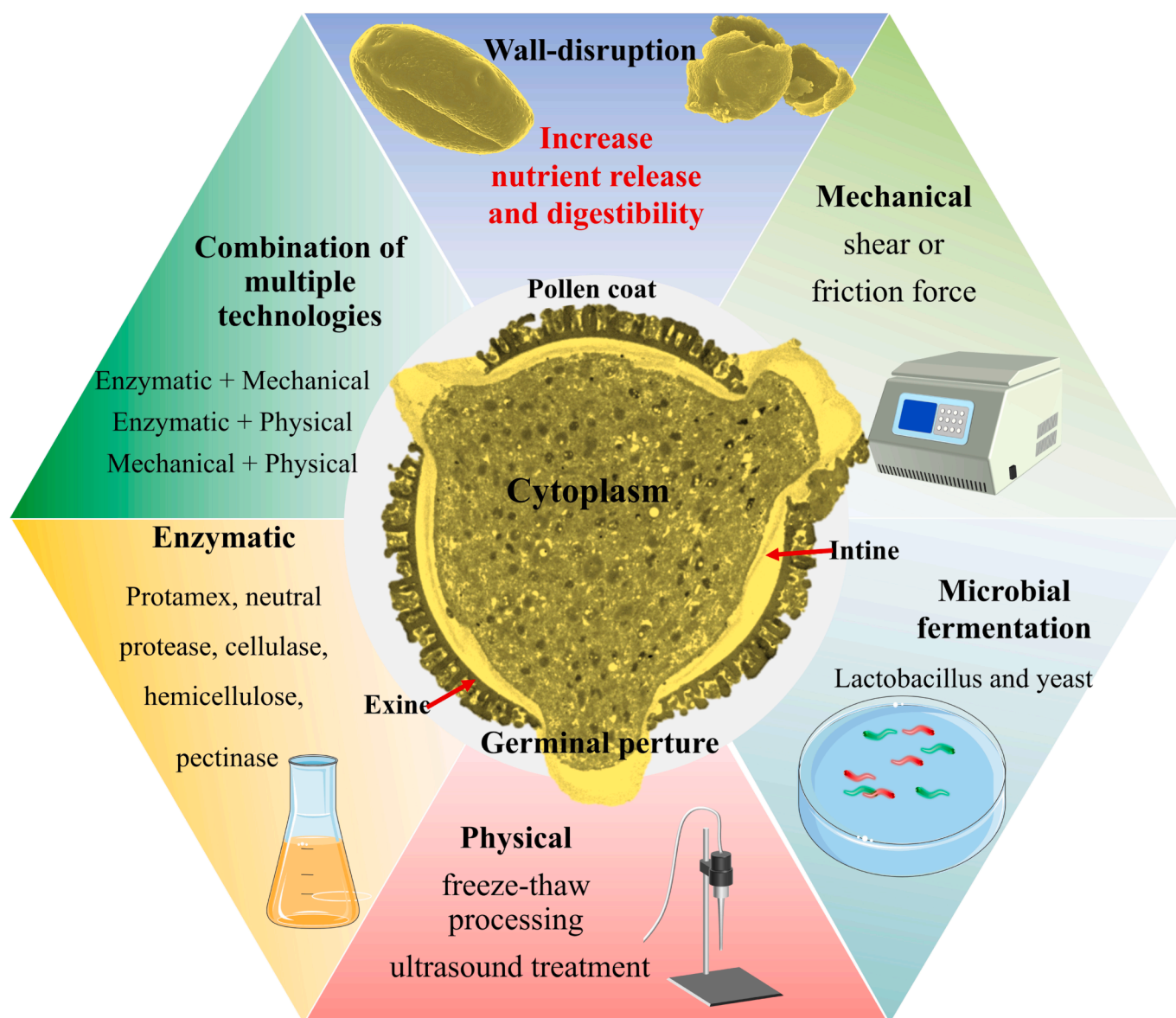


Fig. 2. Structural characteristics of pollen wall and methods for wall-disruption.

**Table 1**  
Bee Pollen composition and nutritional requirements.

Nutrients	RDA or AI levels (mg/day)	Pollen levels (mg/100 g)
Protein	50,000	10000–40000
Carbohydrates	320,000	130000–550000
Crude fibers	30,000	300–30000
Fat	80,000	1000–13000
Sodium	1500	44
Potassium	2000	400–2000
Phosphor	1000	80–600
Calcium	1100	20–300
Magnesium	350	20–300
Zink	8	3–25
Manganese	3.5	2–11
Iron	12.5	1.1–17
Copper	1.2	0.2–1.6
Selenium	0.005	0–0.005
Iodine	0.15	0.7
$\beta$ -Carotin	0.9	1–20
Vit. C	75	7–56
Vit. E	13	4–31
Vit. A	2310 IU	35.6 IU
Vit. B3	15	4–11
Vit. B6	1.4	0.2–0.7
Vit. B1	1.1	0.6–1.3
Vit. B2	1.3	0.6–2
Vit. H	0.045	0.05–0.07
Pantothenic acid	6	0.5–2
Folic acid	0.4	0.3–1

RDA = Recommended Dietary Allowance, AI = Adequate Intakes, IU = International Units;

Bee pollen composition is according to Mamta Thakur and Vikas Nanda (Thakur & Nanda, 2020a) and Campos et al. (Campos et al., 2008).

RDA or AI levels from Institute of Medicine (IOM) (2012), Mamta Thakur and Vikas Nanda (Thakur & Nanda, 2020a) and Bozena Denisowa and Marta Denisow-Pietrzykb (Denisow & Denisow-Pietrzyk, 2016).

(Campos et al., 2010). Bee pollen is rich in essential amino acids (EAAs), providing substantial nutritional value for honeybees and humans (Yang et al., 2013). Almost all EAAs are present in bee pollen (with a few exceptions), ranging from 12 % to 45.02 % of the total amino acid content, which is comparable to the supply of essential amino acids (33.9 %) as defined by the FAO reference protein (Komosinska-Vassev et al., 2015; Thakur & Nanda, 2018).

### 2.3. Lipids

Lipids are the third most abundant component of bee pollen, following after carbohydrates and proteins (Thakur & Nanda, 2020a). Studies have shown that the total fat contents in bee pollen can range from 1 % to 24 % of the pollen's dry weight (Campos et al., 2008); similarly, the crude fat contents ranging from 2 % to 11 % in 20 species of bee pollen (Dong, Yang, et al., 2015).

In recent years, thousands of lipid metabolites have been identified in bee pollen through lipidomics methodologies (Li et al., 2017; Wang et al., 2022). These lipids can be systematically classified into four principal classes, including glycerophospholipids, glycerides, glycolipids, and sphingolipids (Li et al., 2017; Wang et al., 2022). Furthermore, the four classes comprise of twenty distinct subclasses: triglyceride, diglyceride, phosphatidylethanolamine, phosphatidylcholine, phosphatidylserine, phosphatidylglycerol, ceramide, monoglyceride, phosphatidic acid, phosphatidylinositol, cardiolipin, lyso-phosphatidylethanolamine, lyso-phosphatidylcholine, lyso-phosphatidylglycerol, lyso-phosphatidylinositol, lyso-phosphatidic acid, sphingomyelin, hexosyl ceramide, monogalactosyl mono-acylglycerol, and monogalactosyl diglyceride (Li et al., 2017; Wang et al., 2022). Glycerophospholipids emerged as the most prevalent lipid category within bee pollen, representing 48 to 51 % of the total lipids (Li et al., 2017; Wang et al., 2022). Following glycerophospholipids, glycerides accounted for 43 % to 46 %, while glycolipids and sphingolipids

contributed 4.10 % to 5.2 % and 1.4 % to 1.6 %, respectively (Li et al., 2017; Wang et al., 2022). Among the phospholipids, phosphatidylcholine exhibited the highest concentration in the tested bee pollen, ranging from 1.5 mg/g to 4.4 mg/g. It was followed by phosphatidylethanolamine and lyso-phosphatidylcholine, with concentrations ranging from 0.2 mg/g to 2.3 mg/g and 0.2 mg/g to 1.2 mg/g, respectively (Li et al., 2017; Wang et al., 2022).

A previous report reviewed that 3 % of the total lipids in bee pollen were free fatty acids, with about half of them being unsaturated acids, such as oleic, linoleic ( $\omega$ -6), and linolenic ( $\omega$ -3) acids (Bogdanov, 2012). Among the more than 20 types of fatty acids found in bee pollen, the content of  $\omega$ -3 fatty acids is the highest (Campos et al., 2008; Dong, Yang, et al., 2015). Most types of bee pollen have higher levels of unsaturated acids, except sunflower pollen (Dong, Yang, et al., 2015). The concentration of  $\alpha$ -linolenic acid, an  $\omega$ -3, varies widely among different types of pollen, ranging from 0.1 to 4 g/100 g (Manning, 2001). Furthermore, bee pollen has been found to contain docosahexaenoic acid (DHA), commonly found in fish oil (Dong, Yang, et al., 2015; Thakur & Nanda, 2020a). The European regulation EC 1924/06 designates fresh food as a 'source of  $\omega$ -3 fatty acids' if it contains  $\omega$ -3 at 300 mg/100 g concentration. As such, bee pollen is a significant source of  $\omega$ -3 fatty acids (Li et al., 2018; Thakur & Nanda, 2020a). The presence of nervonic acid is a noteworthy discovery in 16 species of bee pollen, with an average level of 0.21 mg/g (Dong, Yang, et al., 2015), highlighting the significance of bee pollen in the nervous system and brain development of human and honeybees.

### 2.4. Phenolic acids

Eighteen phenolic acids and three phenolic glucosides were identified from bee pollen in past studies (Table 2). *p*-Coumaric acid, gallic acid, caffeic acid, tri-hydroxycinnamic acid and ferulic acid are common and have been detected in bee pollen from different botanical and geographical origins. Although these phenolics have been found in bee pollen, their content is pretty low, with many compounds less than the limit of quantification (Li et al., 2018). Among the phenolic acids quantified in bee pollen, cinnamic acid and ellagic acid exhibited the highest concentrations, with 13 mg/100 g and 28 mg/100 g, respectively (Li et al., 2018). However, according to a recent survey of phytochemicals in 20 different monofloral bee pollen from China, phenolic acids were absent in bee pollen; instead, these compounds were exclusively found in conjugated forms as phenolamides in bee pollen (Qiao, Feng, et al., 2023).

### 2.5. Phenolamides

Phenolamides are structurally defined by the linkage of one or more hydroxycinnamic acids (such as *p*-coumaric, ferulic, and caffeic acid) to a polyamine (such as putrescine, cadaverine, spermidine, and spermine) through amide bonds (Adaškevičiūtė et al., 2022; El Ghouizi et al., 2020; Qiao, Feng, et al., 2023; Rodríguez-Flores et al., 2023). The variation of hydroxycinnamic acids and the possibility of one to four N-substitutions on polyamines are responsible for the greater diversity of phenolamides (Qiao, Feng, et al., 2023). Based on recent studies, phenolamides in bee pollen can be subdivided into the following four groups: 9 phenolamides conjugated putrescine, 35 phenolamides conjugated spermidine, 25 phenolamides conjugated spermine conjugated and one phenolamide conjugated agmatine (Table 3). Noteworthy, at least 28 phenolamides were initially identified or unique present in bee pollen (Kim et al., 2018; Qiao, Feng, et al., 2023). Recent multiple reports have indicated that bee pollen is rich in phenolamides; for example, 18 phenolamides in bee pollen from *Quercus mongolica* (Kim et al., 2018), 13 phenolamides in *Mimosa pudica* L. bee pollen (Pereira Gomes et al., 2022), 13 phenolamides in rapeseed bee pollen (Qiao, Feng, et al., 2023), 18 phenolamides in bee pollen collected from Colombia, Italy, and Spain (Gardana et al., 2018), and 64 phenolamides in 20 different types of Chinese bee

**Table 2**  
Polyphenols in bee pollen.

Polyphenols	Molecule weight	Botanical origin	Country or Region	Content (mg/100 g)	Reference
<b>Phenolic acids</b>					
4-methoxy benzoic	136	–	Brazil	–	(Carpes et al., 2013)
Cinnamic acid	148	<i>Anadenanthera</i>	Brazil	13.05	(De-Melo et al., 2018)
$\beta$ -Resorcylic acid	154	<i>Mimosa scabrella</i>	Brazil	12.54	(De-Melo et al., 2018)
Protocatechic acid	154	<i>Mimosa scabrella</i> , rapeseed	Brazil, China	1.50	(De-Melo et al., 2018)
<i>p</i> -Coumaric acid	164	<i>Alternanthera</i> , <i>Helianthus annuus</i> L. Rapeseed, <i>Zea mays</i> , <i>Coriandrum</i> and <i>Daucus</i> sp.	Brazil, Egypt, Morocco	6.68–20	(Aylanc et al., 2023; De-Melo et al., 2018; Kostić et al., 2019)
Vanillic acid	168	<i>Alternanthera</i>	Brazil	6.06	(De-Melo et al., 2018)
Galic acid	170	<i>Mya</i> , rapeseed, <i>Castanea</i> , <i>Rubus</i> and <i>Cistus</i> , <i>Zea mays</i> , <i>Helianthus annuus</i> L.	Brazil, Italy, China, Egypt, Serbia	–	(De-Melo et al., 2018; Thakur & Nanda, 2020b)
Caffeic acid	180	<i>Mimosa caesalpiniaefolia</i> , <i>Zea mays</i> , <i>Castanea</i> , <i>Rubus</i> and <i>Cistus</i> , <i>Ononis spinosa</i> / <i>Astragalus</i> sp.	Brazil, Turkey, Egypt, Italy, Morocco	0.15	(Aylanc et al., 2023; Kostić et al., 2019; Othman et al., 2019; Thakur & Nanda, 2020b)
Ferulic acid	194	<i>Alternanthera</i> , <i>Helianthus annuus</i> L. <i>Zea mays</i>	Brazil, Serbia, Egypt	0.71	(Kostić et al., 2019; Othman et al., 2019; Thakur & Nanda, 2020b)
Hydrocaffeic acid	196	–	Greece	–	(Karabagias et al., 2018)
Tri-hydroxycinnamic acid	196	<i>Cocos nucifera</i> L. ( <i>Arecaceae</i> ).	Brazil	–	(Negri et al., 2018)
Syringic acid	198	<i>Mimosa caesalpiniaefolia</i>	Italy, Brazil	5.36	(De-Melo et al., 2018)
Synapic acid	224	<i>Myrcia</i>	Brazil	0.29	(De-Melo et al., 2018)
Ellagic acid	302	<i>Mimosa scabrella</i>	Brazil	3.41–28.12	(Adaškevičiūtė et al., 2022; De-Melo et al., 2018)
<i>p</i> -Coumaric acid hexoside	326	<i>Coriandrum</i> and <i>Daucus</i> sp.,	Morocco	16–22	(Aylanc et al., 2023)
<i>p</i> -Coumaroyl tyrosine	327	–	Greece	–	(Karabagias et al., 2018)
Carnosic acid	332	–	Italy	–	(Rocchetti et al., 2019)
Coumaroyl quinic acid	338	–	Portugal	–	(Anjos et al., 2019)
Caffeoyl glucose	342	–	Italy	–	(Rocchetti et al., 2019)
Chlorogenic acid	354	<i>Cocos nucifera</i> , <i>Mimosa caesalpiniaefolia</i>	Brazil	4.85	(De-Melo et al., 2018)
Feruloyl glucose	356	–	Italy	–	(Rocchetti et al., 2019)
<b>Flavonoids</b>					
Chrysin	254	<i>Brassica juncea</i>	India	0.07–0.08	(Ketkar et al., 2014; Thakur & Nanda, 2020b)
Apigenin	270	<i>Myrcia</i> , <i>Helianthus annuus</i> L. <i>Zea mays</i>	Brazil, Serbia	0.03–0.23	(De-Melo et al., 2018; Kostić et al., 2019; Othman et al., 2019)
Galangin	270	<i>Helianthus annuus</i> L.	Serbia	2.4–72.8	(Kostić et al., 2019)
Naringenin	272	<i>Helianthus annuus</i> L., <i>Anadenanthera</i> , <i>Mimosa scabrella</i> , <i>Mimosa scabrella</i> , <i>Brassica campestris</i> , <i>Zea mays</i>	Serbia, Brazil, China	4.6	(De-Melo et al., 2018; Kostić et al., 2019; Thakur & Nanda, 2020a)
Phloretin	274	<i>Helianthus annuus</i> L.	Serbia	6.6	(Kostić et al., 2019)
Acacetin	284	<i>Helianthus annuus</i> L.	Serbia	4.0	(Kostić et al., 2019)
Genkwanin	284	<i>Helianthus annuus</i> L.	Serbia	4.2	(Kostić et al., 2019)
Kaempferol	286	<i>Alternanthera</i> , <i>Mimosa caesalpiniaefolia</i> , <i>Helianthus annuus</i> L. Rapeseed, <i>Brassica campestris</i> , <i>Brassica juncea</i> , <i>Zea mays</i>	Serbia, Brazil, China, Slovakia, Egypt	24.2–61.2	(De-Melo et al., 2018; Kostić et al., 2019; Thakur & Nanda, 2020a)
Luteolin	286	<i>Helianthus annuus</i> L. <i>Zea mays</i>	Slovakia, Egypt	5.80–10.60	(Kostić et al., 2019; Rocchetti et al., 2019)
Eriodictyol	288	<i>Helianthus annuus</i> L.	Serbia	12.2–13.6	(De-Melo et al., 2018)
Catechin	290	Rapeseed, <i>Zea mays</i>	China, Egypt, Turkey	0.75	(De-Melo et al., 2018; Thakur & Nanda, 2020a)
Epicatechin	290	<i>Zea mays</i>	Egypt	–	(De-Melo et al., 2018)
Quercetin	302	<i>Cocos nucifera</i> , Rapeseed, <i>Helianthus annuus</i> L., <i>Brassica juncea</i>	Brazil, China, Slovakia, India	261.4–381.6	(De-Melo et al., 2018; Kostić et al., 2019)
Tricetin	302	–	Brazil	–	(Urcan et al., 2018)
Taxifolin	304	<i>Helianthus annuus</i> L.	Serbia	26.1	(Kostić et al., 2019)
Myricetin	318	–	Brazil, Portugal	–	(Anjos et al., 2019)
Isorhamnetin	316	<i>Helianthus annuus</i> L. <i>Brassica campestris</i>	Serbia, China	136.2–143.6	(Kostić et al., 2019; Thakur & Nanda, 2020a)
Dihydromyricetin	320	<i>Anadenanthera</i>	Brazil	–	(De-Melo et al., 2018)
Bis-methylated quercetin	330	<i>Cocos nucifera</i>	Brazil	–	(De-Melo et al., 2018)
<b>Flavonoid glycosides</b>					
Quercetin 3-O-rhamnoside	448	<i>Helianthus annuus</i> L., <i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i>	Serbia, Portugal, Brazil, Morocco	70–77.6	(Anjos et al., 2019; Aylanc et al., 2023; Kostić et al., 2019)
Quercetin 3-O-galactoside	464	<i>Helianthus annuus</i> L.	Serbia	–	(Kostić et al., 2019)
Quercetin 3-O-glucoside	464	Buckwheat, Maize, Sunflower, <i>Olea europaea</i>	China	19–53	(Aylanc et al., 2023; Qiao, Feng, et al., 2023)
Quercetin 3-O-(6'-O-malonyl)-glucoside	550	Chrysanthemum	China	51	(Qiao, Feng, et al., 2023)
Quercetin-O-(malonyl)-hexoside	550	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i> , <i>Helianthemum</i> sp.	Portugal, Morocco	22–84	(Anjos et al., 2019; Aylanc et al., 2023)
Quercetin-3-O-arabinoglucoside	596	Corn poppy	China	64	(Qiao, Feng, et al., 2023)

(continued on next page)

Table 2 (continued)

Polyphenols	Molecule weight	Botanical origin	Country or Region	Content (mg/100 g)	Reference
Quercetin-3-O-glucosyl-6-O-pentoside	596	<i>Alternanthera</i>	Brazil	–	(De-Melo et al., 2018)
Quercetin-O-hexosyl-pentoside	596	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i> , <i>Ononis spinosa</i> / <i>Astragalus</i> sp.	Portugal	17	(Anjos et al., 2019; Aylanc et al., 2023)
Quercetin 3-O-rutinoside (Rutin)	610	<i>Alternanthera</i> , Tea, <i>Olea europaea</i> , <i>Raphanus</i> sp., <i>Ligustrum/Olea</i> sp., <i>Cistaceae</i>	Brazil, China, Italy, Greece, Portugal	21–48	(Aylanc et al., 2023; De-Melo et al., 2018; Kostić et al., 2019; Larbi et al., 2023; Qiao, Feng, et al., 2023)
Quercetin-3-O-rhamnosyl glucoside	610	–	Brazil	–	(Negri et al., 2018)
Quercetin-3-O-sophoroside	626	Watermelon, Corn poppy, Watermelon, Rapeseed, Dandelion, Maize, <i>Phellodendron</i> , Melon, Tea, Melon, Maize,	China, Lithuania, China	36–396	(Čeksterytė et al., 2016; Qiao, Feng, et al., 2023)
Quercetin-3,7-O-diglucoside	626		China	42–83	(Qiao, Feng, et al., 2023)
Quercetin-O-diglucoside	626	<i>Coriandrum</i> and <i>Daucus</i> sp., <i>Olea europaea</i> , <i>Raphanus</i> sp., <i>Helianthemum</i> sp., <i>Ononis spinosa</i> / <i>Astragalus</i> sp., <i>Carduus</i> sp., <i>Ligustrum/Olea</i> sp.	Morocco, Portugal	20–330	(Aylanc et al., 2023; Larbi et al., 2023)
Quercetin-3,4'-O-diglucoside	626	Melon	China	202	(Qiao, Feng, et al., 2023)
Quercetin-O-malonyl deoxyhexosyl-hexoside	696	<i>Cistaceae</i>	Portugal	24	(Larbi et al., 2023)
Quercetin-O-(malonyl)-rutinoside	712	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i>	Portugal	–	(Anjos et al., 2019)
Isorhamnetin-3-O-glucoside	478	Plum, Pear, Hawthorn, Chrysanthemum, <i>Phellodendron</i> , <i>Helianthus annuus</i> L. <i>Ononis spinosa</i> / <i>Astragalus</i> sp.	China, Slovakia, Morocco	24–338	(Aylanc et al., 2023; Kostić et al., 2019; Qiao, Feng, et al., 2023)
Isorhamnetin-O-dihexoside	478	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i>	Portugal	–	(Anjos et al., 2019)
Isorhamnetin-3-O-(6'-O-malonyl)-glucoside	564	Pear, Hawthorn, Chrysanthemum	China	121–1720	(Qiao, Feng, et al., 2023)
Isorhamnetin-O-malonyl hexoside	564	<i>Helianthemum</i> sp., <i>Carduus</i> sp., <i>Cistaceae</i>	Morocco, Portugal	26–39	(Aylanc et al., 2023; Larbi et al., 2023)
Isorhamnetin-O-pentosyl-hexoside	610	<i>Ononis spinosa</i> / <i>Astragalus</i> sp., <i>Carduus</i> sp.	Morocco, Portugal	17–23	(Aylanc et al., 2023; Larbi et al., 2023)
Isorhamnetin-3-O-vicianoside	610	Lotus	China	66	(Qiao, Feng, et al., 2023)
Isorhamnetin-7-O-vicianoside	610	Tea	China	19	(Qiao, Feng, et al., 2023)
Isorhamnetin-3-O-(6''-O-pcoumaroyl)-glucoside	624	–	Brazil	–	(Negri et al., 2018)
Isorhamnetin-3-O-(2''-O-rhamnosyl)-glucoside	624	–	Brazil	–	(Negri et al., 2018)
Isorhamnetin-3-O-rutinoside	624	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i> , <i>Helianthus annuus</i> L.	Portugal, Serbia	3.4–3.9	(Anjos et al., 2019; Kostić et al., 2019)
Isorhamnetin-3-O-neohesperidoside	624	Rose, Tea, Pear, Maize	China	18–143	(Qiao, Feng, et al., 2023)
Isorhamnetin-3-O-hexosyl-deoxyhexoside	624	<i>Cistaceae</i> , <i>Castanea</i> sp.	Portugal	16–101	(Larbi et al., 2023)
Isorhamnetin-di-3,7-O-glucoside	640	–	Brazil	–	(Negri et al., 2018)
Isorhamnetin-3-O-gentiobioside	640	Broad bean, Plum, Apricot, Maize, Pear, Hawthorn, Rose, <i>Phellodendron</i> , Tea	China	18–2360	(Qiao, Feng, et al., 2023)
Isorhamnetin-O-malonyl rutinoside	664	–	Morocco	21	(Aylanc et al., 2023)
Isorhamnetin-3-O-(2''-O-rhamnosylacetyl) glucoside	666	–	Brazil	–	(Negri et al., 2018)
Isorhamnetin-O-malonyl pentosyl-hexoside	696	<i>Carduus</i> sp., <i>Echium</i> sp.	Morocco, Portugal	15–46	(Aylanc et al., 2023; Larbi et al., 2023)
Isorhamnetin-O-acetyl-hexoside	710	<i>Cistaceae</i>	Portugal	16	(Larbi et al., 2023)
Isorhamnetin-3-O-(6'-O-malonyl)-glucosyl-7-O-glucoside	726	Hawthorn, Chrysanthemum, Rose	China	55–91	(Qiao, Feng, et al., 2023)
Isorhamnetin-3-O-(2'',3''-O-di-rhamnosyl)-glucoside	770	–	Brazil	–	(Negri et al., 2018)
Isorhamnetin-3-O-(2'-O-glucosyl)-rutinoside	786	Oil-Tea	China	99	(Qiao, Feng, et al., 2023)
Kaempferol-3-O-rhamnoside	432	<i>Coriandrum</i> and <i>Daucus</i> sp.	Morocco	17–160	(Aylanc et al., 2023; Larbi et al., 2023)
Kaempferol-O-hexoside	448	<i>Carduus</i> sp.	Portugal	16–17	(Larbi et al., 2023)
Kaempferol 3-O-(6'-O-malonyl)-glucoside	534	Chrysanthemum	China	39	(Qiao, Feng, et al., 2023)
Kaempferol-3-O-sambubioside	580	Corn poppy	China	197	(Qiao, Feng, et al., 2023)

(continued on next page)

Table 2 (continued)

Polyphenols	Molecule weight	Botanical origin	Country or Region	Content (mg/100 g)	Reference
Kaempferol 3-O-rhamnosyl-glucoside	594	<i>Mimosa scabrella</i>	Brazil	–	(De-Melo et al., 2018)
Kaempferol-7-O-rutinoside	594	<i>Myrcia</i>	Brazil	–	(De-Melo et al., 2018)
Kaempferol-3-O-rutinoside	594	Apricot, Watermelon, Corn poppy, Melon, Tea, Phellodendron, Echium plantagineum, <i>Ononis spinosa</i> / <i>Astragalus</i> sp., <i>Carduus</i> sp., <i>Ligustrum/Olea</i> sp., <i>Cistaceae</i> , <i>Rubus</i> sp., <i>Echium</i> sp.	China, Morocco, Portugal	17–402	(Aylanc et al., 2023; Larbi et al., 2023; Qiao, Feng, et al., 2023)
Kaempferol-O-dihexoside	610	<i>Carduus</i> sp.	Portugal	20	(Larbi et al., 2023)
Kaempferol-O-diglucoside	610	<i>Raphanus</i> sp., <i>Ononis spinosa</i> / <i>Astragalus</i> sp.	Morocco	22–83	(Aylanc et al., 2023)
Kaempferol-3-O-sophoroside	610	Plum, Apricot, Corn poppy, Rapeseed, Tea, Phellodendron	China	46–1013	(Qiao, Feng, et al., 2023)
Kaempferol-O-malonyl rutinoside	680	<i>Helianthemum</i> sp.	Morocco	19–25	(Aylanc et al., 2023)
Kaempferol-O-malonyl-hexosyl deoxyhexoside	680	<i>Carduus</i> sp., <i>Ligustrum/Olea</i> sp., <i>Rubus</i> sp., <i>Castanea</i> sp.	Portugal	19–124	(Larbi et al., 2023)
Kaempferol-3-O-rutinoside-7-O-glucoside	756	Tea	China	–	(Qiao, Feng, et al., 2023)
Kaempferol-3-O-(2'-O-glucosyl)-rutinoside	756	Apricot, Oil-Tea	China	–	(Qiao, Feng, et al., 2023)
Kaempferol-3-O-glucosyl rutinoside	756	<i>Mimosa scabrella</i>	Brazil	–	(De-Melo et al., 2018)
Myricetin-3-O-rhamnopyranoside	464	<i>Myrcia</i>	Brazil	–	(De-Melo et al., 2018)
Myricetin-O-hexoside	480	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i> , <i>Helianthemum</i> sp.	Portugal, Morocco	0.2	(Anjos et al., 2019; Aylanc et al., 2023)
Myricetin-O-(malonyl)-hexoside	566	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i> , <i>Helianthemum</i> sp., <i>Cistaceae</i>	Portugal, Morocco	25	(Anjos et al., 2019; Larbi et al., 2023)
Myricetin-3-O-rutinoside	626	<i>Helianthemum</i> sp., <i>Cistaceae</i>	Morocco, Portugal	17–80	(Aylanc et al., 2023; Larbi et al., 2023)
Myricetin-O-(malonyl)-rutinoside	712	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i> , <i>Cistaceae</i>	Portugal	19	(Anjos et al., 2019; Larbi et al., 2023)
Syringetin-3-O-glucoside	508	Hawthorn	China	96	(Qiao, Feng, et al., 2023)
Syringetin-3-O-(6"-O-malonyl)-glucoside	594	Hawthorn	China	346	(Qiao, Feng, et al., 2023)
Syringetin-3-O-rutinoside	654	Hawthorn	China	35	(Qiao, Feng, et al., 2023)
Naringenin hexoside	434	<i>Anadenanthera</i>	Brazil	–	(De-Melo et al., 2018)
Naringenin-7-O-glucoside	434	–	Italy	–	(Rocchetti et al., 2019)
Naringin-4'-O-glucoside	434	–	Italy	–	(Rocchetti et al., 2019)
Naringin	580	–	Brazil	–	(De-Melo et al., 2018)
Luteolin-di-O-hexosyl-rhamnoside	432	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i>	Portugal	–	(Anjos et al., 2019)
Luteolin-O-dihexoside	448	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i>	Portugal	–	(Anjos et al., 2019)
Luteolin 7-O-glucuronide	462	–	Italy	–	(Rocchetti et al., 2019)
Luteolin-7-O-6"-acetylglucoside	490	<i>Alternanthera</i>	Brazil	–	(De-Melo et al., 2018)
Luteolin-O-(malonyl)-hexoside	534	<i>Cistus ladanifer</i> , <i>Echium</i> sp. and <i>Apiaceae</i>	Portugal	–	(Anjos et al., 2019)
Apigenin 6-C-glucoside	564	–	Italy	–	(Rocchetti et al., 2019)
Orientin-2-O-xyloside	580	<i>Myrcia</i>	Brazil	–	(De-Melo et al., 2018)
Tricetin-7-O-(pentoside-glucoside)	596	<i>Myrcia</i>	Brazil	–	(De-Melo et al., 2018)
Isovitexin	432	Watermelon, Melon	China	–	(Qiao, Xiao, et al., 2023)
Methyl herbacetin-O-hexoside	478	<i>Rubus</i> sp.	Portugal	18–19	(Larbi et al., 2023)
Methyl herbacetin-O-dihexoside	640	<i>Carduus</i> sp., <i>Rubus</i> sp.	Portugal	24–423	(Larbi et al., 2023)
Methyl herbacetin-O-malonyl-hexosyl-deoxyhexoside	710	<i>Rubus</i> sp.	Portugal	21–22	(Larbi et al., 2023)
Methyl herbacetin-malonyl-dihexoside	726	<i>Carduus</i> sp., <i>Rubus</i> sp.	Portugal	21–205	(Larbi et al., 2023)
Laricitrin-O-malonylhexoside	580	<i>Cistaceae</i>	Portugal	17	(Larbi et al., 2023)
Laricitrin-O-hexosyl-deoxyhexoside	640	<i>Cistaceae</i>	Portugal	22	(Larbi et al., 2023)

pollen (Qiao, Feng, et al., 2023). Based on current knowledge, a total of 70 phenolamides have been thus far reported in bee pollen, exceeding one-third of the total phytochemicals found in bee pollen (Table 3).

A survey of phenolamides in 20 types of monofloral bee pollens from China found that the content of phenolamides ranged from 1.50 mg/g to 39.02 mg/g (Qiao, Feng, et al., 2023). Among these, 11 types of bee pollen contained phenolamides exceeding 1 % of the total weight;

particularly, rose bee pollen with 39.02 mg/g (Qiao, Feng, et al., 2023). Moreover, tri-*p*-coumaroyl spermidine is consistently detected in nearly all documented bee pollen samples, displaying higher concentrations than other phenolamides, for pear pollen with the most elevated levels at 26.89 mg/g (Qiao, Feng, et al., 2023). To our knowledge, bee pollen is currently natural foods' richest source of phenolamides.

**Table 3**  
Phenolamides in bee pollen.

Phenolamides	Molecule weight	Botanical origin	Country or Region	Content (mg/100 g)	Reference
N-Feruloyl putrescine	264		China	–	(H. Zhang et al., 2023)
<i>p</i> -Coumaroyl agmatine	276		China	–	(H. Zhang et al., 2023)
N(Z), N'(Z)-di- <i>p</i> -coumaroyl putrescine	380	Broad bean	China	69–298	(Qiao, Feng, et al., 2023)
N(Z), N'(E)-di- <i>p</i> -coumaroyl putrescine	380	Broad bean, sunflower, Pear	China	1.50	(Kim et al., 2018; Qiao, Feng, et al., 2023; X. Zhang et al., 2022)
N(E), N'(E)-di- <i>p</i> -coumaroyl putrescine	380	Broad bean, Hawthorn, kiwifruit	Korea, China	6.68–20	(Kim et al., 2018; Qiao, Feng, et al., 2023; X. Zhang et al., 2023)
N- <i>p</i> -coumaroyl-N'-caffeoyl putrescine	396	Broad bean	China	140	(Qiao, Feng, et al., 2023)
N- <i>p</i> -coumaroyl-N'-feruloyl putrescine	410	Broad bean	China	135	(Qiao, Feng, et al., 2023)
N, N'-di-caffeoyl putrescine	412	Broad bean	China	99	(Qiao, Feng, et al., 2023)
N-feruloyl-N'-caffeoyl putrescine	426	Broad bean	China	90	(Qiao, Feng, et al., 2023)
N1(Z), N10(Z)-di- <i>p</i> -coumaroyl spermidine	437	Rapeseed	China	29–833	(Qiao, Feng, et al., 2023; Zhang et al., 2020)
N1(Z), N10(E)-di- <i>p</i> -coumaroyl spermidine	437	Rapeseed	China	5.36	(Qiao, Feng, et al., 2023; Zhang et al., 2020)
N1(E), N10(Z)-di- <i>p</i> -coumaroyl spermidine	437	Rapeseed, Phellodendron	China	0.29	(Qiao, Feng, et al., 2023; Zhang et al., 2020)
N1(E), N10(E)-di- <i>p</i> -coumaroyl spermidine	437	Rapeseed, Phellodendron, Tea, Buckwheat	China	3.41–28.12	(Qiao, Feng, et al., 2023; Zhang et al., 2020)
Coumaroyl caffeoyl spermidine	453	–	China	–	(X. Zhang et al., 2022)
Bis (dihydrocaffeoyl) spermidine	473	–	China	–	(H. Zhang et al., 2023)
N1-acetyl-N5(E), N10(E)-di- <i>p</i> -methoxy coumaroyl spermidine	507	<i>Quercus mongolica</i>	Korea	–	(Kim et al., 2018)
N1-acetyl-N5(Z)-N10(E)-di- <i>p</i> -methoxy-coumaroyl spermidine	507	<i>Quercus mongolica</i>	Korea	–	(Kim et al., 2018)
N1-acetyl-N5(Z), N10(Z)-di- <i>p</i> -methoxy-coumaroyl spermidine	507	<i>Quercus mongolica</i>	Korea	–	(Kim et al., 2018)
N1(Z), N5(Z), N10(Z)-tri- <i>p</i> -coumaroyl spermidine	583	Sunflower, Plums, Pear, Oil-tea, Tea, Phellodendron, Apricot, Hawthorn, kiwifruit, Buckwheat, Rose, <i>Quercus mongolica</i> , <i>Castanea</i>	Korea, China, Iberian Peninsula	85–2689	(El Ghouizi et al., 2020; Kim et al., 2018; Qiao, Feng, et al., 2023; Rodríguez-Flores et al., 2023; Zhang et al., 2020)
N1(Z), N5(Z), N10(E)-tri- <i>p</i> -coumaroyl spermidine	583	Sunflower, Plums, Pear, Oil-tea, Tea, Moroccan Phellodendron, Apricot, Hawthorn, kiwi fruit, Broad bean, Buckwheat, Rose, <i>Quercus mongolica</i> , <i>Castanea</i> Moroccan	Korea, China, Iberian Peninsula	2.4–72.8	(El Ghouizi et al., 2020; Kim et al., 2018; Qiao, Feng, et al., 2023; Rodríguez-Flores et al., 2023; Zhang et al., 2020)
N1(E), N5(Z), N10(E)-tri- <i>p</i> -coumaroyl spermidine	583	Sunflower, Plums, Pear, Oil-tea, Tea, Phellodendron, Apricot, Hawthorn, kiwifruit, Broad bean, Melon, Buckwheat, Rose, <i>Quercus mongolica</i> , Moroccan	Korea, China, Iberian Peninsula	4.6	(El Ghouizi et al., 2020; Kim et al., 2018; Qiao, Feng, et al., 2023; Rodríguez-Flores et al., 2023; Zhang et al., 2020)
N1(E), N5(E), N10(E)-tri- <i>p</i> -coumaroyl spermidine	583	Sunflower, Plums, Pear, Oil-tea, Tea, Phellodendron, Apricot, Hawthorn, kiwi fruit, Broad bean, Melon, Buckwheat, Rose, <i>Quercus mongolica</i> , <i>Castanea</i> , <i>Rubus</i> sp.	Korea, China, Iberian Peninsula, Moroccan, Brazil	6.6	(El Ghouizi et al., 2020; Kim et al., 2018; Larbi et al., 2023; Negri et al., 2018; Negri et al., 2011; Qiao, Feng, et al., 2023; Qiao, Xiao, et al., 2023; Rodríguez-Flores et al., 2023; Zhang et al., 2020)
N1, N10-di- <i>p</i> -coumaroyl-N5-caffeoyl spermidine	599	Apricot, Rose, Oil-tea, Broad bean, Tea, Phellodendron,	China, Brazil	38–2617	(El Ghouizi et al., 2020; Negri et al., 2018; Qiao, Feng, et al., 2023)
N1(E), N10(E)-di- <i>p</i> -coumaroyl-N5(E)-caffeoyl, spermidine	599	<i>Quercus mongolica</i>	Korea	4.2	(Kim et al., 2018)
N1(E), N10(Z)-di- <i>p</i> -coumaroyl-N5(Z)-caffeoyl spermidine	599	<i>Quercus mongolica</i>	Korea	24.2–61.2	(Kim et al., 2018)
N1- <i>p</i> -methoxybenzoyl-N5(Z)-N10(E)-di- <i>p</i> -methoxy-coumaroyl spermidine	599	<i>Quercus mongolica</i>	Korea	5.80–10.60	(Kim et al., 2018)
N1, N5-di- <i>p</i> -coumaroyl-N10-caffeoylspermidine	599	<i>Ononis spinosa</i> / <i>Astragalus</i> sp.	Morocco, Portugal		(Aylanc et al., 2023; Larbi et al., 2023)
Di-coumaroyl dihydrocaffeoyl spermidine	602	–	China	–	(X. Zhang et al., 2022)
N1, N5-di- <i>p</i> -coumaroyl- N10-feruloyl spermidine	613	Oil-tea, Tea, <i>Echium</i> sp.	China, Portugal	23–26	(Larbi et al., 2023; Qiao, Feng, et al., 2023)
N1- <i>p</i> -coumaroyl-N5, N10-di-caffeoyl spermidine	615	Broad bean, Oil-tea, Tea, Phellodendron, Buckwheat, <i>Castanea</i>	China, Brazil, Morocco	16–186	(El Ghouizi et al., 2020; Negri et al., 2018; Qiao, Feng, et al., 2023; Qiao, Xiao, et al., 2023; Rodríguez-Flores et al., 2023)

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Table 3 (continued)

Phenolamides	Molecule weight	Botanical origin	Country or Region	Content (mg/100 g)	Reference
N1(E)- <i>p</i> -coumaroyl-N5(Z), N10(E)-di-caffeoyl, spermidine	615	<i>Quercus mongolica</i> , <i>Castanea</i> , <i>Ononis spinosa</i> / <i>Astragalus</i> sp.	Korea	–	(Aylanc et al., 2023; Kim et al., 2018; Rodríguez-Flores et al., 2023)
N1(E), N5(E)-di-caffeoyl-N10(E)- <i>p</i> -coumaroyl spermidine	615	<i>Quercus mongolica</i> , <i>Castanea</i> , <i>Ligustrum/Olea</i> sp.	Korea, Iberian Peninsula, Portugal	26.1	(Kim et al., 2018; Larbi et al., 2023; Rodríguez-Flores et al., 2023)
N1, N5, N10-(Z)-tri- <i>p</i> -methoxy-coumaroyl spermidine	625	<i>Quercus mongolica</i>	Korea	–	(Kim et al., 2018)
N1, N5-di- <i>p</i> -coumaroyl-N10-hydroxyferuloyl spermidine	629	Tea	China	75	(Qiao, Feng, et al., 2023)
N'-caffeoyl-N''-feruloyl-N'''-coumaroyl spermidine	629	–	Brazil, China	–	(Negri et al., 2018; X. Zhang et al., 2022)
Tri-caffeoyl spermidine	631	Apricot, Tea, Phellodendron, Buckwheat, <i>Ligustrum/Olea</i> sp., <i>Castanea</i> , <i>Quercus mongolica</i> , <i>Castanea</i>	Brazil, China, Portugal	27–371	(Larbi et al., 2023; Negri et al., 2018; Qiao, Feng, et al., 2023; Zhang et al., 2020)
N1(E), N5(E), N10(E)- tri-caffeoyl spermidine	631	<i>Quercus mongolica</i> , <i>Castanea</i>	Korea, Iberian Peninsula	–	(Kim et al., 2018; Rodríguez-Flores et al., 2023)
N1(E), N5(Z), N10(E)- tri-caffeoyl spermidine	631	<i>Quercus mongolica</i> , <i>Castanea</i>	Korea, Iberian Peninsula	–	(Kim et al., 2018; Rodríguez-Flores et al., 2023)
Coumaroyl di-feruloyl spermidine	643	–	China	–	(X. Zhang et al., 2022)
N',N''-di-caffeoyl-N'''-feruloyl spermidine	645	<i>Castanea</i> sp.	China, Portugal	34	(Larbi et al., 2023; Negri et al., 2018; Rodríguez-Flores et al., 2023)
Caffeoyl di-feruloyl spermidine	659	–	China	–	(X. Zhang et al., 2022)
Tri-feruloyl-spermidine	673	<i>Rhus chinensis</i>	China, Brazil	116	(Negri et al., 2018; Qiao, Feng, et al., 2023; Zhang et al., 2020)
N1, N10-di-feruloyl-N5-hydroxyferuloyl spermidine	689	<i>Rhus chinensis</i>	China	56	(Qiao, Feng, et al., 2023)
N1, N10-di-hydroxyferuloyl-N5-feruloyl spermidine	705	<i>Rhus chinensis</i>	China	1320	(Qiao, Feng, et al., 2023)
N1, N14-di- <i>p</i> -coumaroyl-N5-hydroxyavenalumoyl spermine	682	Corn poppy	China	317	(Qiao, Feng, et al., 2023)
N1(Z), N14(Z)-di- <i>p</i> -coumaroyl-N5, N10-di-acetyl spermine	578	Corn poppy	China	553	(Qiao, Feng, et al., 2023)
N1(Z), N14(E)-di- <i>p</i> -coumaroyl-N5, N10-di-acetyl spermine	578	Corn poppy	China	202	(Qiao, Feng, et al., 2023)
N1(E), N14(E)-di- <i>p</i> -coumaroyl-N5, N10-di-acetyl spermine	578	Corn poppy	China	24	(Qiao, Feng, et al., 2023)
N1, N5, N10-tri- <i>p</i> -coumaroyl spermine	640	<i>Chrysanthemum</i> , <i>Ononis spinosa</i> / <i>Astragalus</i> sp.	China, Morocco	19–161	(Aylanc et al., 2023; Qiao, Feng, et al., 2023; X. Zhang et al., 2022)
N1, N10-di- <i>p</i> -coumaroyl-N14-caffeoyl spermine	656	Rapeseed	China	41	(Qiao, Feng, et al., 2023; X. Zhang et al., 2022)
N1-feruloyl-N5, N14-di- <i>p</i> -coumaroyl spermine	670	Rapeseed	China	22	(Qiao, Feng, et al., 2023)
Coumaroyl caffeoyl dihydrocaffeoyl spermine	674	–	China	–	(X. Zhang et al., 2022)
N1, N10-di- <i>p</i> -coumaroyl-N14-hydroxyferuloyl spermine	686	Rapeseed, Buckwheat	China	83–164	(Qiao, Feng, et al., 2023; Zhang et al., 2020)
Coumaroyl feruloyl dihydrocaffeoyl spermine	688	–	China	–	(X. Zhang et al., 2022)
N1- hydroxyferuloyl-N5- <i>p</i> -coumaroyl-N14-caffeoyl spermine	702	Rapeseed	China	111	(Qiao, Feng, et al., 2023)
N1-hydroxyferuloyl-N5- <i>p</i> -coumaroyl-N14-feruloyl spermine	716	Rapeseed, Buckwheat	China	33–111	(Qiao, Feng, et al., 2023)
N1(Z), N5(Z), N10(Z), N14(Z) tetra- <i>p</i> -coumaroyl spermine	786	<i>Chrysanthemum</i> , <i>Quercus mongolica</i>	China	11–735	(Qiao, Feng, et al., 2023)
N1(E), N5(Z), N10(Z), N14(Z) tetra- <i>p</i> -coumaroyl spermine	786	<i>Chrysanthemum</i> , Tea, Sunflower	China	–	(Qiao, Feng, et al., 2023)
N1(E), N5(Z), N10(Z), N14(E) tetra- <i>p</i> -coumaroyl spermine	786	<i>Chrysanthemum</i> , Tea, Sunflower, Buckwheat	China	3.4–3.9	(Qiao, Feng, et al., 2023)
N1(E), N5(E), N10(Z), N14(E) tetra- <i>p</i> -coumaroyl spermine	786	<i>Chrysanthemum</i> , Sunflower, Buckwheat	China	18–143	(Qiao, Feng, et al., 2023)
N1(E), N5(E), N10(E), N14(E) tetra- <i>p</i> -coumaroyl spermine	786	<i>Chrysanthemum</i> , Sunflower, Buckwheat	China	16–101	(Qiao, Feng, et al., 2023)
tetra- <i>p</i> -coumaroyl spermine	786	<i>Helianthemum</i> sp.	Morocco	14–23	(Aylanc et al., 2023)
N1, N5, N10-tri- <i>p</i> -coumaroyl-N14-hydroxyferuloyl spermine	832	Rapeseed	China	69	(Qiao, Feng, et al., 2023)
N1-caffeoyl-N5, N10-di- <i>p</i> -coumaroyl-N14-hydroxyferuloyl spermine	848	Rapeseed	China	25	(Qiao, Feng, et al., 2023)
Tetra-caffeoyl spermine	850	Rapeseed	China	74	(Qiao, Feng, et al., 2023)
N1, N5, N10-tri-caffeoyl-N14-feruloyl spermine	864	Rapeseed	China	38	(Qiao, Feng, et al., 2023)

(continued on next page)

Table 3 (continued)

Phenolamides	Molecule weight	Botanical origin	Country or Region	Content (mg/100 g)	Reference
N1, N5, N10-tri-caffeoyl-N14-hydroxy feruloyl spermine	880	Rapeseed	China	106	(Qiao, Feng, et al., 2023)
N1-feruloyl-N5, N10-dicafeoyl-N14-hydroxyferuloyl spermine	894	Rapeseed	China	21	(Qiao, Feng, et al., 2023)
N1, N14-di-hydroxyferuloyl-N5, N10-di-cafeoyl spermine	910	Rapeseed	China	11	(Qiao, Feng, et al., 2023)

## 2.6. Flavonoids

Flavonoids were considered the predominant bioactive compounds in bee pollen (Ćirić et al., 2022; El Ghouizi et al., 2023). Prior research has documented the existence of 98 flavonoids within bee pollen, comprising 19 non-glycosylated flavonoids and 79 glycosylated flavonoids (Table 2). Glycosylated flavonoids are the most significant number of identified phytochemicals in bee pollen. The aglycones of flavonoid glycosides in bee pollen are primarily composed of isorhamnetin, quercetin, and kaempferol, with 21, 16, and 15 compounds, respectively. Noteworthy, isorhamnetin-3-O-glucoside, isorhamnetin-3-O-gentiobioside, quercetin-3-O-sophoroside, kaempferol-3-O-rutinoside, and kaempferol-3-O-sophoroside are found almost ubiquitously in bee pollen of various species and regions (Qiao, Feng, et al., 2023). The previous studies showed the contents of flavonoid glycosides with relatively high levels, ranging from 0.05 % to 3 %, particularly isorhamnetin-3-O-gentiobioside reaching 23.61 mg/g (Li et al., 2018; Qiao, Feng, et al., 2023). Glycosylation of flavonoids renders them less reactive and more polar, protecting against cytoplasmic damage and ensuring safe storage of flavonoids within the cell vacuole (Cavaliere et al., 2005). This explains why almost all flavonoids in bee pollen are in glycoside forms. Furthermore, 11 anthocyanins have been identified in bee pollen from Brazil and Italy, including 3 cyanidin glycosides, 4 delphinidin glycosides, 2 petunidin glycosides, and 1 each of patuletin and pelargonidin glycosides (De-Melo et al., 2018; Rocchetti et al., 2019).

## 2.7. Others

Bee pollen also contains abundant carotenoids, minerals, and vitamins. The content varies significantly depending on the botanical source and geographical origin. The minerals in bee pollen, sodium, calcium, magnesium, phosphorus, zinc, iron, copper, and manganese show noteworthy variations (Table 1) (Bogdanov, 2012; Thakur & Nanda, 2020a). The vitamins in bee pollen primarily include provitamin A, vitamin E, niacin, thiamine, folic acid, and biotin (Table 1). Among them, group B vitamins present the highest levels, especially niacin, which shows promise as a potential supplement for pellagra (Chantarudee et al., 2012). The carotenoids in bee pollen are primarily  $\beta$ -carotene. Noteworthy, squalene is present in bee pollen, with an approximate content of 90  $\mu\text{g/g}$  detected in lotus bee pollen (Keskin & Özkök, 2020; Xu et al., 2011).

## 3. Functional properties

Historically, bee pollen is a traditional medicine, and its medicinal value can be traced back thousands of years. The therapeutic properties of bee pollen predominantly involve antioxidant, anti-inflammatory, anti-tyrosinase, antibacterial, anti-prostatitis, anti-radiation, hepatoprotective, and cardioprotective effects, and the ability to regulate intestinal microbiota (Fig. 3). Based on web of science, a total of 1860 articles about the functional activities of bee pollen were published within the timeframe spanning from 2014 to 2023 (Fig. 4). Investigations into the antioxidant activity of bee pollen exhibit a notable concentration with 945 publications, following antibacterial and gut

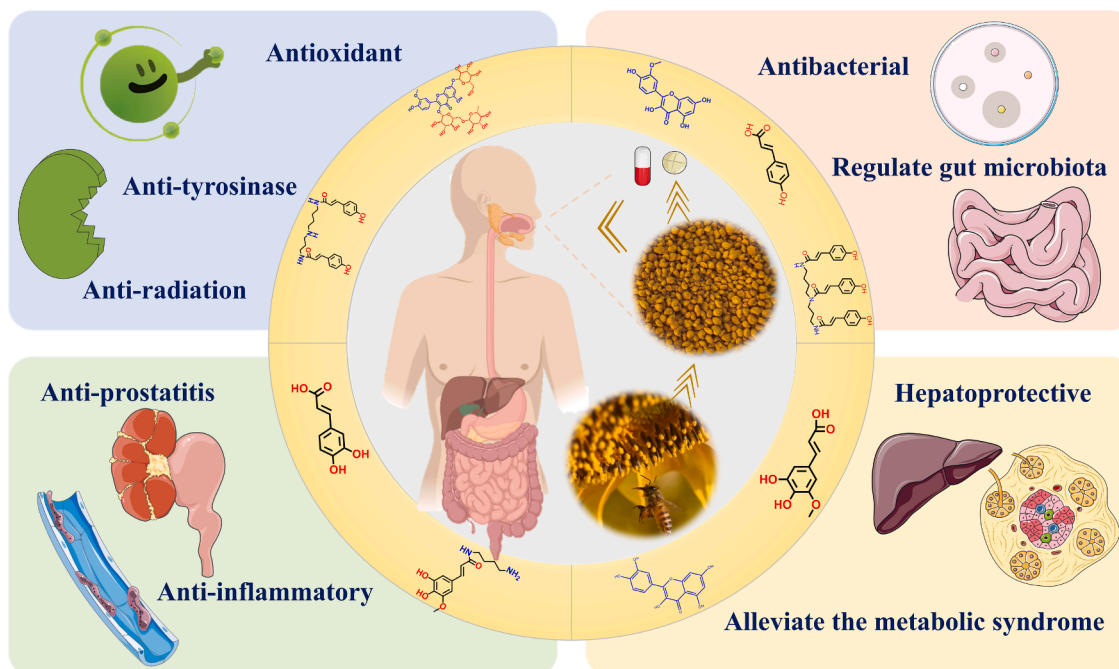


Fig. 3. The health benefits of bee pollen.

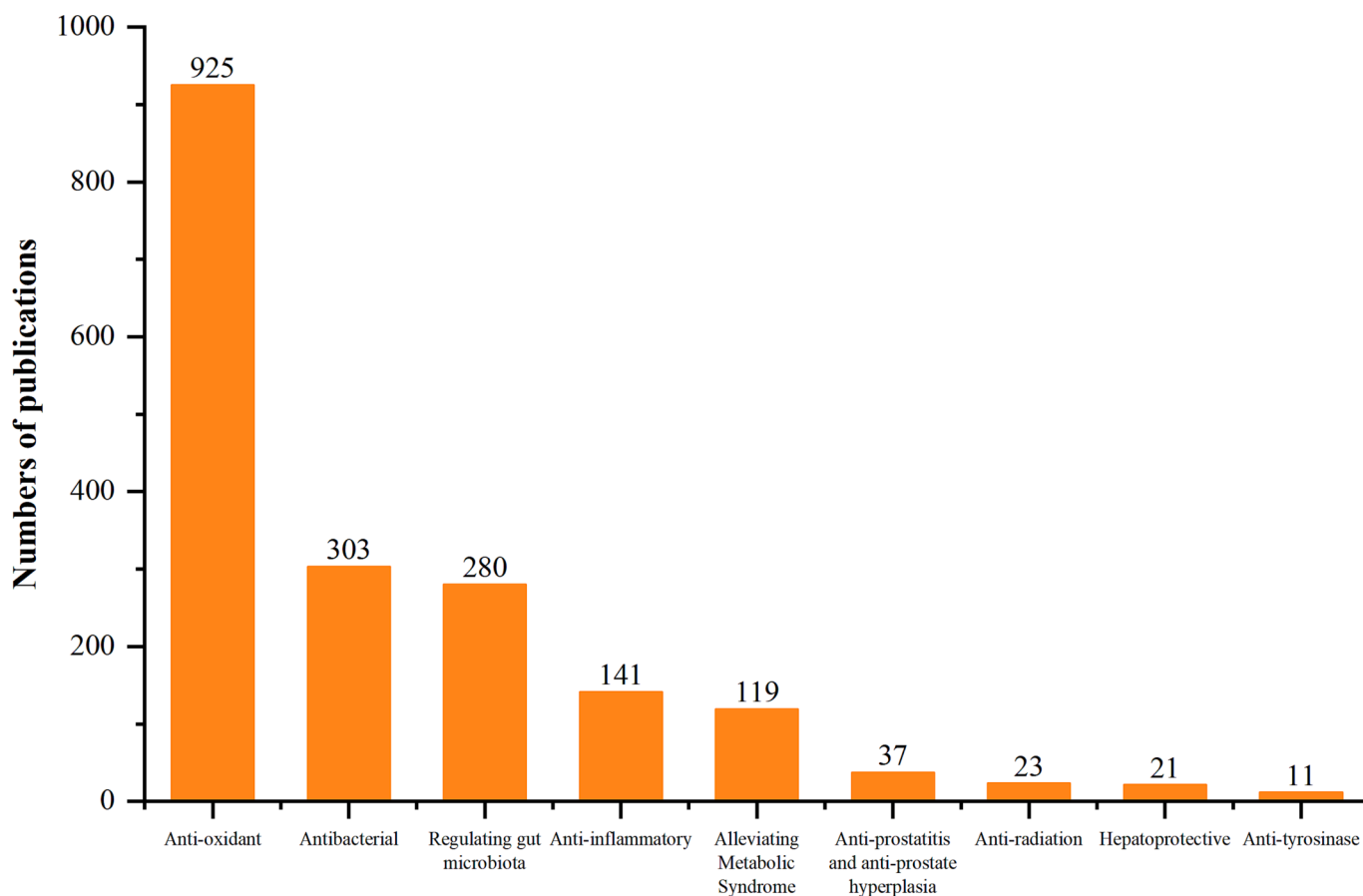


Fig. 4. The number of publications on the functional properties of bee pollen from 2014 to the present, data sourced from the Web of Science.

microbiota regulation contributing to 303 and 280 publications, respectively. These three categories collectively account for over 80 % of the total literature. Studies related to anti-inflammatory activities and metabolic syndrome total 141 and 119 publications. It is worth highlighting that bee pollen has served as a mainstream therapeutic intervention for prostatitis and prostate hyperplasia in China, Japan, and Europe for an extensive period exceeding four decades. However, a relative paucity of research reports in the past decade result in still unclear regarding the underlying mechanism and the substance-based foundation. Hence, future research should emphasize elucidating the substance-based foundation and mechanisms to ameliorate prostatitis and prostate hyperplasia.

### 3.1. Antioxidative effects

Rich antioxidants in bee pollen have been proven *in vitro* and *in vivo* experiments to have excellent antioxidant effects (El Ghouzi et al., 2023; Fatrcová-Sramková et al., 2016). *In vitro* antioxidant studies on ethanolic or methanolic extracts of bee pollen have demonstrated lipid peroxidation inhibiting and free radicals scavenging activities (Tutum et al., 2021). Research conducted by Zhang (H. Zhang et al., 2023) indicates that after the fermentation of rapeseed bee pollen, its antioxidant activity increased. Furthermore, Kawther and coworkers have shown that administering bee pollen extract at 250 mg/kg b.w. can attenuate *in vivo* protein-induced oxidative stress in rats (Abed et al., 2019). Noteworthy, the antioxidant activity of bee pollen is positively correlated with the contents of flavonoids and phenolamides (H. Zhang et al., 2023). Additionally, some antioxidant enzymes in bee pollen such as catalase, superoxide dismutase (SOD), and glutathione (GSH) can enhance antioxidant potential (Khalil & El-Sheikh, 2010).

### 3.2. Antibacterial

The ethanol or methanol extracts of pollen have been widely confirmed to have antibacterial effects on several bacterial strains, such as *Staphylococcus aureus*, *Candida glabrata*, *Escherichia coli*, *Bacillus cereus*, *Bacillus subtilis*, *Salmonella enteritidis*, *Listeria monocytogenes*, and *Pseudomonas aeruginosa* (Fatrcová-Sramková et al., 2016; Pascoal et al., 2014). Moreover, its antibacterial activity is depends on the extracts' concentration. *Staphylococcus aureus* exhibited the highest sensitivity to 70 % ethanol extracts of poppy bee pollen, while *Salmonella enterica* demonstrated the most heightened sensitivity to 70 % methanol extracts of rape bee pollen and 70 % ethanol extracts of sunflower bee pollen (Denisow & Denisow-Pietrzyk, 2016). The antibacterial activity of bee pollen extracts may be attributed to its abundance of phenolics and flavonoids, which have been confirmed to degrade the bacterial cytoplasmic membrane, leading to potassium ion loss and initiating cell autolysis (Denisow & Denisow-Pietrzyk, 2016).

### 3.3. Regulate intestinal microbiota

Previous studies indicate that bee pollen can regulate intestinal microbiota due to its abundant phenolics, polysaccharides, and phenolamides (Chen et al., 2019; Hu et al., 2023; X. Zhang et al., 2023). Rapeseed bee pollen supplementation amended the gut microbial dysregulation in diabetic rats (Hu et al., 2023). Rapeseed bee pollen extracts, particularly phenolic compounds, induced changes in the gut microbial structure of mice with colitis. These changes led to a significant reduction in the abundances of *Allobaculum* and *Bacteroides*, while the abundance of *Lactobacillus* was notably increased (Chen et al., 2019). The polysaccharides of Chinese wolfberry bee pollen significantly enhanced the relative abundances of Family XIII, *Ruminococcaceae*, and

*Saccharimonadaceae*, while reducing the relative abundances of *Tannerellaceae*, *Marinifilaceae*, and *Rikenellaceae*, which are closely linked to immune traits (Zhao et al., 2010). Tri-*p*-coumaroyl spermidine in bee pollen can decrease the *Firmicutes/Bacteroidetes* ratio in mice fed with a high-fat diet, and promote the growth of beneficial bacteria, including *Muribaculaceae* and *Parabacteroides*, while inhibiting the proliferation of harmful bacteria, such as *Peptostreptococcaceae* and *Romboutsia* (X. Zhang et al., 2023). In attention recent research has indicated that rapeseed bee pollen potentially ameliorates chronic non-bacterial prostatitis through the inhibition of pathogenic bacteria and the enhancement of probiotics, notably manifesting in alterations in the *Firmicutes-to-Bacteroidetes* (F/B) ratio and an increased abundance of *Prevotella* (Qiao, Xiao, et al., 2023).

### 3.4. Anti-inflammatory

Numerous compelling evidence has proved the potent anti-inflammatory properties of bee pollen (El Ghouizi et al., 2023; Hu et al., 2023; Li et al., 2018). Phytochemicals in bee pollen exerted beneficial modulatory effects on such crucial cell as macrophages, T cells, B cells, NK cells, hepatocytes, mast cells, basophils, neutrophils, and eosinophils (Denisow & Denisow-Pietrzyk, 2016; Pascoal et al., 2014). These cellular entities play pivotal roles in the host's defense against invading pathogens and actively contribute to various inflammatory processes (Denisow & Denisow-Pietrzyk, 2016). Consequently, phytochemicals have emerged as responsible for the observed anti-inflammatory effects of bee pollen extracts. Additionally, some studies have reported that the anti-inflammatory effects of bee pollen are also related with the presence of fatty acids, phytosterols, and phospholipids (Pascoal et al., 2014). The anti-inflammatory activity of bee pollen can match to some extent such non-steroidal anti-inflammatory drugs as naproxen, analgin, phenylbutazone, or indomethacin (Pascoal et al., 2014). Overall, this outstanding advantage leads to the market recognition of pollen as a dietary supplement and functional foods with anti-inflammatory properties.

### 3.5. Prevention and treatment of the metabolic syndrome

The Metabolic syndrome typically refers to the constellation of obesity, high blood sugar, blood pressure elevation, high triglycerides, and low-density lipoprotein, increasing the risk of heart disease, stroke, and type 2 diabetes (Yan et al., 2021). Numerous studies have documented the potential of bee pollen in the prevention and treatment of metabolic syndrome (El Ghouizi et al., 2023; Kacemi & Campos, 2023; Khalifa et al., 2021), primarily through anti-diabetes, anti-obesity, and cardioprotective domains. Oral ingestion of bee pollen has shown the capacity to lower postprandial blood glucose levels (Algethami et al., 2022). Evidence from *in vivo* studies suggests that bee pollen extract can attenuate blood glucose levels in streptozotocin-induced diabetic rats (J. Zhang et al., 2022). This effect is primarily ascribed to the presence of phenolic compounds and flavonoids within bee pollen, which exhibit inhibitory properties towards enzymes involved in carbohydrate hydrolysis, including starch-degrading enzymes and glucosidases (Algethami et al., 2022). These inhibitory actions culminate in a diminished absorption of carbohydrates in the small intestine, leading to a marked reduction in blood glucose levels. Bee pollen aqueous-ethanol extracts displayed a substantial  $\alpha$ -amylase inhibitory effect with an  $IC_{50}$  value of 4.51 mg/mL, surpassing the control (acarbose) with an  $IC_{50}$  of 6.52 mg/mL (Daudu, 2019). Additionally, the phenolamide extract originating from apricot bee pollen has demonstrated a substantial capacity to ameliorate glucolipid metabolic disruptions in a murine model of obesity induced by a high-fat diet (X. Zhang et al., 2023).

The cardioprotective effects of bee pollen have been substantiated in various animal models through diverse mechanisms (Komosinska-Vashev et al., 2015; Olas, 2022). Bee pollen exhibits hypolipidemic activity, reducing cholesterol levels, triacylglycerol, and total lipids in the body

(Li et al., 2018; Rzepecka-Stojko et al., 2017). Moreover, regular consumption of bee pollen significantly attenuates platelet aggregation and the formation of atherosclerotic plaques (Li et al., 2018; Rzepecka-Stojko et al., 2017). After treatment with isoprenaline, bee pollen (*Schisandra chinensis*) extracts demonstrated significant *in vivo* cardioprotective actions within the heart, upregulated nuclear factor-erythroid 2-related factor 2 (Nrf2), heme oxygenase-1, and B-cell lymphoma 2 (Bcl-2) protein expressions in a dose-dependent manner while concurrently reducing the expression of Bcl2-associated protein (Olas, 2022).

### 3.6. Anti-prostatitis

The best documented healthful benefit of bee pollen for humans is undoubtedly the treatment of prostatitis; for example, pollen consumption can reduce the inflammation, discomfort, and pathology of patients suffering from benign prostatic inflammation. Rapeseed bee pollen extracts can potentially ameliorate the symptoms of chronic nonbacterial prostatitis by downregulating Mfn1 and suppressing DHT, 5 $\alpha$ -reductase, and COX-2 expression (Qiao, Xiao, et al., 2023). Recent research indicates that rapeseed bee pollen alleviates chronic non-bacterial prostatitis by inhibiting pathogenic bacteria and enhancing probiotics, particularly in the *Firmicutes-to-Bacteroidetes* (F/B) ratio and the abundance of *Prevotella* (Qiao, Xiao, et al., 2023).

Bee pollen or extracts have become a prominent medicine for treating chronic prostatitis and prostate hyperplasia (Yang et al., 2014); for example, Pule'an (made entirely from rapeseed bee pollen) and cernilton (ryegrass pollen extracts). Pule'an has been regarded as a medicine for prostate patients with obstructive symptoms and CNP since 2007 in China. Pule'an proved potentially effective with over 90 % symptom relief in clinical trials in China (Qiao, Xiao, et al., 2023; Yang et al., 2014). In Europe and Japan, cernilton has been used for over 40 years to treat nonbacterial prostatitis and prostatic hyperplasia with a success rate of 70 % (El-Khatib et al., 2019; Thorpe & Neal, 2003). Cernilton potential can reduce prostate-specific antigen, COX-2, and MCP-1 levels in the prostate and alleviate pain in preclinical studies (Chabot et al., 2021). Cernilton comprises two distinct fractions of pollen extracts: the water-soluble T60 and the lipid-soluble GBX (Jethon et al.; NAKASE et al., 1990). The primary compound in T60 fraction is identified as feruloyl putrescine (Leander, 1962); however, other components in cernilton remain unclear. Therefore, a current research hot-spot focuses on the bioactive compounds and anti-prostatitis mechanism of bee pollen.

### 3.7. Anti-tyrosinase

Multiple studies have confirmed bee pollen and its extracts to possess anti-tyrosinase activity. Zhang et al. (Zhang et al., 2015) reported that 14 types of bee pollen extracts exhibited various anti-tyrosinase activities, significantly depending on the floral species and extraction solvents. The 75 % ethanol extract of apricot bee pollen showed the highest anti-tyrosinase activity (Zhang et al., 2015). The study on the anti-tyrosinase activity of different extracts (petroleum ether, ethyl acetate, n-butanol, and water fractions) from four types of bee pollen revealed that the ethyl acetate extract from camellia bee pollen exhibited the highest anti-tyrosinase activity (Su et al., 2021). To comprehensively elucidate the phytochemicals of bee pollen that inhibit tyrosinase, the researchers found that phenolamides exhibited exceptionally high correlations with the anti-tyrosinase activity (X. Zhang et al., 2022). In the subsequent research, the anti-tyrosinase activity of 18 phenolamides derived from *Quercus mongolica* bee pollen using mushroom tyrosinase as an *in vitro* assay system (Kim et al., 2018). Phenolamides comprising coumaroyl and caffeoyl showed tyrosinase inhibition with  $IC_{50}$  values of 18.9 to 85.8  $\mu$ M (Kim et al., 2018). The introduction of methoxyl groups to phenolic compounds resulted in a decrease in inhibitory activity. This reduction was observed in compounds such as methoxy coumaroyl and

methoxy benzoyl, which exhibited  $IC_{50}$  values exceeding 100  $\mu$ M (Kim et al., 2018). The highest level of tyrosinase inhibition was observed in four coumaroyl spermidines, followed by spermidines with three phenolic groups and derivatives of putrescine carrying two phenolic groups (Kim et al., 2018). The enzymatic reaction catalyzed by tyrosinase represents the pivotal rate-limiting step in the process of melanin synthesis, serving as a vital mechanism for preventing the accumulation of melanin. Henceforth, bee pollen can be utilized in skin whitening treatments.

#### 4. Wall-disruption

##### 4.1. Necessity of wall-disruption

As nutrient-rich treasure trove, although bee pollen can provide nearly all the essential nutrients needed by honeybees and humans, its digestibility and absorption rate are influenced by the special structure of pollen walls (Wu et al., 2021; Wu et al., 2019). Therefore, the wall disruption of bee pollen continuously attracts researcher's attention and has gradually become a crucial step in the production and processing of bee pollen. Currently, there are two views regarding how to verdict wall-disruption pollen: a broad view and a narrow view (Dong, Gao, et al., 2015). The broad view regards either degrading the coat or opening the germinal apertures as wall-disruption pollen. This view claimed two primary rationales: firstly, the assertion that both humans and animals can assimilate nutrients from bee pollen via pollen germination (Cook et al., 2003; Dong, Gao, et al., 2015); secondly, the contention that the gastrointestinal tract in both humans and animals possesses the capability to disintegrate bee pollen wall naturally (Vit et al., 2016; Wu et al., 2019). However, the previous research indicated that the pollen with opening germination still possesses the intact exine or intine, resulting in difficulty for the digestion and absorption by human body (Vit et al., 2016; Wu et al., 2019). The narrow view regards breaking both the exine and intine as wall-disruption pollen. This view difference results from understanding the effect of complex pollen walls on the release, digestion, and absorption of nutrients.

The mature complex pollen wall is clearly divided into three layers: exine, intine, and pollen coat (Wu et al., 2019) (Fig. 2). The outer and rigid layer, known as the exine, bears a sculptured pattern and is predominantly composed of sporopollenin. The inner layer lies beneath the exine, also is referred as intine, primarily consisting of cellulose. Intine envelopes the protoplast of the male gametophytes, and shares chemical composition similarities with the primary walls of typical plant cells. Surrounding the exine layer, the pollen coat extends extensively and often penetrates deep into the crevices of the highly sculpted exine (Wu et al., 2019). These three domains appear to form highly complex, and can resist high-pressure, high-temperature, corrosion, and degradation of the wall system to protect the intracellular compounds from digestive degradation (Wu et al., 2021; Wu et al., 2019). In fact, honeybees and humans cannot effectively degrade pollen walls in their digestive tracts, and cannot completely digest and absorb nutrients inside pollen walls. Certain researchers claimed that honeybees and humans can digest entire pollen grains within their digestive tract and fully assimilate the nutrients from bee pollen (Wang et al., 2014). However, recent research regarding honeybee feces shows that the vast majority of pollen grains remain intact and undamaged through scanning electron microscopy (SEM), and the nutrients remain unreleased inside pollen grains through transmission electron microscopy (TEM); surprisingly, honeybee can only digest nutrients in pollen coat (Wu et al., 2021). Subsequently, *in vitro* simulations and *in vivo* of human gastrointestinal digestion of bee pollen indicated that the human digestive system also cannot break pollen walls (Wu et al., 2019). Moreover, the imaging technique of time-of-flight secondary ion mass provides compelling evidence that most nutrients are located inside the pollen wall (Wu et al., 2019). Hence, bee pollen should break both the exine and intine. This wall-disruption can facilitate the optimal release of nutritive constituents contained therein,

and augment the digestive absorption efficiency within the biological entity.

##### 4.2. Techniques for wall-disruption

Wall-disruption methods can generally be divided into five types: mechanical, physical, enzymatic, microbial fermentation and a combination of multiple technologies methods (Dong, Gao, et al., 2015; Liu et al., 2014; Wu et al., 2019). Mechanical methods usually crack pollen walls by employing shear or friction force. This technique involves specialized equipment, such as ball mills or high-speed shearers, and mechanically crush the pollen grains, for breaking the tough outer wall. For example, the high shear technique (High-speed Shear Dispersing Emulsifier, HSDE) was previously used for cracking *Brassica napus* L. pollen (Feng et al., 2012). Although this method is simple and the equipment used is inexpensive, the action of shear force may generate lots of heat, leading to the loss of heat-sensitive nutrients (Dong, Gao, et al., 2015).

Physical methods generally include ultrasound treatment and freeze-thaw processing (Dong, Gao, et al., 2015; Feng et al., 2012). Ultrasonic waves, with frequencies of 20 kHz to several MHz, induce cavitation and microstreaming, resulting in mechanical stress on the pollen grains for wall-disruption (Awad et al., 2012). Ultrasonic treatment has been reported to increase the release of various bioactive compounds from bee pollen, including flavonoids, phenolic acids, and vitamins (Yang et al., 2019). Ultrasound treatment seemed to be more efficient to crack the *Pinus massoniana* pollen wall, compared to freeze-thaw processing. Freeze-thaw technique exploits freezing and thawing cycles, and generates the physical stresses by the expansion and contraction of ice, thereby disrupting the cell wall and increasing the accessibility of nutrients (Liu et al., 2014).

Enzymatic methods commonly utilize such enzymes as papain, pro-tamex protease, neutral protease, cellulase, hemicellulose, or pectinase to break bee pollen wall (Dong, Gao, et al., 2015; Gao et al., 2011; Liu et al., 2014). Specifically, cellulases and pectinases can target and degrade the structural components of the pollen wall, resulting in nutrient release; for instance, cellulases hydrolyze cellulose in the intine layer. To improve efficacy, the combined uses of cellulase, pectinase, xylanase, and protease have also been widely explored in pollen wall-disruption (Dong, Gao, et al., 2015; Gao et al., 2011; Liu et al., 2014). Noteworthy, sporopollenin in the exine provides strong resistance to enzymatic degradation, rendering the alone use of enzymes less effective in the exine (Dong, Gao, et al., 2015).

The method of disrupting pollen walls through microbial fermentation is a noteworthy emulation of bee-like behavior by humans. In the honey bee society, honey bees undertake a process to optimize the utilization of nutritional constituents present in flower pollen. Specifically, these industrious honey bees amalgamate the collected bee pollen with nectar and their endogenous secretions, depositing the resulting mixture within the confines of the hive. Subsequently, a fermentation process ensues under the influence of bacteria and yeast. This transformative procedure converts the original bee pollen into a substance known as bee bread, concurrently disrupting the pollen, which is a natural disruption wall. This process enhances the efficacious release of nutrients. (Barta et al., 2022; Di Cagno et al., 2019). The utilization of microbial fermentation to break pollen walls has gained widespread application in recent years (Yan et al., 2019; H. Zhang et al., 2022). This method commonly employs lactic acid bacteria and yeast through either single-strain fermentation or a combination of two different strains (Yan et al., 2019; H. Zhang et al., 2022). Yan et al. found that yeast fermentation exhibited superior wall-disruption effects on bee pollen than fermentation with lactic acid bacteria or mixed microbes (Yan et al., 2019). After microbial fermentation and cell wall disruption, the content of certain nutrients tends to increase, including amino acids, polyunsaturated fatty acids, organic acids, phenolic acids, flavonoid glycosides, and phenolic amides (H. Zhang et al., 2022). However, the content

of glucose and fructose present a significant decrease (Yan et al., 2019), which may be attributed to the consumption of carbon sources during the microbial reproduction process.

Recently, multi-technology amalgamations appeared effectively to break bee pollen walls. Dong et al. research indicates that the combination of protamex hydrolysis and ultrasonication can entirely disrupt both the exine and intine of rapeseed bee pollen (Dong, Gao, et al., 2015). Moreover, a combination of ultrasonication and high shear technique can effectively break both the exine and intine of five species of bee pollen, including rapeseed, lotus, camellia, wuweizi, and apricot bee pollen (Wu et al., 2019).

#### 4.3. Advantages of wall-disruption

Breaking pollen wall seems to be conducive to increasing the release of nutrients; for example, after wall-disruption, a significant increase in the levels of fatty acids, amino acids, proteins, crude fats, reducing sugars,  $\beta$ -carotene, polyphenols, flavonoids, calcium, iron, zinc, and selenium (Wu et al., 2019; Xie et al., 2022; Yang et al., 2019; Yuan et al., 2023). Additionally, using the fermentation process, wall-disruption also results in a minimum increase of 11 % in free amino acids, a higher production of low molecular weight peptides, and a minimum increase of 7 % in nicotinic acid and nicotinamide (Yan et al., 2019). These findings indicate that wall-disruption without exine and intine (Fig. 2) can effectively release pollen nutrients. Moreover, in a comparative *in vitro* simulated digestion study between bee pollen and transformed bee pollen (bee bread), the average bioavailability of total phenols and total flavonoids in bee bread was found to be nearly 10 % higher than that in bee pollen (Aylanc, Tomás, et al., 2021). Bee bread exhibited more accessible in bioactive content than untreated bee pollen in the study (Aylanc, Tomás, et al., 2021), due to microbial activity breaking down the walls during the formation process of bee bread. Many studies show that wall-disruption significantly increases the *in vitro* and *in vivo* digestibility of bee pollen (Ozkan et al., 2018; Wu et al., 2021; Zuluaga et al., 2015).

Noteworthy, wall-disruption can enhance health benefits of bee pollen. Wall-disruption treatments significantly improved the *in vitro* capacity of bee pollen to scavenge DPPH and ABTS radicals (Xie et al., 2022; Yang et al., 2019), and the overall antioxidant activity by a range of 14–46 % (Yuan et al., 2023). Using the aging mice model, wall-disruption treatment can superiorly enhance organ recovery, heighten the enzymatic activity of superoxide dismutase and catalase, and reduce malondialdehyde levels (Yang et al., 2019). Previous research has reported that wall-disruption can significantly enhance the antibacterial activity of bee pollen (Chehraghi et al., 2023). It is worth noting that wall-disrupted rapeseed bee pollen demonstrates a significant therapeutic effect on chronic nonbacterial prostatitis (CNP) in rat model, compared with the non-wall-disruption group (Qiao, Xiao, et al., 2023). Wall-disruption also significantly reduces allergens in bee pollen, such as profilin, cystatin, and alcohol dehydrogenase (Tao et al., 2022). Therefore, bee pollen should be subject to wall-disruption to better release and digest nutrients and exploit bioactivities.

## 5. Conclusion and perspectives

With an ever-growing pursuit of balanced and health-conscious dietary practices, bee pollen has progressively emerged as a subject of heightened scrutiny over the recent decades. Bee pollen is esteemed as a nutritional and functional food, owing to its abundant nutritional content and advantageous effects on human health. To better exploit bee pollen and promote comprehensive utilization, it is imperative to consider the following pivotal aspects in the future. Firstly, distinguished from laboratory wall-disruption methods, bee bread, as a natural wall-disruption product, should be compared with the wall-disruption effect of laboratory methods to achieve a better wall-disruption bee pollen product. Secondly, wall-disruption can augment

the release and digestibility of nutrients in bee pollen, and subsequently elevate its functions. Nonetheless, only a paucity of research focus on comparing the potential health benefits of bee pollen before and after wall disruption. Consequently, future investigations should explore the health advantages associated with wall-disrupted bee pollen. Thirdly, bee pollen has undergone in-depth research on its nutrients over the past few decades. However, there remain still many unknowns about phytochemicals, especially phenolamides, which may play a crucial role in conferring human health benefits. Hence, allocating more research endeavors and resources is imperative toward characterizing phytochemical profiles in bee pollen derived from different geographical regions and botanical sources. Finally, bee pollen is esteemed as a treasure trove of flavonoid glycosides and phenolamides. Hence, future research should focus on the functional activities of these unique phytochemicals for a deeper understanding and more effective utilization of bee pollen.

#### CRedit authorship contribution statement

**Jiangtao Qiao:** Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **Yu Zhang:** Data curation, Validation, Writing – review & editing. **Eric Haubruge:** Conceptualization, Supervision, Visualization, Writing – review & editing. **Kai Wang:** Formal analysis, Methodology, Visualization. **Hesham R. El-Seedi:** Data curation, Methodology, Writing – review & editing. **Jie Dong:** Conceptualization, Formal analysis, Funding acquisition, Validation. **Xiang Xu:** Project administration, Resources, Software, Visualization, Writing – review & editing. **Hongcheng Zhang:** Conceptualization, Formal analysis, Funding acquisition, Project administration, Resources, Software, Supervision, Writing – review & editing.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Data availability

Data will be made available on request.

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