Trends in Food Science & Technology 109 (2021) 464–481

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: www.elsevier.com/locate/tifs

From the hive to the table: Nutrition value, digestibility and bioavailability of the dietary phytochemicals present in the bee pollen and bee bread

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ARTICLE INFO

Keywords:
Bee pollen
Bee bread
Dietary phytochemicals
Digestibility and bioavailability
Safety status

ABSTRACT

Background: Consumption of natural products has increased significantly due to the idea that if nutrition improves, this leads to improved health, general well-being and reduces the risk of developing certain diseases. Bee products, especially bee pollen (BP) and bee bread (BB), have demonstrated several nutritional and bioactive properties, which make them functional foods par excellence. Thus, understanding the digestibility and the changes of phytochemicals along the digestive tract, which give BP and BB the functional food attribute, is crucial.

Scope and approach: This review describes the digestibility, bioavailability, and absorption behaviors of dietary phytochemicals present in BP and BB. It also addresses possible factors that may adversely affect the human health due to its intake and highlights food practices for the industry.

Key findings and conclusions: Many studies have been conducted on BP and BB, which mostly evaluated the nutritional values and the bioactive compounds. However, few studies have addressed the nutritional and phytochemical content of BP and BB after digestion. Topics such as changes in the digestive tract, post-digestive bioaccessibility, tissue absorption scores and the degree of presence in the circulatory system of the phytochemicals that provide strong biological properties to BP and BB, should be taken into consideration in future researches.

1. Introduction

The collection of bee products by humans is evidenced in rock paintings from ancient times and historical finds, showing that apiculture has a very old history. Mesolithic rock painting from around 7000 BC at Spider Caves (Cuevas de la Araña) located in Valencia (Spain) and wall painting on the Ancient Egyptian temple dating back to 2400 BC highlight the importance of beehive products (Mizrahi & Lensky, 2013). Ancient people used honey and pollen to treat many diseases, including wounds, ulcer and bowel problems (Mizrahi & Lensky, 2013). Despite this traditional use of bee products, apiculture began appropriately when people learned to construct models in beekeeping and preserve the future of bee colonies with particular care and control. In a broader definition, apiculture became the maintenance of honey bees in hives and its management, oriented for honey production and for pollination, as well as the collection of other bee products (bee pollen, bee bread, beeswax, propolis, royal jelly and bee venom) and live material such as queen bees, swarms and packaged bees (Formato & Smulders, 2011). Although important developments were made in beekeeping practice and bee products since the 16th century (Crane, 1992), the true origins of bee products were not known until a few centuries ago and their detailed chemical composition was only determined in the late 1900s (Mizrahi & Lensky, 2013).

The development and advancement of civilizations lead to new lifestyles and innovative food trends. The diet is shaped by various factors such as regional traditions, socioeconomic factors, cultural and educational activities and wellbeing. Indeed, there is an intense relationship between diseases and the composition of consumed foods. Proper and adequate diet has a significant effect on physical and mental development, at the same time that it has a protective effect against many diseases. Recently, special interest in bee pollen (BP) and bee bread (BB) has been given with the detailed definition and revelation of the nutritional values and therapeutic properties of these bee products (Gardana, Del Bo, Quicazán, Corrrea, & Simonetti, 2018; Khalifa et al., 2020; Kieliszek et al., 2018; Mărgăoan et al., 2019; Thakur & Nanda, 2020). Both BP and BB are characterized by their high nutritional value, containing macro and micronutrients, phenolic acids and polyphenols (Kieliszek et al., 2018).

Since both bee products contain almost all of the metabolic necessary

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https://doi.org/10.1016/j.tifs.2021.01.042
Received 26 October 2020; Received in revised form 23 December 2020; Accepted 18 January 2021
Available online 22 January 2021

Abbreviations

BB	bee bread
BP	bee pollen
CBG	cytosolic β-glucosidase
GIT	gastrointestinal tract
LPH	lactase phlorizin hydrolase
ROS	reactive oxygen species
TFC	total flavonoid content
TPC	total phenolic content

nutrients and phytochemicals, their directly or indirectly use in foods has an important therapeutic and pharmacological role in the prevention or reduction of several diseases (Bogdanov, 2011). Many studies have been conducted on BP and BB obtained in different geographic areas throughout the world. In general, they focused on microbiology, physicochemical properties, plant origin, extraction methods, biological and its therapeutic activities, but it lacks a detailed discussion on the nutritional value, digestibility and bioavailability of the phytochemicals in BP and BB. Therefore, the aim of this work is a comprehensive review of the nutritional value, digestibility and bioavailability of dietary phytochemicals in BP and BB, as well as their absorption. Besides that, this review assesses the fundamental knowledge of BP and BB consumption and safety, and its potential for the food industry.

2. Bee pollen and bee bread

Bee pollen is known as one of the oldest nutritional supplements in history and contains almost all nourishing components for a diet (Bakour, Fernandes, Barros, Sokovic, & Ferreira, 2019). Pollens are units of male gametophytes of flowering plants. Bees mix the pollen grains with their own secretions after collecting it from the flowers; this process allows pollen to moisten and become pellets; then these pellets stick to the pollen basket on the hind leg of the bees and are transported to the hive (Campos et al., 2008). This new product, which bees collect from flowers and combine with their own secretions, is called bee pollen. The BP is the background source of nutrients necessary for honey bee to grow during their larvae stage and to develop sufficiently during their youth (Tomás, Falcão, Russo-Almeida, & Vilas-Boas, 2017) at the same time it presents important nutritional and therapeutic characteristics for humans (Denisow & Denisow-Pietrzyk, 2016). Beekeepers place pollen traps at the entrance of hives to retain the BP transported by bees, enabling the commercial collection of pollen, Fig. 1.

BP is often characterized by its high protein content, rich nutritional value and a good source of bioactive compounds, all varying accordingly to its botanical origin, geographical and climatic characteristics (Mayda, Özkök, Bayram, Gerçek, & Sorkun, 2020). It contains protein and amino acids (10–40% w/w), lipids (1–13% w/w), vitamins (0.02–0.7%), several minerals (K, P, Mg, Ca, Na, S, Fe, Cu, etc.), and significant phenolic acids and polyphenols (Kieliszek et al., 2018). Nevertheless, carbohydrates are the main components of BP composing 13–55% of dry weight (Campos, Frigerio, Lopes, & Bogdanov, 2010), which includes polysaccharides, oligosaccharides and dietary fiber. For example, cellulose, an important polysaccharide, has a content in pollen of about 3–4% being the main component of the layers of pollen grains, and its presence significantly affects the digestibility of BP (Kieliszek et al., 2018).

BP can present different colors, such as white-black, brown, yellow, orange, yellow-blue, or yellow-brown, depending on the plants visited by bees (Campos et al., 2008). Pollen has a variable general appearance, normally with a spherical shape and diameters ranging from 0.01 mm to 0.1 mm (Ibrahim, Balasundram, Abdullah, Alias, & Mardan, 2012). A bee colony can collect between 50 g and 250 g of pollen per day, and 15–40 kg of pollen per year (Thakur & Nanda, 2020), with the worldwide production of pollen being approximately 1500 tons per year (Kieliszek et al., 2018).

Once inside the beehive, the BP is stored in the honeybee combs cells. The stored pollen is mixed with the digestive enzymes secreted by bees, honey, and organic acids. Furthermore, under anaerobic conditions, BP is converted to BB by lactic acid fermentation caused by bacteria (*Pseudomonas* spp. and *Lactobacillus* spp.) and yeasts (*Saccharomyces* spp.) (Detry, Simon-Delso, Bruneau, & Daniel, 2020; Di Cagno, Filannino, Cantatore, & Gobbetti, 2019; Mărgăoan, Cornea-Cipcigan, Topal, & Kösoğlu, 2020; Tomás et al., 2017), (Fig. 1). As the BP turns into BB, it goes through a number of biochemical stages which is completed in about 7 days: i) growing microorganisms such as lactic acid bacteria, *Escherichia*, aerobic bacteria and yeasts in the first half day, ii) using nutrient by bacteria and drop in pH, iii) loss of *Streptococcus* bacteria and growth of *Lactobacillus* bacteria, and iv) death of lactic acid bacteria and some yeasts due to the produced lactic acid (Khalifa et al., 2020).

BB contains protein and amino acids, carbohydrates, lipids, vitamins, minerals and phenolic acids and polyphenols (Tomás et al., 2017; Zuluaga et al., 2015b), similar to BP, but with a higher nutrient-rich content (Adaškevičiūtė, Kaškonienė, Kaškonas, Barčauskaitė, & Maruška, 2019). Another important point is the BB higher digestibility and degree of absorption by humans since the multi-layered wall surrounding the pollen grain is destroyed by natural fermentation, which gives special features to the BB (Khalifa et al., 2020; Kieliszek et al., 2018; Mizrahi & Lensky, 2013). Recent studies have reported that BP and BB have anti-inflammatory, anti-obesity, anticancer, antimicrobial, antioxidant and gastroprotective properties as well as neuroprotective

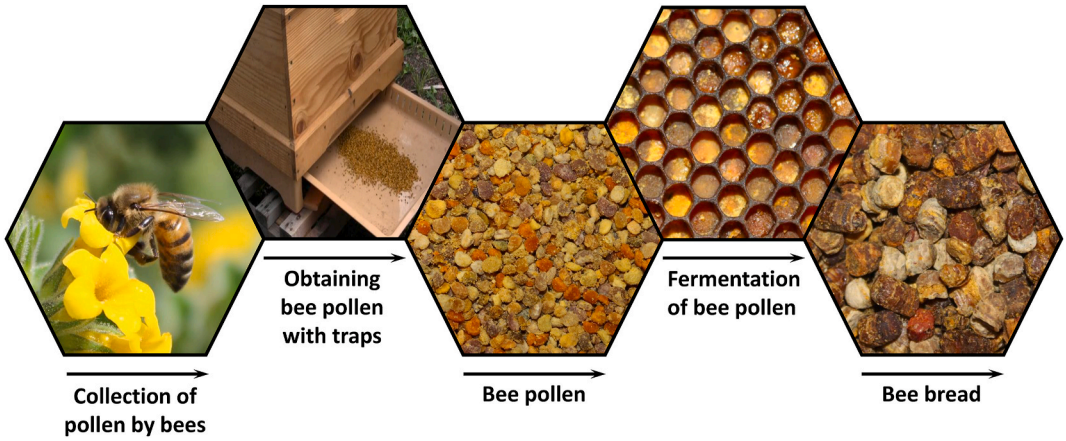

Fig. 1. Pollen chain: from collection of pollen by bees to the formation of bee bread.

and anti-aging activity (Bacha et al., 2020; Bakour et al., 2019; Eleazu et al., 2020; Kurek-Górecka, Górecki, Rzepecka-Stojko, Balwierz, & Stojko, 2020; Othman et al., 2020; Selamoglu, 2017; Sobral et al., 2017; Tomás et al., 2017).

3. Differences between bee pollen and bee bread

BP and BB have similar composition due to their similar origin of plant pollen. Albeit their similarity, there are remarked differences, Table 1. The breakdown of the multi-layered wall of BP during fermentation and the formation of BB make it more digestible than BP (Khalifa et al., 2020). This process increases the bioavailability of BB and results in a higher degree of absorption by human intestinal epithelial cells (Zuluaga, Serrato, & Quicazan, 2015). Cellulose, which forms the inner layer (intine) of BP, is broken down by bacteria, reducing the cellulose ratio of BB compared to BP (Benavides-Guevara, Quicazan, & Ramírez-Toro, 2017). Furthermore, during this transformation process some new products are formed. For example, some of the proteins in BP are reduced to amino acids by digestive enzymes, so the protein content in BP is higher, while in BB a higher amount of amino acids can be found (Kieliszek et al., 2018). The study conducted by DeGrandi-Hoffman, Eckholm, and Huang (2013) showed that the concentration of leucine and threonine in BB is about 60% higher than in BP. In the same study, it was emphasized that other amino acids such as valine, alanine, aspartic acid, and glutamine have a higher concentration in the BB. Differences in sugar content can also be found: BP is mixed with honey when stored in comb cells, as a result BB is richer in sugar than BP (Khalifa et al., 2020; Thakur & Nanda, 2020).

The fermentation process of BB leads to a high content of lactic acid as a result of the metabolism of microorganisms, which will give a long time protection against microorganisms, as well as contributing to the nutritional properties of BB (Khalifa et al., 2020; Mayda et al., 2020). However, lactic acid decreases the level of pH. While the pH of BP varies between 4 and 6, the pH of BB is around 4.2 (Khalifa et al., 2020; Kieliszek et al., 2018). Moreover, BB has a richer content in vitamins than BP, for example, BB has a higher content in terms of vitamin K (Khalifa et al., 2020) which may result from pollen degradation. Concerning fatty acids, BP and BB have a similar content (Kieliszek et al., 2018).

Table 1
Composition of bee pollen and bee bread.

Composition	Bee pollen	Bee bread	References
Carbohydrates	13–55%	24–35%	Campos et al. (2010); Khalifa et al. (2020)
Proteins	10–40%	14–23%	Campos et al. (2010); Tomás et al. (2017); Zuluaga et al. (2015a)\
Lipids	1–13%	2–14%	Bakour et al. (2019); Campos et al. (2010); De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018); Tomás et al. (2017)
Dietary fiber	14–31%	3–20%	Anjos, Paula, Delgado, and Esrevinho (2019); Salazar-González and Díaz-Moreno (2016); K. Yang et al. (2013)
Vitamins	0.02–0.7%	0.4–3%	Farag and El-Rayes (2016); Urcan et al. (2018)
Amino acids	3.2%	n.i.	K. Yang et al. (2013)
Organic acids	1%	0.4	Bakour et al. (2019); Moita et al. (2014)
Flavonoids	0.2–3.2%	n.i.	Bogdanov (2011)
Lactic acid	0.6%	3%	Kieliszek et al. (2018)
Free acidity (mEq/kg)	105–146	400	Bakour et al. (2019); Bárbara et al. (2015); Martins, Morgano, Vicente, Baggio, and Rodriguez-Amaya (2011)
pH	4–6.3	3.8–4.2	Khalifa et al. (2020); Kieliszek et al. (2018)

n.i.: no information.

The process of production from the hive is also distinct and clearly more difficult in BB than BP. The placed traps at the entrance of the hives are often sufficient to obtain BP. But BB is tightly packed and fixed with beeswax in combs by bees, therefore more laborious techniques are required to obtain it, such as manual crushing of the combs after freezing or machinery separation. As a result, BB has a higher price commercially than other bee products such as BP, honey, or beeswax.

4. Plant origin

The information of BP and BB botanical origin is crucial because it can work as an indicator of nutritional values, phytochemicals, biological activity and may influence its commercial quality (Campos et al., 2010). The pollen collected by bees differ in color, size, appearance, biological activity and physicochemical features (Čeksteryte et al., 2016). This difference is due to geographical, seasonal conditions and genetics of flower species that are visited by bees, which have unique characteristics (De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al., 2018). Also, morphological aspects such as the pore structure and the thickness of the multiple layers of the pollen grains depend on botanical source.

BP is called monofloral when only one single botanical taxonomy characterizes the pollen loads while preserving the physical and biochemical properties of the plant, whereas mix-pollen loads from various flowers are called polyfloral (Carpes et al., 2013). At commercial level, BP and BB are mostly sold as polyfloral, as a result of the mixture of pollen pellets collected in the traps or storage by the bees in the same honeycomb.

The traditional approach to access the botanical origin of both pollen products is based on microscopic analysis, which is time-consuming and requires good palynology analysis expertise. With advances in molecular biology and new analytical methods, new approaches are under development. One of these is based on the use of free amino acids, minerals, and aroma compounds, but it introduces both complex and expensive materials (Laha et al., 2017). DNA barcoding technology and next-generation sequencing of amplicons seems more promising (Laha et al., 2017) with higher sensitivity and resolution than microscopic analysis. However, some limitations remain due to the incomplete plant database, access to laboratory equipment, and evaluation of mixed pollen samples originating from more than one plant species (Keller et al., 2015).

5. Structure and digestibility of the pollen grain

BP grains are surrounded by a strong outer layer called exine and an inner layer called intine, both protecting the pollen grains against physical and chemical agents. The exine layer consists of chemically inert biopolymer sporopollenin and has a flexible and solid structure, while the intine layer consists of cellulose and pectin and has a more sensitive structure compared to the exine layer (Fig. 2) (Benavides-Guevara et al., 2017; F.-S.; Li, Phyo, Jacobowitz, Hong, & Weng, 2019; Zuluaga et al., 2015b). This multi-layered structure ensures that the pollen grains are resistant to bacteria, and also preserve the pollen content against environmental factors like temperature, pH-changes, or ultraviolet radiation (Zuluaga-Domínguez, Serrato-Bermudez, & Quicazán, 2018). Indeed, this protection is also effective against human digestion: the absence of specific enzymes, in the human gastrointestinal tract (GIT), for the digestion of the multiple layers surrounding the pollen grains reduces the effectiveness of the digestion (Benavides-Guevara et al., 2017; Rzepecka-Stojko, Stojko, Kurek-Górecka, Górecki, Kabała-Dzik et al., 2015). Differently, BB is more digestible by humans than BP because it is subject to the fermentation process in the combs (Khalifa et al., 2020). The botanical origin may also affect the digestibility degree of bee products (Thakur & Nanda, 2020). Pollen grains with more and larger pores may be easier and faster to digest because digestive enzymes can penetrate easier into the cytoplasmic

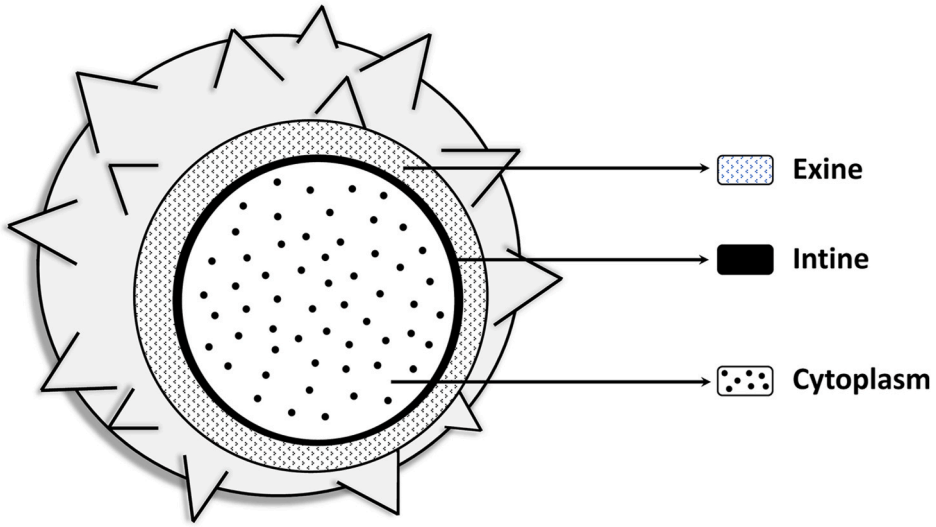

Fig. 2. Cross-section through a pollen grain and its multi-layered structure.

content, resulting in the more effective release of the inner content of pollen grains. On the other hand, pollen with thinner layers is destroyed more effectively by fermentation bacteria, consequently, their bioaccessibility degree may also be higher (Benavides-Guevara et al., 2017; Di Cagno et al., 2019).

Several studies have reported that fermentation is an effective method for the destruction of the pollen layers in order to reach the rich cytoplasmic content of pollen grains, however, this mechanism has not been entirely revealed yet. For instance, Z. Zhang et al. (2017) used fermentation through *Ganoderma lucidum* and *Saccharomyces cerevisiae* in order to break the BP layer and reported a yield of about 85% for *G. lucidum* and 88% for *S. cerevisiae*. In another study (Kaškonienė, Adaškevičiūtė, Kaškonas, Mickienė, & Maruška, 2020), the antibacterial, antifungal and antioxidant activities of BP were evaluated before and after fermentation with *Lactococcus lactis* and *Lactobacillus rhamnosus* bacteria. According to the obtained results, the total phenolic and flavonoid content increased significantly after the fermentation process and thus, an increase in antioxidant, antibacterial and antifungal activity, was observed. In addition, different methods have been proposed to increase the digestibility and consequently bioavailability of BP grains, such as the mechanical breakdown of the pollen layer, thermal shocks, penetration with digestive enzymes, or the disintegration of the pollen layers with osmotic shock (T'ai & Cane, 2000).

Breaking the layers of BP may increase digestibility, but it should be considered that the use of thermal shocks or chemical agents may negatively affect phytochemical compounds in BP (Clement, Olatunde, Obigwa, & Orijajogun, 2017), besides, without layers BP will be more sensitive to harmful environmental factors and microbial contaminations, which may limit the shelf time of the product.

6. Content of dietary phytochemicals in bee pollen and bee bread

Today, botanical resources are explored as dietary sources rich in macro and micro nutrients and particularly phytochemicals (Bakour et al., 2019; Gardana et al., 2018; Khalifa et al., 2020). Phytochemicals are plant secondary metabolites which accumulate in different structures, especially in the skin part of the plant that may play little or no role in plant metabolism (Crozier, Del Rio, & Clifford, 2010). In BP and BB, phytochemicals are very diverse and strongly dependent on the botanical origin of the pollen visited and collected by bees (Carpes et al., 2013), including phenolic acids, flavonoids, carotenoids or vitamins.

6.1. Phenolic compounds

Phenolic compounds have a chemical structure that includes aromatic ring(s) carrying one or more hydroxyl groups. Over 8000 phenolic compounds, which are spread over a wide range in the plant world, have been identified, and may be classified differently according to the number of carbon atoms or structural elements between the phenol rings (Tsao, 2010). In addition, these may be found in different structures, from low molecular weight to complex high molecular weight phenolic derivatives. Phenolic compounds are basically divided into two main groups: flavonoids and phenolic acids (Fig. 3). Flavonoids are the most common compounds in the plant-derived diet (Crozier, Jaganath, & Clifford, 2009; Tsao, 2010). They are chemically attached to two benzene rings by a three-carbon bridge with a skeleton containing 15 carbons (C6–C3–C6). Sugars, like glucose, rhamnose or arabinose, or organic acids (e.g. glucuronic acid) are generally attached to flavonoids (Stahl et al., 2002). Depending on attached hydroxyl groups, position and saturation level, dietary flavonoids can be sub classified as flavonols, flavones, flavan-3-ols, anthocyanidins, flavanones and isoflavones. Phenolic acids (C6–C1) are derivatives of hydroxycinnamic or hydroxybenzoic acids. The most common hydroxycinnamic acids are caffeic acid, ferulic acid, *p*-coumaric acid and synaptic acid, while benzoic acid, syringic acid, vanillic acid and gallic acid are the most common hydroxybenzoic acid derivatives (Abbas et al., 2017; Crozier et al., 2009).

BP and BB are characterized by a rich phenolic profile which is reflected on the therapeutic and biological properties (Araújo et al., 2017; Baltrušaitytė, Venskutonis, & Čeksterytė, 2007; Denisow & Denisow-Pietrzyk, 2016). The total phenolic content (TPC) and total flavonoid content (TFC) of these bee products are on one hand strongly dependent on the botanical origin of the pollen (Gardana et al., 2018), but also on the solvent used in the extraction methodology applied for their determination, Table 2. Observed values for TPC and TFC of BP range between 0.7 and 136 mg GAE/g and 0.1–78 mg QE/g, respectively, while for BB, those values vary between 4.4 and 84 mg GAE/g and 1.7–96 mg QE/g, respectively. Besides, considering the reported studies, BP and BB samples with high TFC and TPC exhibit higher antioxidant activity (Baltrušaitytė et al., 2007).

As previously specified, flavonoids are the major group of phenolic compounds found in BP and BB (Rzepecka-Stojko, Stojko, Kurek-Górecka, Górecki, Kabała-Dzik et al., 2015). Table 3 list the richness of those phytochemical found in BP and BB across the world with a clear dominance of flavonols, particularly the derivatives of kaempferol, quercetin, isorhamnetin and myricetin (Anjos, Fernandes, et al., 2019;

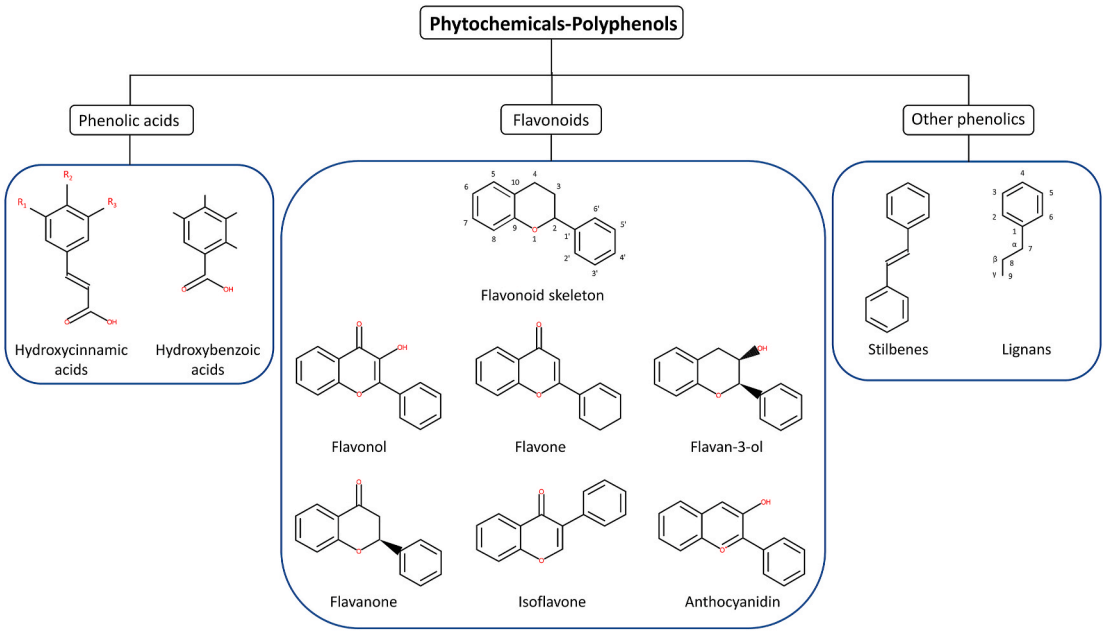

Fig. 3. Classification and chemical structure of some dietary phytochemicals present in bee pollen and bee bread.

Bakour et al., 2019; Čeksteryte et al., 2016; Karabagias, Karabagias, Gatzias, & Riganakos, 2018; Kostić et al., 2019; Negri, Barreto, Sper, Carvalho, & Campos, 2018; Othman et al., 2020; Sobral et al., 2017; Urcan et al., 2018). Flavones are also frequently present, particularly with derivatives of apigenin and luteolin.

Dietary bioactive flavonoids present in BP and BB have different pharmacological and medical roles such as antioxidant activity, enzyme activation, gene expression, hormone regulation, anti-inflammation, neuroprotective, anticancer and antidiabetic (Abouda, Zerdani, Kalalou, Faid, & Ahami, 2011; Bacha et al., 2020; Denisow & Denisow-Pietrzyk, 2016; Kieliszek et al., 2018; Othman et al., 2020), but its effectiveness to prevent diseases, is highly dependent on the degree of bioavailability and assimilation by humans (Carbonell-Capella, Buniowska, Barba, Esteve, & Frígola, 2014; Crozier et al., 2010). Choi, Tai, Cuong, Kim, and Jang (2012) studied the anti-oxidative and anti-inflammatory effects of dietary quercetin and its glycosides as *in vitro*, with quercetin showing poor antioxidant activity compared to its glycosides. On the other hand, quercetin was higher in inducible nitric oxide synthesis and nuclear factor kappa B activation than its glycosides which may be associated with higher anti-inflammatory activity. In addition, other reports have shown that quercetin has anti-carcinogenic activity on different cancer cell lines and tumors (Dajas, 2012). Also, Zang, Zhang, Igarashi, and Yu (2015) investigated the anti-obesity and anti-diabetic effects of kaempferol and glycosides in mice, and they reported that kaempferol glycosides have the potential to reduce the aggregation of adipose tissue, hyperlipidemia and diabetes by enhancing lipid metabolism.

Isorhamnetin, another dominant flavonoid in BP and BB, a methylated form of quercetin, is known to have activities such as anti-cancer, anti-proliferative and anti-inflammation (Hämäläinen, Nieminen, Vuorela, Heinonen, & Moilanen, 2007). Besides that, stimulation of phase II antioxidant enzyme expression and protective properties against oxidative damage of isorhamnetin was examined by J. H. Yang et al. (2014). They concluded that isorhamnetin induces the expression of phase II antioxidant enzyme and is effective in protecting hepatocytes against oxidative stress by preventing the accumulation of reactive oxygen species (ROS) with the activation of NF-E2-related factor-2. Given the above, it is clear that the active diet phytochemicals in BP and BB may play a key role in the prevention, treatment and management of different diseases.

6.2. Carotenoids

Carotenoids are a group of pigmented compounds consisting of a single carbon chain synthesized by plants and some microorganisms (e.g., bacteria and algae). Carotenoids protect plants against oxidative stress and photo-damage (Abd Alla & Salem, 2020). Approximately 100 dietary carotenoids are included in people's diet within coloring foodstuffs (Bohoyo-Gil, Dominguez-Valhondo, Garcia-Parra, & González-Gómez, 2012). BP and BB are rich sources of dietary carotenoids, which are responsible for its different colors, such as yellow, orange, brown and many others, which vary according to its botanical origin (Thakur & Nanda, 2020). β-cryptoxanthin, lutein and lycopene are the most common types of carotenoids found in these bee products (Mărgă;oan et al., 2014), Table 4. The amount of carotenoids found for BP samples in literature is set in the range between 5 and 1233.0 μg/g (Sattler et al., 2015), nevertheless, there are no results reported regarding the quantitative analysis on carotenoid content of BB.

Carotenoids are known to play a key role in cell growth, regulation of dysfunction on a cellular basis, and preventing common diseases such as cancer (Ross, 2010). Previously, Y. Zhang et al. (2016) evaluated *in vitro* and *in vivo* the use of β-carotene with 5-fluorouracil (a used drug in cancer treatment) in the treatment of human esophageal cancer and reported that its combined use increased the inhibition activity on esophageal cancer cells compared to individual use of them. Carotenoids have also strong antioxidant activity, due to the presence of the conjugated double bond system in their structure. They are known as scavengers of ROS and contribute greatly to the prevention of many common chronic diseases (Ross, 2010).

6.3. Vitamins

Vitamins are a group of organic compounds with diverse biochemical roles and strong antioxidant activity. Although vitamins are included in the human diet in small amounts, they are vital micro compounds for the development and maintenance of health (Gey, 1998). Vitamins are naturally found in foods, especially vegetables and fruits, or plant-derived foods, and play a role in managing and regulating metabolic and cellular energy processes (Gey, 1998). The beneficial effects on health are correlated with their optimal diary uptake. The shortage and excess of vitamins disrupt some metabolic processes and consequently,

Table 2
Summary of total phenolic content (TPC) and total flavonoid content (TFC) of bee pollen and bee bread from different botanical origins throughout worldwide.

Bee product	Country	Bee specie	Botanical source	Extraction solvent	Range quantification		References
					Total phenolic content (TPC)	Total flavonoid content (TFC)	
BP	Brazil	*Apis mellifera*	*M. caesalpiniifolia, Cocos nucifera, Mimoza scabrella, Okaliptiis,* Asteraceae, *Eupatoryum, Coffea, Myrcia,* Poaceae, Rubiaceae, *Cecropia, A. aculeatissimum, Astronyum, Mimoza verrucosa,* Fabaceae, Myrtaceae, *M. scabrella, Richardia, Piper, Elephantopus, Syagrus, Vernonia, Ilex, Schinus,* Arecaceae, *Anadenanthera,* Malvaceae, *Alternanthera, Ricinus, Montanoa, Machaerium, Antigonon, Brassica,* Apiaceae, *Baccharis,* Anacardiaceae, Loranthaceae, *Sebastiania* and Melastomataceae	Ethanol	6.7–29.2 mg GAE/g	0.9–17.5 mg QE/g	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
	USA	n.i.	*Mesquite, Yucca, Palm, Terpentine Bush, Mimosa* and *Chenopod*	Methanol	15.91–34.85 mg GAE/g	n.i.	LeBlanc, Davis, Boue, DeLucca, and Deeby (2009)
	Poland	n.i.	Brassicaceae, Asteraceae, *Taraxacum, Centaurea cyanus, Fagopyrum, Trifolium,* Apiaceae, Poaceae, *Tilia,* Rosaceae and *Aesculus*	Water, ethanol and methanol	2.95–31.52 mg GAE/g	n.i.	Borycka, Grabek-Lejko, and Kasprzyk (2015)
	Portugal	n.i.	*Cistus ladanifer, Echium,* Apiaceae, Brassicaceae spp., *Cichorieae* spp., Asteraceae spp., *Lavandula* spp., *Plantago* spp. and *Silene* spp.	Ethanol	35.05 mg GAE/g	6.99 mg QE/g	Anjos, Fernandes, et al. (2019)
		n.i.	*Rubus* spp., *Castanea sativa, Cistus* spp., *Leontondon* spp., *Echium* spp., *Echium* spp., *Eucalyptus* spp., *and Erica* spp.	Methanol	14.83–43.97 mg GAE/g	2.49–11.83 mg CAE/g	Anjos, Paula, et al. (2019)
		Apis mellifera	*Cistus, Echium, Prunus, Castanea, Leontodon, Trifollium, Erica, Quercus, Mimosa, Eucalyptus* and *Rubus*	Methanol	12.90–19.80 mg GAE/g	4.50–7.0 mg CAE/g	Feás, Vázquez-Tato, Estevinho, Seijas, and Iglesias (2012)
	Brazil	*Apis mellifera*	*Cocos nucifera, Miconia* spp., *Spondias* spp., *Myrcia* spp., *Saccharum* spp., *Eucalyptus* spp., *Mikania* spp., and *Mimosa* spp.	Methanol	33.73–75.60 mg GAE/g	1.42–9.05 mg QE/g	Araújo et al. (2017)
		Apis mellifera	Brassicaceae, Asteraceae *Elephantopus,* Asteraceae *Eupatorium,* Asteraceae *Gochnatia,* Myrtaceae *eucalyptus* and Loranthaceae *Struthanthus*	Ethanol	30.55–48.76 mg GAE/g	8.55–28.43 mg QE/g	Carpes et al. (2013)
	Italy	n.i.	*Castanea* sp., *Rubus* sp., *and Cistus* sp.,	Ethanol	13.53–24.75 mg GAE/g	n.i.	Domenici et al. (2015)
	Poland	n.i.	n.i.	Ethanol	13.24–27.03 mg GAE/g	11.22–77.88 mg QE/g	Rzepecka-Stojko, Stojko, Kurek-Górecka, Górecki, Sobczak, et al. (2015)
	Spain and Portugal	n.i.	Cistaceae, Fabaceae, Ericaceae and Boraginaceae	Methanol	18.55–32.15 mg GAE/g	3.71–10.14 mg CAE/g	Pascoal, Rodrigues, Teixeira, Feás, and Estevinho (2014)
	Romania	n.i.	*Brassica napus, Taraxacum officinale, Malus domestica, Rubus idaeus, Taraxacum officinale* and *Rosa canina*	Ethanol	10.08–20.48 mg GAE/g	n.i.	Stanciu, Marghitas, and Dezmirean (2008)
	Turkey	n.i.	Chenopodiaceae, *Cistus* sp., *Convolvulus* sp., *Scabiosa* sp., *Rhododendron* sp., *Euphorbia* sp., *Astragalus* sp., *Coronilla* sp., *Hedysarum* sp., *Lotus* sp., *Melilotus* sp., *Onobrychis* sp., *Trifolium* sp., *Vicia* sp., *Castanea sativa,* Geraniaceae, Hypericaceae, Lamiaceae *Salvia* sp., *Teucrium* sp.,	Ethanol	26.69–43.42 mg GAE/g	2.62–4.44 mg QE/g	Mayda et al. (2020)

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Table 2 (*continued*)

Bee product	Country	Bee specie	Botanical source	Extraction solvent	Range quantification		References
					Total phenolic content (TPC)	Total flavonoid content (TFC)	
			Thymus sp., *Laurus* sp., Liliaceae, *Loranthus* sp., *Tilia* sp., *Eucalyptus* sp., Papaveraceae, Plantaginaceae, *Zea* sp., *Rumex* sp., Ranunculaceae, Rosaceae, *Salix* sp., Scrophulariaceae, *Linaria* sp., and Solanaceae				
	Denmark, Italy, Switzerland, Slovakia, Poland Spain, Lithuania, Ukraine and Latvia	n.i.	n.i.	Methanol	33.14–55.04 mg RUE/10 g	10.68–48.31 mg RUE/10 g	Adaškevičiūtė et al. (2019)
	Lithuania	n.i.	*Brassica napus, Trifolium repens, Carum carvi* L., *Trifolium pratense, Fagopyrum esculentum* and *Salix* spp.	Methanol	23.30 mg GAE/g	n.i.	Čeksteryte et al. (2016)
	China	n.i.	n.i.	Ethanol	12.57 mg GAE/g	22.89 mg RUE/g	Sun, Guo, Zhang, and Zhuang (2017)
	Egypt	n.i.	*Trifolium alexandrinum* L.	Ethanol, ethyl acetate, dichloromethane and petrolium ether	0.8–2.3 mg GAE/g	0.1–0.85 mg QE/g	AbdElsalam, Foda, Abdel-Aziz, and Abd (2018)
	Greece	n.i.	*Papaver rhoes, Chamomila recutita, Sinapis arvensis, Cistus* sp., *Trifolium* sp., *Dorycnium* sp., *Cichorium* sp., *Convolvulus* sp., *Circium* sp., *Malva sylvestris, Fumana* sp., *Eucalyptus camaldulensis, Anemone* sp., *Ononis* sp., *Asphodelus* sp. and *Quercus ilex*	Ethanol	15.20–60.20 mg GAE/g	6.00–57.60 mg QE/g	Karabagias et al. (2018)
	Malaysia	Stingless bee (*Trigona apicalis*, *Trigona itama* and *Trigona thoracica*)	n.i.	Ethanol	33.46–135.93 mg GAE/g	15.28–31.80 mg QE/g	Harif Fadzilah, Jaapar, Jajuli, and Wan Omar (2017)
	India	n.i.	*Brassica juncea*	Ethanol	18.29 mg GAE/g	n.i.	Ketkar et al. (2014)
	Serbia	*Apis mellifera*	*Helianthus annuus* L.	Methanol and ethanol	2.91–3.82 mg GAE/g	0.84–0.87 mg QE/g	Kostić et al. (2019)
	Slovakia	n.i.	*Helianthus annuus* L.	Ethanol	0.69–0.80 mg GAE/g	n.i.	Fatrcová-Šramková, Nôžková, Máriássyová, and Kačániová (2016)
	China	n.i.	*Brassica campestris* L.	Acetone	33.646 mg GAE/g	n.i.	Yan et al. (2019)
BB							
	Morocco	n.i.	n.i.	Ethanol	4.88 mg GAE/g	1.67 mg QE/g	Bakour et al. (2017)
	Poland	n.i.	n.i.	Ethanol	6.15–27.80 mg GAE/g	n.i.	Kowalski and Lukasiewicz (2017)
		n.i.	Brassicaceae, Asteraceae, *Taraxacum, Centaurea cyanus, Fagopyrum, Trifolium,* Apiaceae, Poaceae, *Tilia,* Rosaceae and *Aesculus*	Water, ethanol and methanol	4.37–9.59 mg GAE/g	n.i.	Borycka et al. (2015)
	Romania	n.i.	n.i.	Methanol, ethanol, water	8.32–22.72 mg GAE/g	n.i.	Stanciu, Marghitas, and Dezmirean (2007)
	Ukraine	n.i.	n.i.	Ethanol	12.36–25.44 mg GAE/g	13.56–18.24 μg QE/g	Ivanišová et al. (2015)
	Poland	n.i.	n.i.	Ethanol	33.43–36.52 mg GAE/g	n.i.	Markiewicz-Żukowska et al. (2013)
	Colombia	*Apis mellifera*	n.i.	Ethanol	8.9 mg GAE/g	3.2 mg QE/g	Zuluaga et al., (2015a)
	Portugal	*Apis mellifera iberiensis*	*Castanea sativa, Plantago* sp., *Rubus* sp., *T. Cytisus striatus, Hedera helix, T. Solanum nigra, Plantago* sp., *T. Ulex europaeus, Erica* sp., *Lavandula* sp., *Salix* sp., *Crataegus monogyna, Echium* sp., *T. Anthemis arvensis, Brassica* sp., *T. Raphanus raphanistrum, Sesamoides* sp., *Jasione*	Ethanol	14–84 mg GAE/g	11–96 mg QE/g	Tomás et al. (2017)

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Table 2 (*continued*)

Bee product	Country	Bee specie	Botanical source	Extraction solvent	Range quantification		References
					Total phenolic content (TPC)	Total flavonoid content (TFC)	
			montana and *T. Calendula arvensis*				
	Brazil	*Apis mellifera*	Poaceae, Rubiaceae, Myrtaceae sp., Asteraceae, Mimosaceae sp., Myrtaceae sp., Fabaceae sp., Bignoniaceae, Sapindaceae, Amaranthaceae and Caryophyllaceae	Ethanol	n.i.	578.8–1495.9 mg QE/kg	Bovi et al. (2020)
	India and Romania	*Apis mellifera* and *Apis dorsata*	*Brassica* sp., Poaceae, *Eucalyptus* sp., *Citrus* sp., Asteraceae, *Tilia* sp., Rosaceae, *Plantago*, Fabaceae, *Lotus*, *Centaurea montana*, *Salix* sp., *Prunus* sp. and *Quercus* sp.	Methanol	5.67–12.83 mg GAE/g	23.64–36.19 mg QE/g	Urcan et al. (2018)
	Romania	n.i.	n.i.	Ethanol	13.92 mg GAE/g	n.i.	Stanciu et al. (2008)
		n.i.	n.i.	Methanol	15.33 mg GAE/g	5.13 mg QE/g	Cocan, Marghitas, and Dezmirean (2006)
	Turkey	n.i.	*Cistus* sp., *Convolvulus* sp., *Scabiosa* sp., Chenopodiaceae, *Rhododendron* sp., *Euphorbia* sp., *Astragalus* sp., *Coronilla* sp., *Hedysarum* sp., *Lotus* sp., *Melilotus* sp., *Onobrychis* sp., *Trifolium* sp., *Vicia* sp., *Castanea sativa*, Geraniaceae, Hypericaceae, *Teucrium* sp., *Thymus* sp., *Laurus* sp., Liliaceae, *Loranthus* sp., *Tilia* sp., *Eucalyptus* sp., Papaveraceae, Plantaginaceae, *Zea* sp., *Rumex* sp., Rosaceae, *Salix* sp., Scrophulariaceae, *Linaria* sp., and Solanaceae	Ethanol	8.26–12.71 mg GAE/g	1.81–3.74 mg QE/g	Mayda et al. (2020)
	Lithuania	n.i.	n.i.	Methanol	19.63–22.16 mg RUE/10 g	7.88–15.67 mg RUE/10 g	Adaškevičiūtė et al. (2019)
		n.i.	*Brassica napus*, *Trifolium repens*, *Carum carvi* L., *Trifolium pratense*, *Fagopyrum esculentum* and *Salix* spp.	Methanol	21.20 mg GAE/g	n.i.	Čeksteryte et al. (2016)
		n.i.	n.i.	Ethanol	306–394 mg GAE/100 g	n.i.	Bartkiene et al. (2020)
	Romania	*Apis mellifera* and *Apis dorsata*	n.i.	Methanol	19.72–28.61 mg GAE/g	n.i.	Bobis et al. (2017)
	Malaysia	Stingless bee (*Heterotrigona itama*)	n.i.	Ethanol and water	14.19–22.54 mg GAE/g	2.88–26.57 mg QE/g	Othman, Noordin, Ghazali, Omar, and Mohamed (2019)

n.i., no information; GAE, gallic acid equivalent; QE quercetin equivalent; RUE, rutin equivalent; CAE, catechin equivalent.

different diseases can occur (Rizvi, Raza, Faizal Ahmed, Abbas, & Mahdi, 2014). Therefore, an adequate intake of all vitamins is necessary for the functions of cells and tissues. Many studies have demonstrated that BP and BB are rich in vitamins, with an ideal vitamin content that may fulfill this necessity (Melo & Almeida-Muradian, 2010; Oliveira et al., 2009; Tomás et al., 2017).

Both of them contain fat-soluble vitamins (A, D, E, and K) and water-soluble vitamins (C and B complex), as well as vitamins such as vitamin P (Khalifa et al., 2020; Thakur & Nanda, 2020), depending its contents on the botanical origin and collection season of the polen by the bees, as already mentioned. Both bee products contain vitamin E (Khalifa et al., 2020; Oliveira et al., 2009; Sattler et al., 2015), which is fat-soluble and is considered an antioxidant vitamin. Vitamin E can be stored in the body, so no daily intake is needed. Furthermore, it has many biological activities, including neuroprotective, anticancer, immune-enhancing and anti-inflammatory (Gey, 1998; Rizvi et al., 2014). The vitamin E family is collectively named tocochromanols, (tocopherols and tocotrienols). BP contains especially the tocopherols group (α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol), being α-tocopherol and γ-tocopherol the main compounds (Rizvi et al., 2014). Sattler et al. (2015) reported that α, β, γ and δ-tocopherol contents of more than 20 samples of BP collected from different apiaries from southern Brazil presented 5–73 μg/g, 1–10 μg/g, 2–12 μg/g and 1–84 μg/g, respectively. In another study, the tocopherol content of BB from northern Portugal also set the higher value for δ-tocopherol with ranges between 1 and 37 mg/g for α-tocopherol, 1–35 mg/g for β+γ-tocopherol and 77–293 mg/g for δ-tocopherol (Tomás et al., 2017).

Vitamin C, another vitamin found in BP and BB, is a water-soluble vitamin and has a strong antioxidant property, which has been reported in different studies (Gey, 1998; Grosso et al., 2013; Sesso et al., 2008). BP content in vitamin C can vary between 14 and 797 μg/g (Melo & Almeida-Muradian, 2010; Sattler et al., 2015), while in BB is reported to be much lower, around 0.06–0.11 mg/g (Haydak & Palmer, 1942). Vitamin C plays a role as a co-factor in the synthesis of amino acids,

Table 3
Phenolic compounds present in the bee pollen and bee bread.

Phenolic compounds	Bee specie	Source	Extraction solvent	Spectral analysis	References
Flavonols					
Quercetin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS; HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018); Kostić et al. (2019)
	n.i.	BB	Methanol	LC-MS	Čeksteryte et al. (2016)
Quercetin 3-*O*-galactoside	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Quercetin-3-*O*-glucoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Quercetin 3-*O*-rhamnoside	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
	Apis mellifera iberiensis	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Quercetin 3-*O*-rutinoside (Rutin)	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS; HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018); Kostić et al. (2019)
	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Quercetin-3-*O*-rhamnosyl glucoside	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Quercetin-*O*-dihexoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Quercetin-3-*O*-sophoroside	n.i.	BP	Methanol	LC-MS	Čeksteryte et al. (2016)
	Apis mellifera and *Apis dorsata*	BB	Ethanol	HPLC/DAD	Urcan et al. (2018)
Quercetin-*O*-hexosyl-pentoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Quercetin-3-*O*-glucosyl-6-*O*-pentoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Quercetin-*O*-(malonyl)-rutinoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Quercetin-*O*-hexosyl-*O*-hexoside	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Quercetin-*O*-hexosyl-*O*-rutinoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Quercetin-*O*-(malonyl)-hexoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Bis-methylated quercetin	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Isorhamnetin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
	Stingless bee (*Heterotrigona itama*)	BB	Methanol	LC-MS	Othman et al. (2020)
Isorhamnetin-3-*O*-glucoside	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS Orbitrap	Kostić et al. (2019)
	Apis mellifera iberiensis	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Isorhamnetin-di-3,7-*O*-glucoside	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Isorhamnetin-3-O-(6″-*O*-*p*-coumaroyl)-glucoside	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Isorhamnetin-3-*O*-(2″-*O*-rhamnosyl)-glucoside	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Acetyl isorhamnetin-*O*-hexoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Isorhamnetin-3-*O*-(2″,3″-*O*-dirhamnosyl)-glucoside	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Isorhamnetin-3-*O*-(2″-*O*-rhamnosyl acetyl) glucoside	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Isorhamnetin-3-*O*-rutinoside (Narcissin)	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Isorhamnetin-*O*-dihexoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Isorhamnetin-*O*-hexosyl-*O*-rutinoside	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Isorhamnetin-3-*O*-rhamnoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Isorhamnetin-*O*-(malonyl)-hexoside isomer 1	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Isorhamnetin-*O*-(malonyl)-hexoside isomer 2	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Isorhamnetin-*O*-pentosyl-hexoside	*Apis mellifera iberiensis*	BB	Methanol	LC-DAD–ESI/MS; HPLC-DAD-ESI/MS	Bakour et al. (2019); Sobral et al. (2017)
Isorhamnetin-*O*-rhamnoside-hexoside	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Kaempferol	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS; HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018); Kostić et al. (2019)
	Apis mellifera/Stingless bee (*Heterotrigona itama*)	BB	Methanol	LC-MS	Čeksteryte et al. (2016); Othman et al. (2020)
Acetyl kaempferol-*O*-deoxyhexosyl-hexoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Kaempferol-3-*O*-glucosyl-rutinoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Kaempferol-*O*-pentosyl-deoxyhexoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Kaempferol-3-*O*-rhamnosyl-glucoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)

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Table 3 (*continued*)

Phenolic compounds	Bee specie	Source	Extraction solvent	Spectral analysis	References
Kaempferol-3-*O*-rhamnoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Kaempferol-7-*O*-rutinoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Kaempferol-*O*-hexosyl-*O*-rutinoside	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Kaempferol-3-*O*-rutinoside	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Kaempferol-*O*-dihexoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Kaempferol-3-*O*-glycoside	*Apis mellifera* and *Apis dorsata*	BB	Ethanol	HPLC/DAD	Urcan et al. (2018)
Galangin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Myricetin	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
	Apis mellifera and *Apis dorsata*	BB	Ethanol	HPLC/DAD	Urcan et al. (2018)
Myricetin-*O*-rutinoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Myricetin-3-*O*-rutinoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Myricetin-3-*O*-glucoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Myricetin-*O*-hexoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Myricetin-*O*-(malonyl)-rutinoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Myricetin-*O*-(malonyl)-hexoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Myricetin-3-*O*-α-L-rhamnopyranoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Patuletin-3-*O*-rhamnosylglucoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Methyl herbacetrin-*O*-dihexoside	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Methyl herbacetrin-3-*O*-rutinoside	n.i.	BB	Methanol	LC-DAD–ESI/MS	Bakour et al. (2019)
Herbacetin-3-*O*-glycoside	*Apis mellifera* and *Apis dorsata*	BB	Ethanol	HPLC/DAD	Urcan et al. (2018)
Methyl herbacetrin-*O*-hexosyl-rutinoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Methyl herbacetrin-3-*O*-glucoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Flavanols					
Procyanidin dimer B1	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Catechin	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Epicatechin	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Flavanonols					
Pinobanksin-3-*O*-butyrate	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Pinobanksin-3-*O*-propionate	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Taxifolin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Dihydroflavonols					
Dihydromyricetin	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Pinobanksin-5-methylether-3-*O*-acetate	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Dihydroquercetin-3-*O*-rhamnoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Dihydroquercetin	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti, Castiglioni, Maldarizzi, Carloni, and Lucini (2019)
Flavanones					
Naringin	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
	n.i.	BB	Ethanol	HPLC	Tavdidishvili, Khutsidze, Pkhakadze, Vanidze, and Kalandia (2014)
Naringenin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS; SPME–GC/MS	Kostić et al. (2019); LeBlanc et al. (2009)
Naringin 6′-malonate	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Naringenin hexoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
4′,5-dihydroxy-7-methoxyflavanone	n.i.	BP	Methanol	SPME–GC/MS	LeBlanc et al. (2009)
Eriodictyol	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Naringin-4′-*O*-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Naringenin-7-*O*-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Hesperidin	n.i.	BP	Ethyl acetate	HPLC	Fanali, Dugo, and Rocco (2013)
Dihydrochalcones					
Phloretin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Flavones					
Luteolin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
	Apis mellifera and *Apis dorsata*	BB	Ethanol	HPLC/DAD	Urcan et al. (2018)
	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)

(*continued on next page*)

Table 3 (*continued*)

Phenolic compounds	Bee specie	Source	Extraction solvent	Spectral analysis	References
Apigenin 7-*O*-(6″-malonyl-apiosyl-glucoside)					
Apigenin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
	Apis mellifera/Stingless bee (*Heterotrigona itama*)	BB	Methanol	LC-MS; HPLC/UV/MS	Baltrušaitytė et al. (2007); Othman et al. (2020)
Apigenin 6-C-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Tricetin	*Apis mellifera* and *Apis dorsata*	BB	Ethanol	HPLC/DAD	Urcan et al. (2018)
Tricetin-7-*O*-(pentoside-glucoside)	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Acacetin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Rutin	n.i.	BB	Ethanol	HPLC	Tavdidishvili et al. (2014)
Chrysin	n.i.	BP	Methanol	HPLC-PDA	Ketkar et al. (2014)
	n.i.	BB	Methanol	HPLC/UV/MS	Baltrušaitytė et al. (2007)
Genkwanin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Luteolin-*O*-dihexoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Luteolin 7-*O*-glucuronide	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Luteolin-di-*O*-hexosyl-rhamnoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Luteolin-*O*-(malonyl)-hexoside	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Luteolin-7-*O*-6″-acetylglucoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Orientin-2-*O*-xyloside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Tetramethylscutellarein	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Laricitrin-3-*O*-rhamnoside	*Apis mellifera iberiensis*	BB	Methanol	HPLC-DAD-ESI/MS	Sobral et al. (2017)
Anthocyanins					
Cyanidin-3-rutinoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
6-*O*-caffeoyl glucoside	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Petunidin-3-*O*-galactoside	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Petunidin 3-*O*-arabinoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Cyanidin 3-*O*-xyloside/arabinoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Delphinidin 3-*O*-(6″-*p*-coumaroyl-glucoside)	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Pelargonidin 3-*O*-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Delphinidin 3-*O*-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Delphinidin 3-*O*-glucosyl-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Delphinidin 3-*O*-rutinoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Cyanidin 3-*O*-sophoroside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Isoflavonoids					
7,8,2′,4′-Tetrahydroxyisoflavone	n.i.	BP	Methanol	SPME–GC/MS	LeBlanc et al. (2009)
Formononetin	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Genistin	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Hydroxycinnamic acid					
Caffeic acid	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
		BB	Methanol	LC-MS	Othman et al. (2020)
Caffeic acid 4-*O*-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Hydrocaffeic acid	n.i.	BP	Ethanol	HPLC/ESI-MS	Karabagias et al. (2018)
p-coumaric acid	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS; HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018); Kostić et al. (2019)
	n.i.	BP	Methanol	HPLC/UV/MS	Baltrušaitytė et al. (2007)
Trihydroxycinnamic acid	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Ferulic acid	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
	Stingless bee (*Heterotrigona itama*)	BB	Methanol	LC-MS	Othman et al. (2020)
Feruloyl glucose	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Sinapic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Cinnamic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
2-feruloyl-1-sinapoylgentiobiose	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Caffeoyl glucose	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
p-coumaroyl tyrosine	n.i.	BP	Ethanol	HPLC/ESI-MS	Karabagias et al. (2018)
Hydroxycinnamic acid derivatives 1, 2, 3, 4, 5	*Apis mellifera* and *Apis dorsata*	BB	Ethanol	HPLC/DAD	Urcan et al. (2018)
Hydroxybenzoic acids					
Gallic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Vanillic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Syringic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	

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Table 3 (*continued*)

Phenolic compounds	Bee specie	Source	Extraction solvent	Spectral analysis	References
					De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Ellagic acid	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Dihydroxybenzoic acids					
Protocatechuic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
β-resorcylic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Benzoic acids and derivatives					
4-methoxy benzoic	*Apis mellifera*	BP	Ethanol	GC-MS	Carpes et al. (2013)
Other polyphenols					
Aesculin	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Urolithin B	n.i.	BP	Ethanol	HPLC/ESI-MS	Karabagias et al. (2018)
Chlorogenic acid	*Apis mellifera*	BP	Ethanol; methanol	HPLC-PDA	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
Coumaroyl quinic acid	n.i.	BP	Ethanol	UHPLC-DAD-ESI-MS	Anjos, Fernandes, et al. (2019)
Glucoraphanin	*Apis mellifera*	BP	Ethanol	HPLC-MS	De-Melo, Estevinho, Moreira, Delerue-Matos, Freitas, et al. (2018)
5-*O*-caffeoylquinic acid	*Apis mellifera*	BP	Methanol; ethanol	UHPLC/MS-MS	Kostić et al. (2019)
Isopimpinellin	n.i.	BP	Ethanol	HPLC/ESI-MS	Karabagias et al. (2018)
Polyamines					
N′,N″,N‴-tris-caffeoyl spermidine	n.i.	BP	Ethanol/water	LC/DAD/ESI-MS	El Ghouizi, El Menyiy, Falcão, Vilas-Boas, and Lyoussi (2020)
N′,N″-dicaffeoyl,N‴-coumaroyl spermidine	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
N′,N″-dicaffeoyl,N‴-feruloyl spermidine	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
N′-caffeoyl-N″-feruloyl,N‴-coumaroyl spermidine	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
N′-caffeoyl-N″,N‴- dicoumaroyl spermidine	n.i.	BP	Ethanol/water	LC/DAD/ESI-MS	El Ghouizi et al. (2020)
N′,N″,N‴-tris-*p*-coumaroyl spermidine	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
N′,N″,N‴-tris-*p*-feruloyl spermidine	*Apis mellifera*	BP	Dichloromethane; methanol/water	RP-HPLC-DAD-ESI-MS/MS	Negri et al. (2018)
Tyrosols					
Hydroxytyrosol 4-*O*-glucoside	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Curcuminoids					
Curcumin	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)
Lignans					
Sesamol	n.i.	BP	Methanol	UHPLC-ESI-QTOF	Rocchetti et al. (2019)

n.i., no information.

cholesterol, collagen and some hormones (Grosso et al., 2013). Hence it should be taken regularly with the diet. According to the dietary reference intake, daily vitamin C intake is 90 mg for men and 75 mg for women (Russell et al., 2001). Vitamin C has many different therapeutic properties, such as anticarcinogenic, improving neurotransmission and slowing macular degeneration (Evans & Lawrenson, 2017). Also, there are several research's investigating whether vitamin C has any effect on cardiovascular diseases. Sesso et al. (2008) investigated if long-term vitamin C intake reduced the risk of major cardiovascular diseases, revealing that there is no effect in the short or long term vitamin C intake.

7. Digestion and bioavailability of phytochemicals in bee pollen and bee bread

The concept of phytochemicals bioavailability comprises its release from the food matrix, their alteration in the GIT, bioaccessibility, absorption, tissue distribution with systemic circulation, and finally their effect (i.e. bioactivity) on the tissues (Stahl et al., 2002). The bioaccessibility depends largely in the effectiveness of the digestion which may occur at three different levels, in the mouth, stomach or in the intestines. In the oral stage, when chewed, the food is mixed with saliva containing α-amylase and lingual lipase enzymes initiating several degradation processes such as the hydrolyze of carbohydrates (C. Li, Yu, Wu, & Chen, 2020). The gastric digestion starts with the decrease of pH due to the secretion of hydrochloric acid, followed by the action of enzymes such as pepsin and gastric lipase, and finally the mechanical digestion due to the contraction activity of the stomach (C. Li et al., 2020). The intestinal phase involves also the action of enzymes produced by the pancreas to digest proteins, fats and carbohydrates, but also bile salts and hormones that regulate several metabolisms of sugars and fats. This stage occurs along the small intestine, through mixing and transport of intraluminal contents and absorption of nutrients (Yonekura & Nagao, 2007).

With today's advanced analytical methods and instrumentation, it is possible to measure the bioavailability of dietary phytochemicals, however, some practical limitations may occur in the access of the bioaccessibility and biological activities in living systems. The interaction of phytochemicals with other compounds like proteins and carbohydrates in the GIT can alter their bioavailability. Besides, these can be absorbed and metabolized directly by the intestinal cells in the colon without passing to plasma and urine (Carbonell-Capella et al., 2014; Crozier et al., 2009). In the case of BP and BB, the strong multi-layered structure of pollen grains limits the release of bioactive compounds from its interior and the interaction of digestive enzymes with these food components (Bogdanov, 2011). Thereby the morphology of dietary foods significantly affects the degree of digestion and, consequently, bioavailability, which, in the case BP and BB, may require the use of specific methods to increase digestibility, as referred in more detail in section 5.

Table 4
Carotenoids existing in bee pollen and bee bread, their amounts and botanical origins.

Carotenoids	Bee specie	Bee product	Botanical source	Range quantification	Spectral analysis	References
Carotenes						
β-Carotene	n.i.	BP	Asteraceae, Fabaceae, Brassicaceae, Rubiaceae, *Caesalpineaceae,* Caricaceae, Ulmaceae, Myrtaceae, Aquifoliaceae, Anacardiaceae, Melastomataceae, Mimosaceae, Loranthaceae, Piperaceae, Poaceae, Burseraceae and Rosaceae	0.5–112.7 μg/g	HPLC	Sattler et al. (2015)
	n.i.	BP	*Cistus ladanifer, Echium, Achillea, Taraxacum, Carduus, Cirsium, Vicia, Quercus ilex, Quercus r., Rubus,* Pinaceae, *Filipendula, Trifolium incarnatum, Trifolium pratense, Trifolium repens, Prunus, Pyrus, Malus* and *Oxalis*	n.i.	UHPLC-DAD	Gardana et al. (2018)
	Apis mellifera	BP	n.i.	3.14–77.88 μg/g	HPLC	Melo and Almeida-Muradian (2010)
	n.i.	BP	Rosaceae, Fabaceae, Asteraceae, Brasicaceae, Ericaceae and Salicaceae	0.17–18.18 μg/g	HPLC-PDA	Mărgă;oan et al. (2014)
	n.i.	BB	Dandelion, horse-chestnut, pine, heather,fireweed and birch	n.i.	TLC	Barene, Daberte, and Siksna (2015)
α-Carotene	n.i.	BP	Asteraceae, Myrtaceae, Fabaceae, Loranthaceae, Aquifoliaceae, Arecaceae, Piperaceae, Anacardiaceae, Rubiaceae and Burseraceae	3.3–324.7 μg/g	HPLC	Sattler et al. (2015)
γ – Carotene	*Apis mellifera*	BP	Sunflower, clover, sesame and maize	53.81–128.7 mg/g	Spectrophotometric	Abd Alla and Salem (2020)
ξ – Carotene				44.95–115.81 mg/g		Abd Alla and Salem (2020)
ε – Carotene				58.06–123.91 mg/g		Abd Alla and Salem (2020)
Lycopene				38.44–121.5 mg/g		Abd Alla and Salem (2020)
	Apis mellifera	BP	Multifloral and monofloral bee pollen	0.59–16.17 μg/g	UHPLC-DAD	Bohoyo-Gil et al. (2012)
Xanthophylls						
Zeaxanthin	n.i.	BP	*Cistus ladanifer, Echium, Achillea, Taraxacum, Carduus, Cirsium, Vicia, Quercus ilex, Quercus r., Rubus,* Pinaceae, *Filipendula, Trifolium incarnatum, Trifolium pratense, Trifolium repens, Prunus, Pyrus, Malus* and *Oxalis*	n.i.	UHPLC-DAD	Gardana et al. (2018)
	Apis mellifera	BP	Multifloral and monofloral bee pollen	0.14–2.26 μg/g	UHPLC-DAD	Bohoyo-Gil et al. (2012)
	Apis mellifera	BP	Sunflower, clover, sesame and maize	48.79–312.43 mg/g	Spectrophotometric	Abd Alla and Salem (2020)
Lutein	n.i.	BP	Rosaceae, Fabaceae, Asteraceae, Brasicaceae, Ericaceae and Salicaceae	44.52–476.30 μg/g	HPLC-PDA	Mărgă;oan et al. (2014)
	Apis mellifera	BP	Multifloral and monofloral bee pollen	0.14–0.31 μg/g	UHPLC-DAD	Bohoyo-Gil et al. (2012)
	n.i.	BP	*Cistus ladanifer, Echium, Achillea, Taraxacum, Carduus, Cirsium, Vicia, Quercus ilex, Quercus r., Rubus,* Pinaceae, *Filipendula, Trifolium incarnatum, Trifolium pratense, Trifolium repens, Prunus, Pyrus, Malus* and *Oxalis*	n.i.	UHPLC-DAD	Gardana et al. (2018)
Capsantine	*Apis mellifera*	BP	Multifloral and monofloral bee pollen	0.20–2.04 μg/g	UHPLC-DAD	Bohoyo-Gil et al. (2012)
β-cryptoxanthin	*Apis mellifera*	BP	Sunflower, clover, sesame and maize	40.77–85.42 mg/g	Spectrophotometric	Abd Alla and Salem (2020)
	n.i.	BP	Rosaceae, Fabaceae, Asteraceae, Brasicaceae, Ericaceae and Salicaceae	1.02–35.43 μg/g	HPLC-PDA	Mărgă;oan et al. (2014)
	Apis mellifera	BP	Multifloral and monofloral bee pollen	0.59–16.17 μg/g	UHPLC-DAD	Bohoyo-Gil et al. (2012)
Isocryptoxanthin	*Apis mellifera*	BP	Sunflower, clover, sesame and maize	31.18–80.59 mg/g	Spectrophotometric	Abd Alla and Salem (2020)
Isozeaxanthin				38.06–265.40 mg/g		Abd Alla and Salem (2020)
Lactucaxanthin				31.71–97.94 mg/g		Abd Alla and Salem (2020)
Neoxanthin				44.53–72.19 mg/g		Abd Alla and Salem (2020)
Violaxanthin				48.32–105.99 mg/g		Abd Alla and Salem (2020)
Antheraxanthin				40.12–91.46 mg/g		Abd Alla and Salem (2020)
Astaxanthin				36.88–90.12 mg/g		Abd Alla and Salem (2020)
Canthaxanthin				45.05–96.12 mg/g		Abd Alla and Salem (2020)

n.i., no information.

7.1. Phenolic compounds

Once the phenolic compounds are released from the pollen grains cytoplasm, they can suffer structural changes in the GIT through different mechanisms, for example, enzyme activities, transformation by bacteria in the colon or interactions with macro and micronutrient compounds in the digestive tract, and consequently may cause them to exhibit different biological activities. The digestibility and absorption of phenolic compounds depend on their physicochemical properties (Carbonell-Capella et al., 2014). For instance, its molecular weights may affect its behave differently: low molecular weight phenolic compounds are water-soluble, but those with high molecular weight may be insoluble in water. Furthermore, the conjugation with other compounds, glycosylation, or exposure to oxidation by enzymes such as polyphenol oxidase, are additional factors affecting the digestible and absorption degree of polyphenolic compounds (Stahl et al., 2002).

Dietary flavonoids from plant-based foods are predominantly present as conjugated glycoside, which generally allow them to be absorbed in the small intestine and pass into the circulatory system (Donovan, Manach, Faulks, & Kroon, 2006). Catechins, in the flavans subgroup, are one exception with partial or no change in the presence of saliva in the first phase of digestion in the mouth and resistant to hydrolysis in the stomach (Rechner, Spencer, Kuhnle, Hahn, & Rice-Evans, 2001). When occurs, absorption is associated with the hydrolysis of the glycosylates structure and the release of aglycons as a result of the lactase phlorizin hydrolase (LPH) activity in the brush-border of small intestinal epithelial cells. After which, the process is followed by the passage of passive diffusion into the intestinal epithelial cells due to improved lipophilicity and proximity to the cellular membrane (Crozier et al., 2010; Stahl et al., 2002). Another option of hydrolysis is cytosolic β-glucosidase (CBG), which is found in epithelial cells. In order for hydrolysis to take place, polar glycosides should be transported to epithelial cells with the participation of an active sodium-dependent glucose transporter through the mediation of CBG (Crozier et al., 2009). Therefore, the presence of aglycons in the intestinal epithelial cells after hydrolysis of flavonoid conjugates may be explained in two possible ways: LPH/passive diffusion and CBG/transport (Stahl et al., 2002). Flavonoids and their metabolites that pass into the large intestine without being absorbed in the small intestine can be absorbed here, but the conjugate parts of flavonoids will be fragmented by the bacterial microflora in the large intestine and then exposed to ring fission, resulting in the production of different phenolic acids (Crozier et al., 2010; Donovan et al., 2006).

Quercetin is one of the most common polyphenols compounds in various plant sources including both BP and BB and therefore is one of the most researched flavonoids. A study by Hollman, de Vries, van Leeuwen, Mengelers, and Katan (1995) showed that quercetin is better absorbed than quercetin glycosides, mostly due to the different glycosides moieties linked to them which are depending on the sources of quercetin. In the research conducted by Shi and Williamson (2015), the digestibility and bioavailability of quercetin was compared applying naturally glycosylated quercetin (in meal form) and aglycon quercetin (dietary supplement in tablet form) to six male people. Urine samples were collected for 24 h and the quercetin amount was calculated by liquid chromatography-mass spectrometry. According to the obtained results, 100 g of onion gives a comparable amount of quercetin to a 500 mg quercetin aglycone supplement. This means that BP and BB, rich in conjugated glycoside quercetin, can reach a similar level of bioavailability in the diet as quercetin aglycone supplement.

As shown in Table 3, also kaempferol is one of the most common bioactive flavonoids in both bee products. Along with quercetin, kaempferol is usually found in the human diet, showing many positive effects on human health. A recent study reported a decrease in necro-inflammatory and collagen accumulation after kaempferol injection into mice (Xu et al., 2019). Thus, kaempferol may be an effective agent in the treatment of common diseases such liver fibrosis. Concerning the absorption and excretion of kaempferol, DuPont, Day, Bennett, Mellon, and Kroon (2004) investigated it on four healthy men and four women. In the study, kaempferol showed a better absorption rate than quercetin, even at low doses, being the 3-glucuronide derivative the most dominant form of kaempferol in plasma.

On the other hand, lower molecular weight phenolic acids like gallic acid are more easily absorbed in the intestine than other phenolic compounds. Otherwise, some phenolic acids, such as hydroxycinnamic acid derivatives, which can be in the form of polymers, present a high resistance for penetration through the intestinal cells with LPH or CBG activity, limiting their absorption in the small intestine (Călinoiu & Vodnar, 2018). Studies on the digestibility and absorption of phenolic acids revealed that the strong bonds that linked these compounds to lipids, organic acids or sugars are broken by the intestinal microflora, contributing to their digestibility (Crozier et al., 2009; Marín, Miguélez, Villar, & Lombó, 2015; Rechner et al., 2001). Nevertheless, the esterification of chlorogenic acid and caffeic acid reduces the absorption of these phenolic acids, resulting their absorption from the microbial activities in the colon after hydrolysis with esterases (Manach, Williamson, Morand, Scalbert, & Rémésy, 2005). A study on the metabolites of chlorogenic acid, quercetin-3-*O*-rutinoside and black tea phenols was conducted by Olthof, Hollman, Buijsman, Van Amelsvoort, and Katan (2003) on 20 healthy people. They found that half of the chlorogenic acid and 43% of black tea phenols have been converted to hippuric acid, while quercetin-3-*O*-rutinoside was metabolized to phenylacetic acids (mostly 3-hydroxyphenylacetic acid). Also, traces of phenolic acids and their metabolites were found in the urine after the intake of chlorogenic acid and quercetin-3-*O*-rutinoside by volunteers without colon. These results clearly show that a significant portion of dietary polyphenols is hydrolyzed to different metabolites by the intestinal microflora.

7.2. Carotenoids

The bioavailability of dietary carotenoids depends on internal and external factors, resulting in different absorption values. Events such as pH change, enzymatic processes, or degradation of the pollen wall during the BP transformation into BB by natural fermentation will change the carotenoid content of BB and consequently its bioavailability. Furthermore, a low proportion of carotenoids have been reported to be bioaccessible (Carbonell-Capella et al., 2014). The dietary carotenoids release from these natural products follows the process of integration of gastric emulsions into lipid droplets. Then, as a result of the activity of bile salts released into the intestinal lumen, lipid droplets are transferred to mixed micelles. After the carotenoids dissolve in micelles, they are absorbed by the intestinal epithelial cells, packed into chylomicrons and introduced into the lymphatic system (Yonekura & Nagao, 2007). Each of these processes may restrict the bioavailability and absorption rate of carotenoids. The fat amount and type in the surroundings are other important factors affecting the bioavailability of carotenoids, with a minimum amount of fat required for absorption (Fernández-García et al., 2012). Hence, an oily matrix can significantly increase the absorption of carotenoids and may result in a higher bioavailability score (Carbonell-Capella et al., 2014).

There are no *in vitro* or *in vivo* studies on the digestion, bioavailability or absorption of dietary carotenoids in BP and BB, in the literature. But many studies have examined the lipid content of BP and BB in detail, revealing the amount and types of lipids (Bakour et al., 2019; Campos et al., 2008; Mayda et al., 2020; Tomás et al., 2017). Considering that carotenoids bioavailability depends significantly on lipid content, it is likely that both bee products may show a high level of bioaccessibility. However, it is clear that studies on the bioavailability level of carotenoids present in both bee products are needed.

7.3. Vitamins

Like carotenoids, vitamin E from natural sources such as BP and BB is

solubilized into micelles by bile salts and amphipathic lipids before access the lymphatic system (Rigotti, 2007). Many factors have an impact on the absorption of vitamin E, for example, bile acids and pancreatic fluid (Stahl et al., 2002). Also, lipids play an important role in the vitamin E absorption, depending it on its different types (Rigotti, 2007). Mărgă;oan et al. (2014) showed that medium-chain fatty acids present in BP such as caproic (6:0), caprylic (8:0), capric (10:0) and lauric (12:0) acids, make the vitamin E absorption more effective than long-chain fatty acids demonstrated in previous studies (Kuksis, Shaikh, & Hoffman, 1979).

For Vitamin C, a polar molecule with a relatively high molecular weight, the passage through the cell membrane by passive diffusion is not easy. Therefore, the flow of vitamin C in or out the cell is controlled by different mechanisms. After BP and BB are ingested, vitamin C enters the circulation through membrane proteins like facilitative glucose transporters and sodium vitamin C cotransporters in the small intestine (Y. Li & Schellhorn, 2007; Stahl et al., 2002). On the other hand, due to the resistant pollen wall of the BP, the bioaccessibility can be affected if no digestion is observed while passing through the stomach and ileum (Yesiltas et al., 2014). This is partially valid for BB, because this bee product has an increased degree of digestibility by natural fermentation.

8. Food applications and safety status of bee pollen and bee bread

8.1. Legislation and food applications

Recently, with the reveal of the nutritional and therapeutic properties of BP and BB, expanding interest in these products has emerged. Following the interest, some regulations have been framed individually in many countries, especially regarding the use of BP. For example, Argentina (Artículo 785 - Res 1550, 12.12.90), Brazil (Legislation: Instrução Normativa n.3, de 19 de Janeiro de 2001), China (Legislation: NY 5137–2002 and GB/T 19330–2008), Poland (Legislation: PN-R-78893 “Obnoza pylkowe” -Polish legislation for bee-pollen) and Switzerland (Legislation: Swiss Food Manual: Pollen Bienenprodukte, BAG Swiss Federal Office for Public Health) are among the countries with high producing rates of BP and where related regulations have been made (Ghosh & Jung, 2017). At international level, aiming to harmonize internationally recognized criteria, the International Standard Organization, ISO, have recently established a working group within the sub-committee ISO/TC 35/SC 19, focused in pollen. These concerning regulations define the sensory requirements (color, taste and smell), physical and chemical indexes (moisture, ash, protein, pH, etc.), microbial limits but also packing and storage conditions. Generally, there are also no established standards concerning the safety and use of BP and even less regulation for BB.

BP and BB are usually marketed in their raw form. However, in the last years, with the increase in the supply of functionalized foods, studies have focused on developing new food products by mixing natural sources of bioactive compounds such as BP and BB, with the final goal of increasing the nutritional value of the food products and thus the positive effects on health, as well as food preservative activity.

Conte, Del Caro, Balestra, Piga, and Fadda (2018) determined the physicochemical and sensory properties of gluten-free bread enriched with polyfloral BP at 1, 2, 3, 4 and 5%, thus emphasizing that this bread may be placed in the gluten-free products market against the health problems caused by gluten. Krystyjan, Gumul, Ziobro, and Korus (2015) added BP to biscuits to show their potential as dietary supplements and verify that there was no change in the fat content of the biscuits, while there was a significant increase in the content of sugar, protein, fiber, polyphenols and antioxidant potential of biscuits. In a similar study on bakery products, different rates (16% and 32%) of BP were mixed with wheat flour to produce cookies. Besides the nutritional, technological and sensory properties of cookies, antioxidant activity was highly linked to the percentage of added pollen (Solgajová, Nôžková, & Kadáková, 2014). In addition, Anjos, Fernandes, et al. (2019) and Turhan, Sariçaoglu, Mortas, Yazici, and Genccelep (2017) demonstrated that BP can be used as a natural antioxidant in meat products, playing a role as anti-lipid oxidation and antimicrobial agent, thereby enabling to extend the shelf life in meat products. Moreover, Yerlikaya (2014) added BP to fermented milk and reported that BP had a positive effect on probiotic viability with no negative effect on the physicochemical properties of fermented milk.

8.2. Risk in consumption

BP and BB are natural products of plant origin mainly sold for humans as food supplements, nevertheless there are some concerns about its use for dietary purposes. At the top of these concerns is anxiety that it causes allergic reactions. Normally BP and BB are well tolerated by humans (Bogdanov, 2011), however, there have been reports of some allergic reactions caused by BP, including anaphylaxis and also people suffering from hay fever (Greenberger & Flais, 2001; Jagdis & Sussman, 2012). Excluding those people with hay fever, the allergic reactions to those that consume BP is low, with ratios similar to other foods. In a survey of BP allergy in Polish beekeepers and their families, only 2 out of 493 beekeepers received negative reactions after pollen intake and only 22 cases of BP intolerance were seen from the customers of beekeepers, with 0.6% of BP allergy occurred in family members of beekeepers (Basista, Filipek, & Sodzawiczny, 2012). More importantly, to this date, there have been no report of serious health problems or deaths due to the use and consumption of bee products, especially BP and BB.

Other factor of risk in this bee products, are the concerns about bacterial contaminants, fungal toxins, or heavy metals and pesticides, which may have a negative impact on health. Collection, processing, or storage conditions of BP and BB in unhygienic conditions can provide a suitable environment for microbial growth. The consumption of fresh BP is not generally recommended, yet dry BP is known to be microbiologically safe (Mauriello, De Prisco, Di Prisco, La Storia, & Caprio, 2017). The status for BB is different because it is a natural fermented product with a lower pH and a higher lactic acid content compared to BP, which enables higher resistance to possible microbial contaminations (Khalifa et al., 2020).

Pesticides and heavy metals are among the main pollutants in BP and BB, coming from the environment and from agricultural practices (de Oliveira, do Nascimento Queiroz, da Luz, Porto, & Rath, 2016). Researches on BP and BB samples obtained in different geographical regions around the globe described pesticide residues at different levels in both bee products (de Oliveira et al., 2016). Around two hundred samples of BP and BB obtained from different apiaries and in different seasons across China were tested for pesticide residues with different types of pesticides detected at different concentrations, with the higher contamination found in BP (Tong et al., 2018). A similar study in Luxemburg enable also the detection of more than one hundred pesticides residues in BP (Beyer et al., 2018), but similar occurrences were also reported in North and South America, Asia and Europe (de Oliveira et al., 2016; Mullin et al., 2010; Roszko, Kamińska, Szymczyk, & Jędrzejczak, 2016). More important, pesticides are known to cause negative effects not only in human health (dermatological, neurological, carcinogenic, respiratory, and reproductive systems) (Nicolopoulou-Stamati, Maipas, Kotampasi, Stamatis, & Hens, 2016), but also in honey bees even at sub-lethal dosage (Pettis, Johnson, & Dively, 2012). Concerning the presence of heavy metals, the study conducted by Dinkov and Stratev (2016), identified the presence of lead and cadmium in BP, which was corroborated by several other studies in BP and BB (Harmanescu, Bordean, & Gergen, 2007; Zhelyazkova, 2018), but in general with values below the maximum residue limit. However, the risk of BP and BB consumption in terms of microbiological and environmental contaminants is present, it is not at a level that can affect human health considering the reported studies.

9. Future perspective and conclusion

Concerns over synthetic food additives and consumer demand for a more balanced and healthy diet may have triggered the acceleration of studies on natural products like BP and BB over the past decade. Therefore, researchers are making an effort to reveal its nutritional value and health-promoting properties. However, the amount of studies addressing the mechanisms of interaction of BP and BB constituents with the human body and its link with the medical and pharmacological action is still scarce. In the future, to meet this demand in the and to expand the field of technological application of these two bee products, some points should be taken in account: i) research and classification of nutritional and biological activities based on botanical and geographical origin, ii) BP and BB standardization using techniques with higher accuracy and precision, and internationally recognized, iii) developing innovative approaches to increase the bioavailability, especially for BP, and iv) focused studies on the transformation and absorption/assimilation in the digestive system following the ingestion, and their bioactivity, will greatly contribute to the development of both bee products.

In brief, BP and BB present a variety of dietary phytochemical compounds with functional properties such as carotenoids, vitamins, phenolic acids and especially flavonoids. Therefore, considering the food industry and the positive effects on human health, these bee products, which have tremendous potential for the production and use as natural and functional ingredients, offer a wide field of study.

Funding

The authors are grateful to the Foundation for Science and Technology (FCT, Portugal) for financial support, through national funds FCT/MCTES, to CIMO (UIDB/00690/2020). Thanks to the Programa Apícola Nacional 2020–2022 (National Beekeeping Program) for funding the project "NormBee-Standardization of production procedures and quality parameters of bee products" and to Project PDR2020–1.0.1-FEADER-031734: "DivInA-Diversification and Innovation on Beekeeping Production". National funding by FCT- Foundation for Science and Technology, through the institutional scientific employment program-contract with Soraia I. Falcão.

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