

Review

A narrative review on the physicochemical profiles, bioactive compounds, and therapeutic potentials of stingless bee honey

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Abstract

Stingless bee honey (SBH) is an intriguing type of honey produced by various genera of stingless bees. SBH has traditionally been used for its reputed therapeutic properties; yet scientific exploration on this honey remained less widespread compared to other types. This review aims to report recent physiochemical and phytochemical properties of SBH across various species and geographical origins. This review also aims to delve into the therapeutic potential of SBH, with a specific focus on its antioxidant, antibacterial, anticancer, and antidiabetic properties. By examining various studies on the medicinal attributes of SBH, this paper offers compelling evidence of its efficacy in treating diverse conditions, such as infections, inflammation, and many more. Furthermore, the distinctive composition of SBH was explored in detail, shedding light on its contribution to its remarkable medicinal characteristics. Ultimately, this review underscores the promising therapeutic potential of SBH and advocates further research to comprehensively comprehend its medicinal properties and unlock its potential for various medical applications.

Keywords Stingless bee honey · Phenolic compound · Flavonoid · Antioxidant

Abbreviations

| | |
|-------------------------------|-----------------------------------|
| AKT | Protein kinase B |
| BDNF | Brain-derived neurotrophic factor |
| BMM | Bone marrow-derived macrophages |
| CA | Caffeic acid |
| COX-2 | Cyclooxygenase-2 |
| DNA | Deoxyribonucleic acid |
| DPPH | 2,2-Diphenyl-1-picrylhydrazyl |
| FRAP | Ferric reducing antioxidant power |
| GAE | Gallic acid |
| GI | Glycaemic Index |
| GLUT4 | Glucose transporter type 4 |
| H ₂ O ₂ | Hydrogen peroxide |
| HCHF | High-carbohydrate high-fructose |

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| | |
|---------------|----------------------------------------------------|
| HFD | High fat diet |
| HMF | Hydroxymethylfurfural |
| LPS | Lipopolysaccharide |
| MAPK | Mitogen-activated protein kinase |
| MBC | Minimum bactericidal concentration |
| MIC | Minimum inhibitory concentration |
| MMP-1 | Matrix metalloproteinase-1 |
| NHDF | Normal human dermal fibroblast |
| NO | Nitric oxide |
| OSCC | Oral squamous cell carcinoma |
| RANKL | Receptor activator of nuclear factor-kb ligand |
| ROS | Reactive oxygen species |
| SAM | Salicylic acid microcapsules |
| SBH | Stingless bee honey |
| STAT3 | Signal transducer and activator of transcription 3 |
| T2DM | Type-2 diabetes mellitus |
| TFC | Total flavonoid content |
| TNF- α | Tumour necrosis factor- α |
| TPC | Total phenolic content |
| TRAIL | TNF-related apoptosis-inducing ligand |

1 Introduction

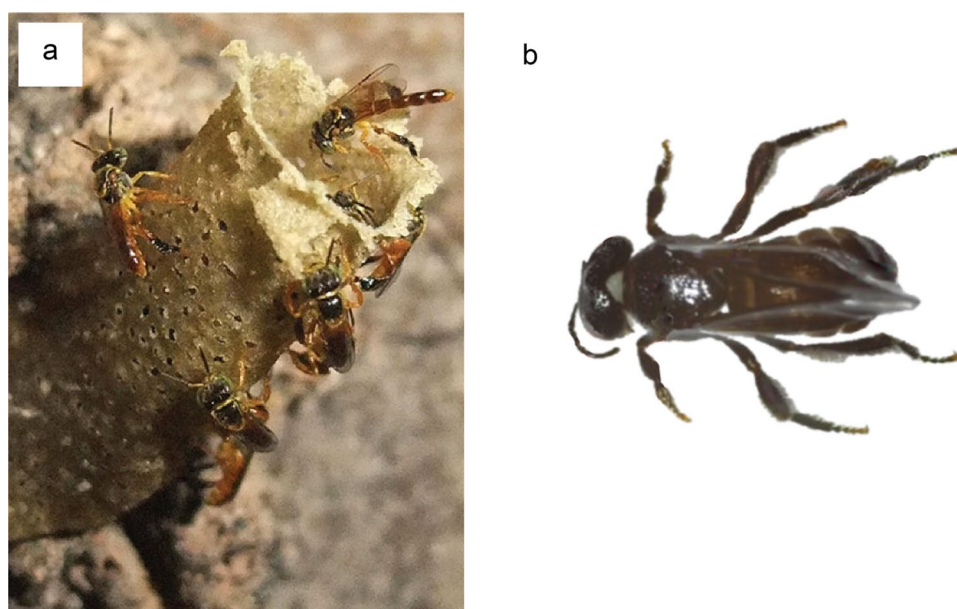
Honey produced by stingless bees, also known as meliponines, comes from the most abundant group of eusocial bees within the family Apidae and the tribe Meliponini. Although stingless bees and honey bees both belong to the family Hymenoptera, they differ at the subfamily level: honey bees are part of the *Apis* subfamily, whereas stingless bees belong to the *Meliponinae* subfamily. These fascinating bees are widely distributed across the Neotropical, Afrotropical, and Indo-Australian regions [1]. In particular, the genus *Melipona* composed a significant number of species, surpassing the common honey bee (*Apis mellifera* Linnaeus) [1, 2]. However, because of their predominantly tropical habitats, stingless bees have received less research interest than their relatives, bumble bees (*Bombini*), and honeybees (*Apini*) [3]. Additionally, their lower honey yield compared to honeybees make them less economically appealing to humans [4, 5].

Stingless bee honey (SBH) is a distinctive natural product that sets itself apart from *A. mellifera* bees honey in terms of chemical composition [6]. Currently, around 600 species of stingless bees have been discovered [3], with ongoing discoveries of new genera, subgenera, and species occurring annually. Stingless bees comprise of multiple genera, including *Melipona*, *Scaptotrigona*, and *Trigona* [7]. Among these *Melipona* and *Trigona* are the most domesticated worldwide, while approximately 100 species remain unstudied [1]. The Indo-Australian region alone is home to 89 species from 15 genera of stingless bees [8]. In Malaysia, approximately 35 stingless bee species have been documented [9] with commercially reared species, including *Geniotrigona thoracica*, *Heterotrigona itama*, *Lepidotrigona terminata*, and *Tetragonula laeviceps* [10]. There are a variety of names by which SBH is referred to in different geographical regions, such as “kelulut” in Malay, Malaysia; “klanceng” in Java; “emmu” in Sulawesi; “lukut” in Tagalog, Philippines; and “damar” in Hindi, India [11, 12].

Stingless bees can be distinguished from other bee species by their unique physical characteristics such as the absence or lack of submarginal cross veins and a second recurrent vein in the forewing [1]. In addition, they are relatively smaller than those of honeybees (*Apis*) and lack a stinger [13]. These bees construct their nests in the form of spherical pots made of cerumen, which is why their honey is often referred to as pot honey [14] (see Fig. 1). Additionally, it has a distinct sweetness combined with an acidic and sour flavour [15]. SBH can range from light amber to amber brown, and darker shades have higher ash values than lighter shades [16, 17]. Comparatively, SBH has been observed to be darker in colour than honey produced by honey bees [18]. The variation in colour is influenced by factors such as moisture content, saccharides, minerals, pollen, and polyphenolic compounds [19].

The United States Standards for Grades of Extracted Honey, 1985 [20] specify that the colour of extracted honey is not regarded as a criterion for determining quality in colour grade designations. However, studies have highlighted the potential significance of honey colour in variety of honey samples. Investigations have indicated that darker honey samples are associated with higher pH values, more mineral content, and increased phenolic content, which contribute to

Fig. 1 Stingless bees. **a** *Tetragonisca angustula* (Figure adopted from Lavinás et al. [36]), **b** *Heterotrigona itama* (Figure adopted from Saiful-lizan et al. [37])



enhanced antioxidant activities [21–24]. The colour of honey influences its flavour, with darker varieties typically having a sweeter taste and being regarded as higher quality due to their greater mineral and sugar content [25, 26].

SBH has traditionally been used due to its reputed therapeutic properties, including to treat respiratory conditions, infections, gastrointestinal disorders, sore throat, wounds as well as its deworming effects [27, 28]. Several studies have also emphasized its antimicrobial [29], antidiabetic properties [30, 31], anticancer [32], and antioxidant activities [33, 34], among other beneficial effects. These medicinal benefits are attributed to the polyphenols present in SBH. As previously reported by Biluca et al. [15] and Kek et al. [7], SBH have higher polyphenol content than other honey types. This is attributed to the bees' smaller body size, which allows them to access a wider range of flowers, including smaller blossoms, thereby enhancing their foraging diversity. However, this can also be a drawback, as smaller foragers have significantly shorter maximum foraging and recruitment distances [35]. Multiple other variables, including geographical location, nectar sources, collection season, storage, and processing, may have an influence on the variations in phenolic content between various honey samples [7].

Honey, including SBH, is highly exploited in apitherapy to treat various ailments, improve health, and enhance overall well-being. Recently, scientific research on the diverse therapeutic properties of SBH has attracted significant interest. The growing interest in SBH not only has the potential to benefit the meliponiculture industry financially but also encourages further investigation into its purported medicinal properties, ultimately contributing to the conservation and survival of stingless bees.

2 Method of review

Extensive exploration of online databases, including Google Scholar, Wiley Online Library, Scopus, ScienceDirect, ACS Publications, Web of Science, PubMed, Springer Link, Nature Communications, and PLoS One, was conducted to gather relevant literature. The search employed specific keywords such as "stingless bee honey", "stingless bee species", "pot honey", "kelulut", "phytochemical properties of stingless bee honey", "physicochemical properties of stingless bee honey", "sugar profiles", "trehalulose", "therapeutic properties", "medicinal values", "flavonoids", "phenolic acids", "phenolic compounds", "antioxidant", "oxidative stress", "anti-bacterial", "anti-cancer", "anti-microbial", "anti-inflammatory", "anti-diabetic", "inflammation", "bioactive compounds", and "nutritional composition". Snowball referencing was also done from relevant articles obtained from the search results. Articles that reported other products of stingless bee like bee bread, propolis and etc. were excluded. Relevant literatures published prior to January 2025 were collected, curated, and critically evaluated to extract essential information for the review.

3 Physicochemical characteristics of stingless bee honey

Earlier studies have reported the physicochemical characteristics of SBH [38, 39]. It is well-established that the bee species and botanical sources significantly influence the physicochemical properties, organic acid content, and antioxidant properties of honey [40]. Compared to honeybee honey, SBH generally exhibits higher moisture, ash content, and free acidity levels, whereas its pH and total soluble solid content are typically lower [18, 41, 42]. Similarly, Chuttong et al. [39] reported that SBH samples from 11 native Southeast Asian stingless bee species exhibited pH values ranging from 3 to 5. The low pH and high acidity of SBH contribute to its extended shelf life by inhibiting microbial growth, thereby enhancing its medicinal potential [43]. The elevated water content in SBH can lead to chemical instability during storage and encourage microbial proliferation, particularly yeast [39, 41, 44] thus requires careful handling and storage practices. However, study also mentioned that, this does not appear to compromise the overall quality of honey [45].

To inhibit the microbial growth in honey, the application of thermal treatment should be considered. Previous study has shown that exposing honey samples to thermal treatment effectively reduces microbial load without compromising the quality or unique characteristics of the honey [46]. Furthermore, heat treatments have been shown to have no significant impact on the total phenolic and flavonoid contents or antioxidant activities in most honey samples. However, consistent reduction of antibacterial activities was observed [47]. This reduction is possibly influenced by the degradation of heat-sensitive components in SBH, such as amino acids, enzymes, and organic acids. Despite this, thermal treatment remains a viable alternative preservation method for honey, enabling its conservation while minimizing potential alterations.

SBH primarily consists of monosaccharides, with fructose and glucose being the predominant sugars [48]. Several studies have quantified the concentration of these reducing sugars, with values differing across species and geographical origins. Some reports indicated that the total sugar content falls below the standards established by the Codex Alimentarius Commission for honey [39, 49]. According to this standard, pure honey must contain more than 60 g of total glucose and fructose per 100 g, while sucrose should not exceed 5 g per 100 g [50]. The reference values set by Codex Alimentarius for moisture, pH, free acidity, and sugar content do not account for the naturally higher moisture content, lower pH, higher free acidity, and distinct sugar composition of SBH, as highlighted in numerous studies [51].

In addition to monosaccharides, researchers have recently discovered a rare natural disaccharide, trehalulose, in SBH samples. Notably, a study by Fletcher et al. [11] identified the disaccharide trehalulose as a significant component of SBH from Malaysia, Australia, and Brazil. Additionally, another study confirmed the presence of trehalulose in all analysed Malaysian *H. itama* samples [52]. Furthermore, a study reported that honey produced by *Geniotrigona thoracica* contained significantly higher levels of trehalulose compared to other species examined, including *H. itama*, *Tetragonula carbonaria*, and *Tetragonula hockingsi* [51]. In contrary, one study reported that trehalulose was either not detected or present in very low quantities in Malaysian SBH samples from *H. itama* and *G. thoracica*, despite being analysed using ^{13}C nuclear magnetic resonance spectroscopy [53].

Trehalulose is produced through the enzymatic isomerization of sucrose. A study examining this process incubated sucrose solutions with macerated body parts (head, thorax, and abdomen) of the stingless bee (*T. carbonaria*). While both the head and thorax extracts contained the enzyme necessary for sucrose-to-trehalulose conversion, the head exhibited greater efficiency in producing trehalulose [54]. Other study on the origin of trehalulose reported that when stingless bees were experimentally fed with glucose and fructose mixtures, trehalulose were not detected in honey [55]. This justified that stingless bees with natural access to floral nectar high in sucrose will produce honey high in trehalulose, with its associated beneficial properties.

Trehalulose, a naturally occurring isomer of sucrose [56], releases monosaccharides into circulation at a significantly slower rate compared to sucrose [11]. It has a relative sweetness of approximately 70% compared to sucrose [57] and does not cause a sudden spike in blood glucose levels owing to its low insulinemic and glycaemic indices [58, 59]. This is especially important for diabetes management. The presence of trehalulose, as a key SBH component, is therefore a likely contributor to health benefits associated to this type of honey. Trehalulose is particularly noteworthy for its non/low-cariogenic properties, meaning it does not contribute to tooth decay. This has been demonstrated in rat models infected with oral bacteria (*Streptococcus mutans* and *Streptococcus sobrinus*), as these bacteria are unable to effectively metabolize trehalulose [60], thus preventing tooth decay. Additionally, trehalulose possesses antioxidant activity and is commonly added to human and animal food products to enhance the shelf life and aging stability [61, 62] all of which indirectly contribute to the therapeutic potential of SBH.

Other components, including enzymes, proteins, organic acids, minerals, pollen grains, and phytochemicals were also presented in the SBH samples [63, 64]. Furthermore, prior investigation on SBH samples from nine different species of stingless bees identified 16 free amino acids, including phenylalanine (5.20–1231 mg kg⁻¹) and proline (12.1–762 mg kg⁻¹) being the most significant [65]. Amino acids are essential components of food because they serve as the basis for the synthesis of proteins, improve food flavours, and act as precursors to aromatic compounds [66].

Despite the growing interest in SBH, a globally standardized method for characterizing stingless bee products has yet to be established. In 2017, the Department of Malaysian Standards introduced the initial Malaysian quality standards to oversee the trade and distribution of SBH. According to these Malaysian Standards, superior stingless bee honey should possess the following characteristics: moisture content not exceeding 35 g/100 g, a combined fructose and glucose content not surpassing 85 g/100 g, sucrose content not exceeding 7.5 g/100 g, maltose content not exceeding 9.5 g/100 g, ash content not exceeding 1.0 g/100 g, Hydroxymethylfurfural (HMF) content not exceeding 30 mg/kg, pH levels falling within the range of 2.5 to 3.8, and it should naturally contain plant phenolic compounds [67]. These standards outline several requirements for ensuring high-quality SBH. Table 1 summarises the physicochemical properties of honey from multiple species of stingless bee.

4 Phytochemical properties of stingless bee honey

The therapeutic potential of honey is largely attributed to its synergistic effects of its components, including polyphenols and other secondary plant compounds, enzymes, ascorbic acid, Maillard reaction products, carotenoid-like substances, organic acids, amino acids, and proteins [72–74]. Phenolic compounds, such as flavonoids and phenolic acids, are particularly important and are further classified based on their basic structures. They include simple phenols, phenolic acids, coumarins, isocoumarins, naphthoquinones, xanthenes, stilbenes, anthraquinones, flavonoids, and lignins [75]. Polyphenols have gained significant attention in medical and nutritional studies thanks to their valuable characteristics. They not only act as free radical scavengers but also exhibit immunomodulatory effects and can inhibit hormonal reactions [76]. Polyphenols are known for their strong peroxy radical scavenging activity, which is attributed to the high mobility of hydrogen atoms in their molecular structures [77].

Various factors, including the type of flowers from which the nectar originates, the surrounding environment and weather conditions, and the specific species of stingless bees engaged in the honey-making process, significantly affect the physicochemical properties of honey [78]. SBH is believed to contain a higher polyphenol content than other varieties of honey, as the small body size of stingless bees enables them to access various flowers and collect a diverse range of bioactive compounds for the honey pot [7, 15].

The antioxidant capacity and phenolic profile of SBH were first reported by Ranneh and colleagues [79]. Liquid chromatography–tandem mass spectrometry analysis of SBH revealed several potential phenolic compounds including gallic acid, caffeic acid, chrysin, cinnamic acid, 2-hydroxycinnamic acid, kaempferol, *p*-coumaric acid, catechin, quercetin-3-O-rutinoside, caffeic acid phenethyl ester, and 4-hydroxybenzoic acid [80]. Additionally, other studies have identified compounds such as quercetin 3,4'-dimethyl ether, pachypodol, jaceoside, irigenin trimethyl ether, corymboside, chrysoeriol 7-neohesperidoside, and corymboside in SBH [81]. Some of the commonly reported significant compounds in SBH include gallic acid, salicylic acid, *p*-coumaric acid, kaempferol, naringin, luteolin, catechin, apigenin, and taxifolin [15, 34, 82, 83].

Although the investigation of polyphenols and their potential medical applications is gaining momentum, the precise molecular mechanisms underlying their effects on human health are still incompletely understood. Researchers continue to explore the diverse compounds within the polyphenol group to elucidate the interactions of these compounds with molecular targets and to decipher the intricate pathways through which such compounds exert therapeutic effects against various diseases. Advancing our understanding of the molecular mechanisms of polyphenols is crucial for developing targeted interventions and utilising natural compounds for therapeutic purposes.

5 Antioxidative stress

Oxidative stress, characterised by a physiological imbalance between reactive oxygen species (ROS) production and the body's antioxidants defence, is associated with various chronic diseases, including cardiovascular disease, melanoma, and neurodegenerative disorders [84]. Natural sources rich in antioxidants are crucial in counteracting these

Table 1 Physicochemical properties of honey from various species of stingless bee

| Parameters | References | | | | | | | |
|-------------------------------|------------------------------|----------------------|------------------------------|------------------------------|-------------------------------|----------------------------|--------------------|------------------------------|
| | Mello dos Santos et al. [68] | Chuttong et al. [39] | Hasali et al. [69] | Abu Bakar et al. [70] | Shamsudin et al. [40] | dos Santos et al. [71] | Zawawi et al. [51] | Ng et al. [53] |
| Moisture % (w/w) | 24.9 ± 0.00 to 29.9 ± 0.92 | 28–47 | 21.32 ± 1.60 to 31.67 ± 1.50 | 26.50 ± 0.00 to 31.80 ± 0.00 | 19.49 ± 0.70 to 33.93 ± 1.05 | 29.6 ± 0.2 to 40.1 ± 0.3 | 23.75 to 31.01 | 22.50 ± 0 to 28.00 ± 0 |
| Free acidity (mEq/kg) | NA | 25–550 | NA | NA | 64.50 ± 4.00 to 207.67 ± 3.30 | 37.8 ± 1.0 to 123.0 ± 1.0 | 17.0 to 336.2 | 60.67 ± 0.58–95.33 ± 0.58 |
| pH | 3.69 ± 0.00 to 5.90 ± 0.91 | 3.1–3.9 | 3.00 ± 0.05 to 3.05 ± 0.05 | 3.24 ± 0.01 to 3.42 ± 0.01 | 3.17 ± 0.00 to 3.40 ± 0.07 | 3.37 ± 0.08 to 3.92 ± 0.02 | 2.86 to 3.88 | 3.17 ± 0.02 to 3.54 ± 0.01 |
| 5-HMF (mg/kg) | NA | 0.26–46 | NA | NA | 0.11 ± 0.04 to 0.14 ± 0.08 | NA | NA | 11.45 ± 0.37 to 27.10 ± 0.92 |
| Electric conductivity (mS/cm) | 1.24 ± 0.23 to 2.15 ± 0.00 | 0.33–3.1 | NA | NA | NA | 0.20 ± 0.00–0.71 ± 0.00 | 0.23–0.77 | 0.28 ± 0–0.52 ± 0 |
| Diastase activity (un. Göthe) | NA | 0.150–4.9 | NA | NA | NA | NA | NA | 1.83 ± 0.15 to 3.04 ± 0.08 |
| Soluble solids (°Brix) | 70.2 ± 0.92 to 75.1 ± 0.00 | NA | NA | NA | 60.85 ± 0.07 to 72.25 ± 0.92 | NA | NA | 72.00 ± 0 to 77.50 ± 0 |
| Total sugar (g/100 g) | NA | 11 to 68 ± 3.2 | NA | NA | 44.98 ± 1.75 to 61.37 ± 0.63 | 44.7 ± 0.4 to 79 ± 1.1 | 42.3 to 72.5 | 35.36 ± 0.76 to 35.39 ± 0.20 |
| Fructose (g/100 g) | 7.79 to 33.4 | 6 to 17 ± 9.7 | NA | NA | 7.89 ± 0.36 to 13.58 ± 0.33 | 26.2 ± 0.4 to 46.5 ± 0.6 | 0.69 to 25.01 | 37.61 ± 0.20 to 38.25 ± 0.21 |
| Glucose (g/100 g) | 3.36 to 26.8 | 4.1–28 | NA | NA | 6.95 ± 0.34 to 11.69 ± 0.56 | 16.2 ± 0.1 to 30.5 ± 0.1 | 2.12 to 16.91 | NA |
| Sucrose (g/100 g) | NA | 0.03 ± 0.02 to 6 | NA | NA | NA | NA | NA | 0.40 ± 0.57 |
| Maltose (g/100 g) | NA | 37 ± 12 to 53 | NA | NA | 28.96 ± 1.17 to 43.15 ± 2.36 | NA | NA | NA |
| Trehalulose (g/100 g) | 10.0 ± 4.2 to 30.7 ± 5.0 | NA | NA | NA | NA | NA | 17.8 to 57.0 | NA |
| F/G | 1.22 to 2.56 | NA | NA | NA | 0.83 ± 0.002 to 1.56 ± 0.07 | 1.32 ± 0.03 to 1.80 ± 0.02 | NA | 1.06 ± 0.01 to 1.08 ± 0.03 |
| G/W | NA | NAA | NA | NA | 0.24 ± 0.03 to 0.53 ± 0.01 | NA | NA | 1.31 ± 0.01 to 1.38 ± 0.03 |
| Ash content (g/100 g) | NA | 0.22 ± 0.08 to 3.1 | 0.04 ± 0.01 to 0.19 ± 0.01 | 0.15 ± 0.01 to 0.67 ± 0.00 | 0.07 ± 0.007 to 0.24 ± 0.01 | NA | 0.05 to 0.364 | 0.04 ± 0 to 0.18 ± 0.01 |
| Protein (%) | NA | NA | 0.34 ± 0.03 to 0.69 ± 0.03 | 0.096 ± 0.08 to 0.31 ± 0.11 | NA | NA | NA | NA |
| Fat (%) | NA | NA | 0 | 0.03 ± 0.00 to 0.73 ± 0.00 | NA | NA | NA | NA |
| Carbohydrate (%) | NA | NA | 67.03 ± 1.52 to 77.58 ± 1.59 | 67.20 ± 0.11 to 73.01 ± 0.35 | NA | NA | NA | NA |

Table 1 (continued)

| Parameters | References | | | | | | | |
|---------------------|--------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| | Mello dos Santos et al. [68] | Chuttong et al. [39] | Hasali et al. [69] | Abu Bakar et al. [70] | Shamsudin et al. [40] | dos Santos et al. [71] | Zawawi et al. [51] | Ng et al. [53] |
| Energy (kcal/100 g) | NA | NA | 276 ± 0.06 to 317 ± 0.06 | NA | NA | NA | NA | NA |
| TFC (mg QE/100 g) | NA | NA | NA | *53.81 ± 4.12 to 549.05 ± 9.74 | 2.38 ± 0.20 to 9.31 ± 0.10 | NA | NA | NA |
| TPC (mg GAE/100 g) | 22.1 ± 2.94 to 63.8 ± 1.44 | NA | NA | #357.14 ± 3.57 to 520.83 ± 4.49 | 27.33 ± 0.83 to 55.86 ± 2.40 | NA | 223.4 to 1321.3 | 56.78 ± 2.24 to 120.06 ± 1.29 |
| FRAP (mmol Fe2+/kg) | 2.07 ± 0.78 to 9.10 ± 0.39 | NA | NA | NA | 53.80 ± 2.69 to 163.80 ± 1.84 | NA | NA | 1.33 ± 0.01 to 3.58 ± 0.31 |
| DPPH (mmol TE/kg) | 0.70 ± 0.53 to 6.67 ± 0.83 | NA | NA | 52.33 ± 0.07 to 97.30 ± 0.84 | NA | NA | NA | 31.56 ± 0.69 to 37.37 ± 1.50 |
| Country of origin | Australia | Thailand | Malaysia | Malaysia | Malaysia | Brazil | Malaysia and Australia | Malaysia |
| Honey species | <i>Tetragonula carbonaria</i> , <i>Tetragonula hockingsi</i> | <i>Homotrigona fimbriata</i> , <i>Lepidotrigona terminata</i> , <i>Lepidotrigona flavibasis</i> , <i>Lepidotrigona doipaensis</i> , <i>Lisotrigona furva</i> , <i>Tetragonilla colina</i> , <i>Tetragonula fuscobalteata</i> , <i>Tetragonula laeviceps</i> , <i>Tetragonula testaceitarsis</i> , <i>Tetrigona apicalis</i> , <i>Tetrigona melanoleuca</i> | <i>Heterotrigona itama</i> | <i>Heterotrigona itama</i> , <i>Geniotrigona thoracica</i> | <i>Heterotrigona itama</i> , <i>Geniotrigona thoracica</i> | <i>Melipona bicolor</i> , <i>Scaptotrigona bipunctata</i> , <i>Melipona quadrifasciata</i> , <i>Melipona marginata</i> | <i>Heterotrigona itama</i> , <i>Geniotrigona thoracica</i> , <i>Tetragonula carbonaria</i> , <i>Tetragonula hockingsi</i> | <i>Heterotrigona itama</i> , <i>Geniotrigona thoracica</i> |

5-HMF: 5-hydroxymethylfurfural; F/G: ratio of fructose and glucose content; G/W: glucose/water; TFC: total flavonoid content; TPC: total phenolic content; DPPH: 2,2-diphenyl-1-picrylhydrazyl; FRAP: ferric reducing antioxidant power; NA: not available

*Value expressed in mg rutin kg⁻¹ honey

#Value expressed in gallic acid kg⁻¹ honey

harmful species and reducing oxidative stress. SBH is a unique type of honey that stands out for its distinctive flavour and high antioxidant content. The antioxidant effects of SBH can be attributed to the high levels of polyphenols, flavonoids, and other antioxidant compounds. Phenolic compounds fight oxidative stress by acting as antioxidants, directly scavenging free radicals through their chemical structure, which allows them to donate hydrogen atoms to stabilize the radicals, thereby preventing damage to cellular components like proteins, lipids, and deoxyribonucleic acid (DNA) [42, 85, 86]. The remarkable antioxidant and radical scavenging activity of SBH from *Dactylurina schmidtii* were documented by Mduda et al. [87]. The total phenolic content values recorded in this study exceeded those reported for SBH from Brazil [88] and Malaysia [49].

The antioxidant capacity of honey samples correlates with their biochemical constituents, such as total phenol and total flavonoid content, as well as the levels of water-soluble vitamins (vitamins B1, B2, B3, B9, B12, and vitamin C) [33]. These bioactive compounds, primarily polyphenols and flavonoids, are largely influenced by the origin of pollen and nectar [89] as well as the bee species [79]. Tuksitha et al. [90] conducted a study on *H. erythrogastra* and *H. itama* species from Borneo, revealing that their honey exhibited the highest DPPH radical-scavenging activity, as well as high protein and phenolic content, with mean values of 5.66 ± 1.00 and 17.67 ± 0.75 (mg/ml), respectively. Another study indicated that the DPPH antioxidant activity of honey from *T. laeviceps* is influenced by its geographical origin [91]. It was observed that honey with a darker colour generally possesses a higher total phenolic content (TPC) and total flavonoid content (TFC) than lighter-coloured honey [92], consequently exhibiting higher antioxidant activity. Correspondingly, Ferreira et al. [93] noted that darker honey displayed elevated levels of antioxidant agents such as flavonoids, ascorbic acid, and β -carotene, as opposed to lighter honey. A similar result was observed in *Melipona beecheii*, where darker honey contained higher levels of phenols and flavonoids, which in turn influenced its radical scavenging activity and overall antioxidant properties [94]. The timing of honey collection significantly affects its physical and chemical properties, as well as its antioxidant and antimicrobial activities. Honey harvested over an extended period exhibited exceptional antioxidant and antimicrobial effects [95].

The antioxidant activity of a substance is determined by the quantity and configuration of the hydroxyl groups in its molecular structure. Alvarez-Suarez et al. [96] examined five distinct monofloral varieties of Cuban honey, revealing a robust connection between the overall phenolic content and the outcomes of the oxygen radical absorbance capacity assay. The results suggested that phenolic compounds were instrumental in the antioxidant capacity of honey, although they were not the exclusive factors influencing it. Similarly, Chua et al. [33] examined three distinct Malaysian Tualang, Gelam, and Acacia honey. The study revealed a notable correlation between the total flavonoid content and the results of three different antioxidant assays, each utilising a distinct mechanism. These assays included the evaluation of free radical scavenging activity using the DPPH assay, FRAP assay, and β -carotene bleaching assay. These results further support the significance of total flavonoid content as an indicator of antioxidant activity in honey.

Honey treatment led to a significant increase in glutathione (GSH) levels and catalase (CAT) activity, along with a notable reduction in malondialdehyde (MDA) levels in the sleep-deprived group [97]. The elevation of antioxidant enzymes (GSH and CAT) and the decline in MDA levels contribute to enhancing brain oxidative status and alleviating oxidative stress in sleep-deprived rats. The remarkable antioxidant properties of honey can be attributed to its high phenol and flavonoid content. These bioactive compounds effectively scavenge free radicals and mitigate oxidative damage. While the precise mechanisms of action of antioxidants in SBH remain unclear, several potential pathways have been suggested. These include chelation of metal ions, inhibition of oxidative enzymes, and scavenging of reactive oxygen species. Furthermore, the presence of phytochemicals in SBH may enhance antioxidant activity through synergistic interactions with other antioxidants present in honey. Further research is necessary to gain a deeper understanding of the mechanisms by which antioxidants in SBH exert their effects and to evaluate their efficacy in human populations. Nevertheless, existing evidence suggests that SBH has the potential to serve as a valuable dietary supplement for individuals seeking protection against oxidative stress and associated diseases.

The polyphenols and flavonoids present in honey serve as potent antioxidants by neutralising reactive elements through oxidation, resulting in the formation of more stable and less reactive radicals [98]. These bioactive compounds play a crucial role in the antioxidant capacity of honey and contribute to its health promoting properties (Table 2). Among the various classes of phenolic compounds, a total of 16 phenolic acids, 19 flavonoids, and five additional phenolic compounds have been identified in SBHs at varying concentrations [99]. The commonly reported compounds include gallic acid, salicylic acid, p-coumaric acid, kaempferol, naringenin, luteolin, catechin, apigenin, and taxifolin [63, 100–102]. Figure 2 shows the major phenolic acids compounds in different types of SBH.

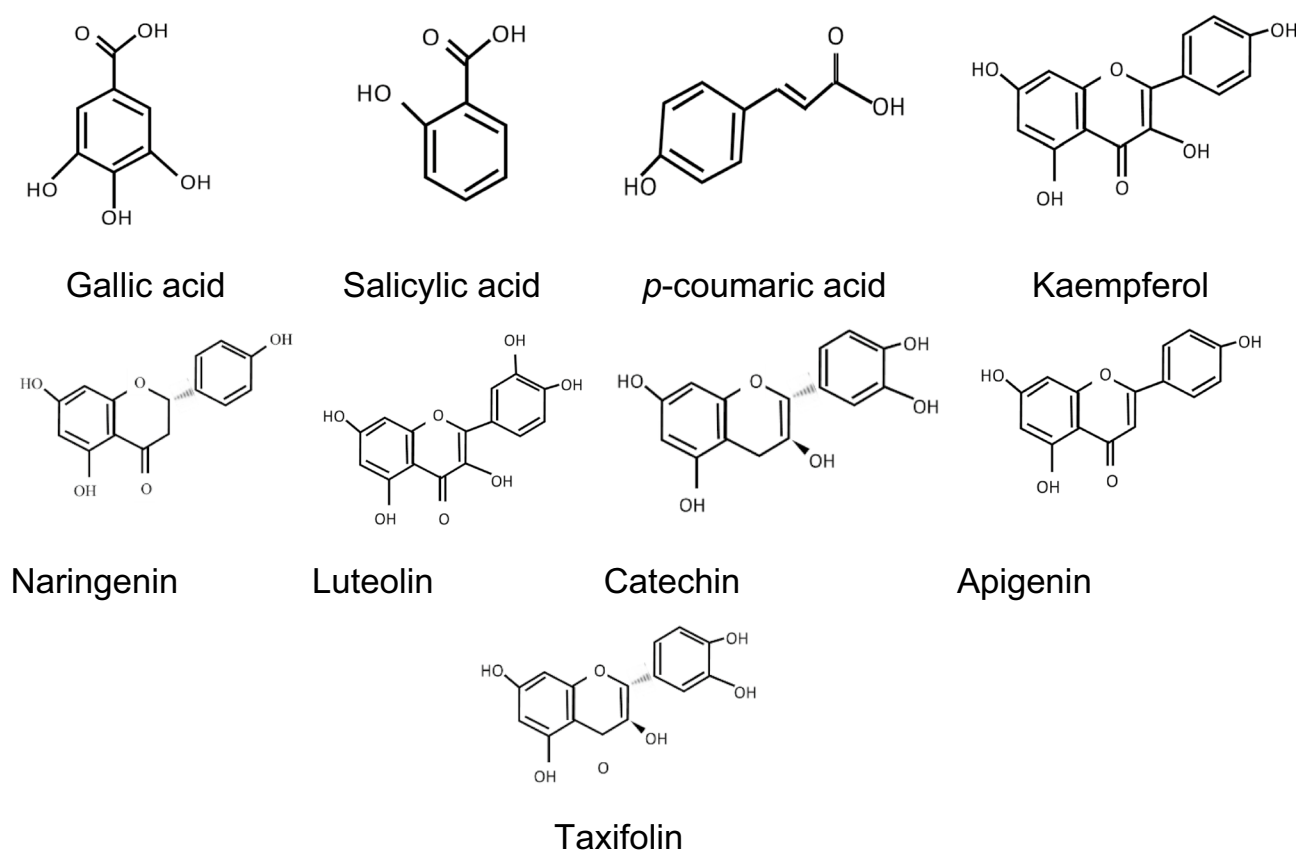


Fig. 2 Major phenolic acids in different types of SBH (Al-Hatamleh et al. [99])

6 Antibacterial

The antimicrobial activity of SBH can partially be attributed to its inherent acidity, as most bacteria thrive poorly in acidic environment. The high concentration of hydrogen ions (low pH) compromises the bacterial structure and function of essential proteins and cell membranes, resulting in cellular damage and ultimately leading to cell death [115]. However, there is little evidence of a link between the high antibacterial activity of SBH and its high acidity [4]. Other factor contributing to antimicrobial activity is the presence of hydrogen peroxide (H_2O_2) in honey, which is generated through glucose oxidation catalysed by glucose oxidase [116, 117]. Study reported a supplementation of bacterial cultures with H_2O_2 inhibited *E. coli* and *Bacillus subtilis* growth in a concentration-dependent manner by inducing oxidative damage causing bacterial growth inhibition and DNA degradation [117], though this process might be also modulated by other components in honey. The antimicrobial activity of SBH is also influenced by its phenolic compounds. This is supported by a study demonstrating that phenolic and protein extracts from *Melipona beecheii* honey exhibit antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* [118]. These factors, combined with its low pH and the presence of H_2O_2 , contribute to the multifaceted therapeutic potential of honey [119, 120].

Several studies have demonstrated that SBH exhibits stronger antibacterial activity than honey produced by *A. mellifera* [102, 121, 122]. A previous study reported that SBH exhibited higher antibacterial activity than Manuka honey, a widely recognised honey produced by *A. mellifera* [121]. The study demonstrated that SBH samples displayed non-peroxide antibacterial activity against *S. aureus*, *Enterococcus faecalis*, *E. coli*, and *Pseudomonas aeruginosa*. Another study also found that all SBH samples inhibited all tested bacterial isolates, whereas only four out of 23 honey bee honeys exhibited similar effectiveness, with *E. coli* being more susceptible than *S. aureus*. Notably, honeydew honey from *H. itama* demonstrated the strongest antibacterial effects, and exhibited synergistic effects when combined with antibiotics against clinical *E. coli* isolates [122]. Although phytochemicals contribute to the non-peroxide antibacterial activity of SBH, their precise mechanism of action remains unclear. Researchers have suggested that the presence of

Table 2 Phenolic compounds found in SBH and their therapeutic values

| Phenolic compounds | Model | Results | Therapeutic values | References |
|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|------------|
| Caffeic acid | Wistar rats fed with a HCHF diet | SBH and CA supplementation effectively counteracted hyperglycaemia and hypertension induced by the HCHF diet. Additionally, SBH reduced brain TNF-α levels while increasing BDNF levels | Antioxidant, anti-inflammatory | [103] |
| Kaempferol | Human cancer derived cell lines (ChaGo-I and KATO-III) | ChaGo-I cell line was sensitive to kaempferol at 10 µg/mL and KATO-III was sensitive to kaempferol and apigenin at the same concentration | Anti-cancer | [104] |
| Phenylalanine | Swiss albino mice | Treated mice exhibited significant improvements in spatial working and reference memory, with enhanced memory consolidation following prolonged supplementation. The study also reported significant upregulation of BDNF and Itpr1 genes and identified phenylalanine as a key precursor for tyrosine, which influences the BDNF receptor | Improves spatial memory | [105] |
| Quercetin | <i>Streptococcus mutans</i> , <i>Streptococcus sanguis</i> , <i>Streptococcus sobrinus</i> , <i>Actinomyces viscosus</i> , <i>Actinomyces naeslundii</i> , <i>Lactobacillus acidophilus</i> , <i>Porphyromonas gingivalis</i> , <i>Fusobacterium nucleatum</i> , <i>Actinobacillus actinomycetemcomitans</i> , <i>Prevotella intermedia</i> and <i>Candida albicans</i> | Quercetin had inhibitory effects on <i>S. mutans</i> , <i>S. sobrinus</i> , <i>L. acidophilus</i> , <i>S. sanguis</i> , <i>A. actinomycetemcomitans</i> , and <i>P. intermedia</i> | Antibacterial | [106] |
| Salicylic acid | <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> | Salicylic acid microcapsules (SAMS) displayed a potent MIC and MBC of 4 mg/mL. SAMS at 1/4 × MIC, 1/2 × MIC, and 1 × MIC effectively inhibited bacterial growth, with increased effectiveness at higher concentrations. At 1 × MIC, SAMS exhibited rapid bactericidal action, reducing the bacterial population by over 99.9% within 10 min causing the disruption of bacterial cell walls and membranes | Antibacterial | [107] |
| Catechin | Normal human dermal fibroblast | (-)-Catechin suppressed MMP-1 activity and prevented TNF-α-induced collagen degradation in NHDF. Its mechanism involved reducing ROS accumulation and inhibiting MAPK, AKT, and COX-2 activation. Additionally, (-)-catechin decreased the expression and secretion of proinflammatory cytokines | Anti-Skin Aging; Antioxidant | [108] |
| Apigenin | Primary effusion lymphoma | Apigenin induced cell death and autophagy in primary effusion lymphoma cells while reducing intracellular ROS levels. Its mechanism involved p53 activation, leading to increased catalase levels and STAT3 inhibition | Anticancer | [109] |

Table 2 (continued)

| Phenolic compounds | Model | Results | Therapeutic values | References |
|--------------------|---------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|------------|
| p-coumaric acid | HFD-induced diabetic rats | P-coumaric acid significantly lowered blood sugar levels, leading to reduced kidney weight and while increased overall body weight in T2DM rats. It also improved histopathological changes and reduced urea, creatinine, and uric acid levels. Additionally, its antioxidant properties mitigated lipid peroxidation and restored antioxidant enzyme activity induced by diabetes | Antidiabetic | [110] |
| Naringin | Human (ER-/PR-/HER2-) breast cancer | Naringin inhibits cell growth, induces apoptosis, and causes G1 cycle arrest by increasing p21 and decreasing survivin levels. It also suppresses the β -catenin signaling pathway, with β -catenin overexpression reversing its tumour-inhibiting effects. In MDA-MB-231-injected xenograft mice, naringin treatment enhanced p21 expression while reducing survivin and active β -catenin levels | Anti-cancer | [111] |
| Luteolin | Lung cancer xenograft mouse model | Luteolin enhances TRAIL-induced anticancer effects in lung cancer cells, significantly inhibiting tumour growth and promoting apoptotic cell death in xenograft models | Anti-cancer | [112] |
| Gallic acid | HFD fed male Wistar rats | Reduction of the perirenal adipose tissues and restored expression of insulin receptor and GLUT4 was observed | Anti-diabetic | [113] |
| Taxifolin | human bone marrow-derived macrophages | Taxifolin inhibits RANKL-induced osteoclast differentiation and function in human BMMs in a dose-dependent manner and prevents bone loss in a mouse model of LPS-induced bone lysis | Anti-inflammatory | [114] |

CA: caffeic acid; HCHF: high-carbohydrate high-fructose; TNF- α : tumour necrosis factor- α ; BDNF: brain-derived neurotrophic factor; SAM: salicylic acid microcapsule; MIC: minimum inhibitory concentration; MBC: minimum bactericidal concentration; NHDF: normal human dermal fibroblast; MAPK: mitogen-activated protein kinase; AKT: protein kinase B; COX-2: cyclooxygenase-2; MMP-1: matrix metalloproteinase-1; STAT3: signal transducer and activator of transcription 3; T2DM: type-2 diabetes mellitus; TRAIL: TNF-related apoptosis-inducing ligand; HFD: high fat diet; GLUT4: glucose transporter type 4; BMM: bone marrow-derived macrophages; RANKL: receptor activator of nuclear factor- κ B ligand; LPS: lipopolysaccharide

benzene ring substitutions and a saturated side chain play a key role in the antibacterial activity of SBH [90]. These structural features enhanced the membranolytic activity against pathogenic bacteria [123].

Nevertheless, an earlier study found no significant difference in the effectiveness of honey produced by *A. mellifera* and *Meliponinae* (*T. angustula*) against the five microorganisms examined: *P. aeruginosa*, *Bacillus cereus*, *Candida albicans*, *Saccharomyces cerevisiae*, and *S. aureus* [124]. Phenolic compounds, particularly flavonoids, are also responsible for the antimicrobial properties of honey, which vary based on the phytogeographic origin of the honey. Thus, the contradictory results of this study may be attributed to the phytogeographic regions in Costa Rica where the honey was sourced.

A past study reported significant antibiofilm activity of SBH against multidrug-resistant pathogens, demonstrating statistically significant log reductions in cell counts for most treated pathogens. Notably, substantial decreases in cell viability were observed for *Candida tropicalis* and *Klebsiella pneumoniae* strains. Scanning electron microscopy further revealed structural disruption of biofilms, highlighting the effectiveness of SBH in inhibiting biofilm formation [125]. In addition to its various antibacterial compounds, such as hydrogen peroxide, methylglyoxal, and phenolic compounds, which contribute to its antimicrobial activity [126], SBH possesses a high sugar content that creates a hyperosmotic environment. This osmotic effect draws water out of bacterial cells, leading to dehydration, metabolic disruption, and ultimately inhibiting bacterial growth and survival [125].

The native bacterial colony found in SBH exhibits strong potential as an antagonist against pathogenic microorganisms. The predominant bacterial genera associated with stingless bee colonies include *Bacillus*, *Streptomyces*, *Weissella* and *Lactobacillus* [127–131]. Rosli et al. [4] identified *Lactobacillus malefermentans*, commonly referred to as “good bacteria,” as the dominant bacterial species in Malaysian SBH samples. The antimicrobial properties of honey are partly attributed to the secretion of bacteriocins by these bacteria as part of their defence mechanism. Multiple studies suggested that bacteriocins may serve as viable alternatives to conventional antibacterial agents for the prevention and treatment of bacterial infections [132, 133]. The antimicrobial activity of bacteriocins has been reported against various pathogens, including *E. coli*, *Salmonella enterica*, and *C. albicans* [134]. A recent report further confirmed that ursoricin, a bacteriocin produced by *Streptococcus ursoris*, exhibits potent activity against methicillin-resistant *S. aureus* and vancomycin-resistant enterococci [135].

The antimicrobial effectiveness of honey can vary significantly, by more than 100 times, depending on factors such as its geographical origin, season, botanical source, health of bees, and conditions related to harvesting, processing, and storage [126, 136]. In Ghana, a clinical study documented that pure SBH of the species *Meliponula boncadei* at concentrations of more than 60% exhibited the strongest inhibition activity against all three isolated eye pathogens (*S. aureus*, *Staphylococcus epidermidis*, and *P. aeruginosa*) compared with eight standard antibiotics [137]. This study supports the claims of SBH in a traditional setting for treating a variety of infectious disorders caused by microorganisms. Mwangi et al. [138] and Keng et al. [139] reported consistent findings, demonstrating that Gram-positive isolates exhibited larger zones of inhibition compared to Gram-negative isolates. This may be credited to the thicker peptidoglycan layer in gram-positive bacteria, which makes them more susceptible to antibacterial agents, whereas gram-negative bacteria possess an outer membrane that provides additional resistance [140].

Recent finding revealed that SBH samples from *Tetragonisca fiebrigi* in Argentina exhibit antimicrobial activity, inhibiting both Gram-positive and Gram-negative bacteria with varying sensitivity levels. Particularly, samples exhibiting high bioactivity were found to exhibit crystallisation, which was positively associated with fungal development and the presence of flavonoids [81]. Further, result consistently showed that SBH derived from *Melipona flavolineata* exhibits antimicrobial properties in vitro against various types of bacteria, encompassing both Gram-positive and Gram-negative strains. This antimicrobial activity was observed not only against general bacterial species but also against strains isolated from bovine mastitis. Scanning electron microscopy revealed the detrimental effects of *M. flavolineata* honey on *S. aureus* cells and its inhibitory influence on cell division [141]. Furthermore, SBH from *Melipona favosa* and *Frieseomelitta nigra* in Tobago exhibited stronger inhibitory and bactericidal activities compared to honey derived from the European honeybee (*Apis mellifera*) and artificial honey (control) against common pathogens such as *S. aureus*, *E. coli*, *Streptococcus pyogenes*, and *Haemophilus influenzae* [142]. Although numerous studies have provided substantial evidences on the antibacterial activity of SBH, most findings are derived from in-vitro and in-vivo studies. The limited application in clinical settings highlights the need for further research to validate its therapeutic potential.

7 Chemo preventive properties of SBH

Chemoprevention refers to the use of natural or synthetic chemicals to stop, slow down, or prevent cancer growth [143]. Increasing evidences suggest that honey (not specific to SBH) has significant potential to be a valuable chemo preventive agent [144, 145]. Oxidative stress and inflammation are closely linked and play a significant role in the cancer pathogenesis. They serve as key contributors to tumour initiation, promotion, and progression through mechanisms such as DNA damage, cell proliferation, angiogenesis, and immune evasion. This interplay creates a vicious cycle in which chronic inflammation induces oxidative stress, which subsequently exacerbates inflammation, ultimately facilitating cancer development [146, 147]. To counteract this, cells employ various defence mechanisms, including radical scavengers such as glutathione, vitamins C and E, antioxidant enzymes such as catalase and superoxide dismutase, and intricate DNA repair mechanisms. The protective effect of SBH against oxidative DNA damage is likely due to its high phenolic content. The significant antioxidant and anti-inflammatory properties of SBH have been extensively documented [63, 101], suggesting that SBH may play a crucial role in mitigating oxidative damage. SBH may protect cells from H₂O₂-induced DNA damage through its potent reducing power and radical-scavenging activities [48, 148].

According to an in-vitro study, SBH may help prevent and treat multiple disorders linked to inflammation and oxidative stress. A study carried out by Ooi et al. [48] demonstrated that SBH pretreatment protected WIL2-NS cells from H₂O₂-induced cell death and DNA damage while also reducing nitric oxide (NO) production by inhibiting inducible nitric oxide synthase expression in lipopolysaccharide-induced RAW 264.7 cells. Nitric oxide synthase is an enzyme that produces NO from L-arginine [149]. NO serves as a key mediator of inflammation, exhibiting both pro- and anti-inflammatory effects depending on the concentration and site of action [150, 151]. However, the surplus of NO production can be harmful, potentially causing damage to surrounding tissues and contributing to the onset of various inflammatory diseases [150].

A prior study on Sprague–Dawley rats with induced colon cancer showed that oral administration of SBH at 1183 mg/kg body weight twice daily for eight weeks significantly reduced aberrant crypt foci, aberrant crypts, and crypt multiplicity, key biomarkers for colorectal cancer [152]. In another study, the most pronounced cytotoxic effect was observed following a 72-h period of honey treatment [153]. The study found that treating U-87MG glioma cells with honey led to nuclear shrinkage, chromatin condensation, and nuclear fragmentation, indicating apoptotic progress of the cells. The study further suggested that the anticancer effect of *H. itama* sp. honey on U-87 MG cells was attributed to its antioxidant capacity, which enabled honey to scavenge free radicals through its phenolic content (including benzoic acid, cinnamic acid, and *p*-coumaric acid) and flavonoids. As evidenced by a previous study, SBH exhibited cytotoxic activity against cervical cancer cell lines (HeLa) even at low concentrations [154]. However, the study also noted that honey bee honey demonstrated superior antioxidant capacity, anticancer potential, and phenolic content when compared to SBH, under similar environmental conditions.

Mahmood et al. [32] explored the chemo preventive potential of Malaysian SBH from *H. itama* species against oral squamous cell carcinoma (OSCC). The study yielded promising results, indicating that SBH could serve as an adjunct chemo preventive agent for OSCC. The findings revealed that a 0.84% dose of honey inhibited 50% of HSC-2 oral squamous cell carcinoma cell lines, while a 10% dose resulted in the highest inhibition. Further, another investigation with two breast cancer cell lines, MDA-MB-231 and MCF-7, discovered the cytotoxic activity of SBH, thereby promoting its chemo preventive potential [155]. The study proposed that the cytotoxic activity of SBH is due to its high concentration of total phenolic content, which acts as both an antioxidant and an anti-inflammatory agent. This finding emphasises the potential of SBH in cancer management and suggest its possible application as an alternative chemotherapeutic approach.

8 Anti-diabetic activity

Honey, in general, is a natural sweetener that has attracted attention for its potential benefits in diabetes treatment. The primary component of SBH is fructose, which has a low glycaemic index (GI) and causes slight increase in blood sugar levels when consumed orally. In general, carbohydrates with a low GI led to a minor rise in blood sugar levels compared to those with a high GI [156]. Although fructose is the sweetest naturally occurring sweetener, it has a GI of 19, compared to 68 for sucrose and 100 for glucose [157]. The fructose in SBH may influence its hypoglycaemic effect or antidiabetic activity. Researches have shown that fructose lowers hyperglycaemia and glucose levels in both humans and rodents with diabetes [158, 159].

Prior study reported that supplementation with SBH from *Tetragonula biroi* significantly reduced bodyweight of diabetic rats, however, no changes were observed in fasting blood glucose levels [156]. The findings of another investigation indicated that obese individuals who follow a diet low in fructose (< 20 g/day) or moderate consumption (50–70 g/day) while incorporating natural fruit supplements experience weight reduction compared to their initial measurements [160]. SBH has been shown to exhibit hypolipidemic effects and provide protection against tissue damage induced by a dyslipidaemic diet [161]. The recent discovery of trehalulose in various SBH samples across different species further reinforces the potential of SBH as an alternative approach for diabetes management [11]. Zulkifli et al. [59] stated that trehalulose can ameliorate insulin function by regulating glucose metabolism, thereby reducing the risk of diabetes. These results suggest that honey may be a natural sweetening alternative to sucrose for diabetic patients. Albeit the growing number of research on the anti-diabetic properties of trehalulose, evidence from clinical settings remains limited.

Along with the carbohydrates content, the high phenolic content in SBH is a key factor contributing to its anti-diabetic effect. Past investigation stated that among the various sources of SBH, mangroves demonstrated the highest phenolic content in their honey, measuring at 141.74 ± 0.03 mg GAE/100 g. On the other hand, honey sourced from coconuts displayed the highest flavonoid content, measuring at 51.33 ± 0.02 mg RE/100 g. Different analysis reported that phenolic-rich extract from SBH showed higher carbohydrate enzymatic inhibition, glucose uptake, and protection against intracellular oxidative stress tested on the 3T3-L1 adipocytes and L6 muscle cells [162]. These results suggest that SBH, primarily due to its high antioxidant content, may serve as an alternative therapeutic agent for managing type 2 diabetes and its related complications. Additionally, prior study postulated that SBH supplementation could potentially have an antidiabetic effect through the inhibition of α -amylase and α -glucosidase, with the highest percentage inhibition observed against α -glucosidase (68.33% at 100 μ g/mL) [163]. Consistent with other report, SBH from *T. biroi* and *T. laeviceps* exhibited the ability to suppress α -glucosidase activity, with the methanol extract from *T. laeviceps* honey showing the greatest suppression of α -glucosidase enzyme activity [164]. These enzymes play a crucial role in the hydrolysis of complex carbohydrates into simple sugars; however, excessive enzyme activity can lead to increased blood glucose levels. Therefore, regulating glucose release and absorption through the modulation of α -amylase and α -glucosidase makes them key targets for diabetes management strategies.

In terms of obesity reduction, the administration of three doses of SBH demonstrated greater efficacy in reducing body mass index, percentage of body weight gain, adiposity index, and relative organ weight than the conventional obesity treatment [10]. Mohd Rafie et al. [10] also determined that a dosage of 750 mg/kg was the optimal concentration for effectively decreasing body weight and minimising the percentage of weight gained. Besides, a separate study revealed that rodents supplemented with SBH from *H. itama* exhibited lower body fat percentage and omental fat, thus preventing adipocyte hypertrophy at week 16 of supplementation [165]. The reduction of body weight is highly associated with the presence of low GI sugars in SBH and its ability to inhibit the overactivity of digestive enzymes such as α -glucosidase, α -amylase.

Other evidence stated that administration of SBH to diabetic male rats inhibited the increase in fasting blood glucose, total cholesterol, triglyceride, and low-density lipoprotein levels were observed in a study. Simultaneously, high-density lipoprotein and serum insulin levels increased in diabetic rats receiving SBH. The same study also revealed also revealed histological changes in the pancreatic islets of the diabetic rats, along with a reduction in the expression of markers associated with oxidative stress, inflammation, and apoptosis [30]. In line with these findings, a study on diabetic rats demonstrated a reduction in fasting blood glucose, total cholesterol, triglyceride, and low-density lipoprotein levels following SBH supplementation. Notably, the study also reported an increase in high-density lipoprotein levels [166]. It can be postulated that low-GI sugars in SBH help stabilize blood glucose levels by preventing rapid spikes and ensuring sustained energy release, which may aid in appetite regulation and fat reduction. Additionally, SBH's ability to inhibit α -glucosidase and α -amylase slows carbohydrate digestion, leading to lower blood sugar levels and improved metabolism. These effects suggest that SBH may support weight management and metabolic health, making it a potential functional food for obesity and diabetes.

9 Conclusion

In conclusion, SBH contains phenolic compounds that enhance its antioxidant properties, potentially reducing the risk of oxidative stress-related diseases. In addition to its antioxidant activity, SBH exhibits significant antimicrobial properties, which may contribute to the prevention and treatment of infections by inhibiting the growth of pathogenic microorganisms. Furthermore, its chemo preventive effects suggest a potential role in reducing cancer risk by modulating

oxidative damage, inflammation, and cellular proliferation. Additionally, SBH has demonstrated antidiabetic properties, potentially aiding in glycaemic control by improving insulin sensitivity and reducing oxidative stress associated with diabetes-related complications. This review highlights the diverse medicinal benefits of SBH, suggesting that it may serve as a valuable natural therapeutic resource. However, further research is required to fully elucidate its mechanisms of action, assess its efficacy especially in clinical settings, and determine optimal methods for its use in the prevention and treatment of various health conditions.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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