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#### Review

### Biological and therapeutic effects of honey produced by honey bees and stingless bees: a comparative review

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#### ABSTRACT

Honey is a natural product produced by both honey bees and stingless bees. Both types of honey contain unique and distinct types of phenolic and flavonoid compounds of variable biological and clinical importance. Honey is one of the most effective natural products used for wound healing. In this review, the traditional uses and clinical applications of both honey bee and stingless bee honey – such as antimicrobial, antioxidant, anti-inflammatory, anticancer, antihyperlipidemic, and cardioprotective properties; the treatment of eye disorders, gastrointestinal tract diseases, neurological disorders, and fertility disorders and wound healing activity are described.

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#### 21 Introduction

Honey is a natural sweetener that is widely available across 22 the world. Among natural products, it is extensively used for 23 various applications, some clinical (Ahmed and Othman, 2013), 24 and contains approximately 200 distinct chemical compounds 25 26 (Ramanauskiene et al., 2012). Honey bee honey is a viscous solu-27 tion containing various molecules, including fructose and glucose (80-85%); water (15-17%); ash (0.2%); proteins and amino acids 28 (0.1-0.4%) and trace amounts of enzymes, vitamins and other sub-29 stances, such as phenolic compounds. However, honey composition 30 varies depending on the types of plants from which the bee con-31 sumes nectar. Nevertheless, nearly all honey worldwide contains 32 similar types of phenolic acids, including caffeic, ellagic, ferulic and 33 p-coumaric acids; flavonoids, such as apigenin, chrysin, galangin, 34 hesperetin, kaempferol, pinocembrin and quercetin; and antiox-35 idants, such as tocopherols, ascorbic acid, superoxide dismutase 36 (SOD), catalase (CAT), and reduced glutathione (GSH). Each con-37 stituent has unique nutritional and medicinal properties, and the 38 components act synergistically, lending honey utility in a variety 39 of applications (Vit et al., 2015a). Nevertheless, the physical prop-40 erties and chemical composition of honeys fluctuate based on the 41

plants from which the bees collect raw material. In addition, differences in the type of flora, climatic conditions and geographical region also influence honey's physical and chemical properties. In a recent study, different methods were used for discrimination of the entomological origins of sting bee and stingless bee honeys (Vit et al., 2011, 2015b) as well as authentication of commercial honeys by nuclear magnetic resonance (Schievano et al., 2015).

Several research studies of honey have confirmed its biological properties, such as antioxidant, anti-inflammatory, anti-bacterial, antiviral, anti-ulcer activities; and antihyperlipidemic, antidiabetic and anticancer properties (Erejuwa et al., 2010; Kishore et al., 2011; Viuda-Martos et al., 2008). It has been reported that honey lowers cardiovascular risk in both healthy patients and in those with increased risk factors. Various parameters, such as plasma glucose, plasma insulin, cholesterol, triacylglycerides (TG), blood lipids, C-reactive proteins and homocysteine, were investigated following in vivo administration of natural and artificial honeys; natural honey was found to have significant ameliorative effects on the aforementioned parameters (Al-Waili, 2004). In particular, Tualang (Koompassia excelsa) honey has been reported to have protective effects in learning and memory, including enhanced morphology of memory-related brain areas, increased levels of brain-derived neurotrophic factor, reduced brain oxidative stress, increased acetylcholine concentration, and reduced acetyl

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Fig. 1. Honey comb (A) of sting bee honey and pot (B) of stingless bee honey.

cholinesterase activity in brain homogenates (Al-Himyari, 2009; Othman et al., 2015).

Stingless bee honev is a precious bee product of the stingless bee. 69 Stingless bee honey is different from that produced by the bees of 70 the genus Apis (i.e., the honey bee) in terms of its color, taste and 71 viscosity (Almeida-Muradian et al., 2014; Guerrini et al., 2009). This 72 valuable bee product has traditionally been consumed directly and 73 used in numerous medical practices: both traditional methods, in 74 which honey is harvested directly from the forest, and in the more 75 76 well-established meliponary (Souza et al., 2006). The honey comb of sting bee honey and honey pot of stingless bee honey are repre-77 sented in Fig. 1. The aim of this review is to summarize information 78 on the traditional and clinical uses of honey bee and stingless 79 bee honey to augment various biological activities and to treat 80 diseases. 81

#### 82 Chemical constituents of honey bee and stingless bee honey

Honey contains approximately 200 compounds, such as vitamins, enzymes, amino acids and minerals, with the major content being water and sugars. Sugars comprise approximately 95–99% of honey's dry matter. Of the sugars in honey, fructose is the most prevalent, comprising approximately 32–38% of its total sugar. In addition to fructose and glucose, several other disaccharides and oligosaccharides, including sucrose, maltose, maltotriose and panose, can be found. Organic acids, minerals and trace elements such as calcium, potassium, sodium, magnesium, phosphorus, sulphur, iron, zinc, copper and manganese are other components present.

In addition, various vitamins, including ascorbic acid (Vitamin C), thiamine (Vitamin B1), pantothenic acid (Vitamin B5), riboflavin (Vitamin B2), nicotinic acid (Vitamin B3), pyridoxine (Vitamin B6), biotin (Vitamin B8), folic acid (Vitamin B9) and cyanocobalamin (Vitamin B12), are present (Ciulu et al., 2011). Enzymes and proteins are minor constituents, with the enzymes playing a vital role in various activities, including antimicrobial activity and facilitating calcium absorption (Ariefdjohan et al., 2008). Many studies have reported (Can et al., 2015; Escriche et al., 2014; Flores et al., 2015; Habib et al., 2014) that the antioxidant capacity of honey is dependent not only on the presence of total phenolic compounds but also on the presence of flavonoids, which play an important role in ameliorating oxidative stress. Interglycosidic linkages in O-glycosil flavones from Tetragonula carbonaria have previously been detected by high-performance liquid chromatography/photodiode-array (Truchado et al., 2015).

A variety of flavonoids and terpenoids have been reported in various honeys. In manuka honey, pinocembrin (1), chrysin (2), pinobanksin (3), 8-methoxykaempferol (4), luteolin (5), isorhamnetin (6), galangin (7), kaempferol, sakuranetin (8), quercetin and magniferolic acid (9) and 3 $\beta$ -hydroxy-24-methylenecycloartan-26-oic acid (10) have been identified (Ahmed and Othman, 2013). The various physicochemical properties of honey bee and stingless bee honey are summarized in Tables 1 and 2. Various types of therapeutic efficacies of honey are depicted in Fig. 2.

Table 1

Physicochemical properties of honey bee (Tualang and Manuka honey) and stingless bee honey.

Physico-chemical properties	TH (Erejuwa et al., 2010)	MH (Stephens et al., 2010)	Stingless bee honey (Souza et al., 2006)	IHC guideline (Bogdanov et al., 1999)
Appearance	Dark brown	Light-dark brown	Amber brown	Colorless to dark brown
Moisture content	23.30% (Ahmed and Othman, 2013)	18.70%	25.02	<20.00
рН	3.55-4.00	3.20-4.20	3.05-4.55	3.40-6.00
Total reducing sugars	67.50%	76.00%	55.00-86.00%	>60.00
Glucose	30.00%	36.20%	8.20-30.98	23.00-32.00
Fructose	29.60%	40.00%	31.11-40.20	31.20-42.40
Sucrose	0.60%	2.80%	0.31-1.26%	0.00-2.80
Maltose	7.90%	1.20%	NA	NA
Calcium	0.18%	1.00%	NA	NA
Potassium	0.51%	1.00%	NA	NA
Sodium	0.26%	0.0008%	NA	NA
Magnesium	0.11%	1.00%	NA	NA
Specific gravity	1.34	1.39	NA	NA
Electrical conductivity (mS/cm)	0.75–1.37	0.53	0.49-8.77	0.80-4.40
HMF (mg/kg)	46.17	40.00	8.80-69.00	<80
Ash content $(g/100 g)$	0.19	0.03	0.01-0.12	<0.6

TH, Tualang honey; MH, Manuka honey; HMF, hydroxylmethylfufural; IHC, International Honey Commission; NA, not available.

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