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Review

Relationships between polyphenols and antioxidant activity of honey produced by Apis mellifera and stingless bees (Meliponini).

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Honey is a matrix of vegetal origin processed by diverse types of bees (Apidae; Hymenoptera). Secondary metabolites of plant origin present in honey are one factor contributing to its antioxidant activity. Antioxidant remedies - food, treatments (a means to prevent, retard progress or revert back to health) - have been found for some diseases caused by oxidative stress. Spectrophotometric methods to measure flavonoid and polyphenol contents are the classic approach. Honey is a polyphenol-rich food and medicine, with a charactersitic flavonoid profile . This review study shows relationships between polyphenols and antioxidant activity of honey produced by *Apis mellifera* and stingless bees (Meliponini).

Key words: Antioxidant activity, *Apis mellifera*, flavonoids, honey, Meliponini, polyphenols.

INTRODUCTION

Polyphenols are natural compounds - secondary plant metabolites - with variable phenolic structures, and are the most abundant antioxidants in our diet. They are common constituents of fruits (apples, blackberries, blueberries, cantaloupe, pomegranate, cherries, cranberries, grapes, pears, plums, raspberries, berries, strawbwrries), vegetables (broccoli, cabage, celery, onion, parsley), grains, cereals, bark, roots (carrots), olive oil, dry legumes, chocolate, honey and beverages, such as green and white tea, coffee, fruit juices and red wine (Manach et al., 2004; Scalbert et al., 2005). Herbs and spices are also important sources of polyphenols (Visioli et al., 2011).

Despite the wide distribution of dietary polyphenols, their health effects have been attentively studied by nutritionists only in recent years. Polyphenols comprise a wide variety of molecules with several hydroxyl groups on aromatic rings. They also comprise molecules with one phenolic ring, such as phenolic acids and phenolic alcohols. Polyphenols are divided into several classes, according to the number of phenolic rings present and to the structural elements connecting the rings to one another (Grassi et al., 2010).

Flavonoids are an important group of polyphenols. Structural categories of flavonoids include flavones (for example, apigenin, luteolin), flavanones (for example, hesperetin), catechins (for example, epicatechin, epigallocatechin-3-gallate (EGCG), and anthocyanins (for example, cyanidin) (Hendrich, 2006). One non-flavonoid polyphenol that has received much attention is resveratrol, a stilbene polyphenol, present in grapes and red wine with demonstrated antioxidant properties (Bournival et al., 2009; Fonseca-Kelly et al., 2012).

Diet is a major source of polyphenol intake and diets rich in fruits and vegetables contain an abundance of various classes of polyphenols, with a daily total intake

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amounting to 1 g/day, which is higher than all other classes of phytochemicals and known dietary antioxidants; this is approximately 10 times higher than the intake of vitamin C and 100 times higher that the intake of vitamin E and carotenoids (Manach et al., 2004).

Current evidence strongly supports a contribution of polyphenols for the prevention of cardiovascular diseases, cancers, and osteoporosis, and suggests a role in the prevention of neurodegenerative diseases and diabetes mellitus. A considerable body of literature supports a role for oxidative stress in the pathogenesis of age-related human diseases and a contribution of dietary polyphenols to their prevention (Scalbert et al., 2005; Stocker and Keaney, 2004; Madamanchi et al., 2005; Grassi et al., 2009). However, it is difficult to evaluate the physiological effects of specific natural phenolic antioxidants, since such a large number of individual compounds may occur even in a single food and their fate *in vivo* cannot be measured. For example, over sixty different chemically distinct flavonoids are known to occur in a given red wine (Burin et al., 2011; Yoo et al., 2012). The polyphenol content of several foods, including honey and bee pollen, is usually evaluated by the Folin-Ciocalteu reagent which correlates well with alternative chemical and biological procedures used to determine antioxidant potential (Brenna and Pagliarini, 2001; Sochor et al., 2011).

Herein, this study reviews polyphenol and flavonoid contents related to the antioxidant activity of honey produced by *Apis mellifera*.

POLYPHENOLS EXTRACTIVE AND QUANTIFICATION TECHNIQUES

Polyphenols are chemical compounds with diverse phenolic structural features. They have been classified into phenolic acids, flavonoids, polyphenolic amides and other polyphenols (Tsao, 2010). Phenolic acids are non-flavonoid polyphenolic compounds divided into two main types, benzoic acid and cinnamic acid (Liu and Hu, 2007). Flavonoids are structured as a common carbon skeleton of diphenyl propanes, two benzene rings joined by a linear three-carbon chain usually forming an oxygenated heterocycle nucleus, the flavan nucleus. Depending on the structural complexity of flavonoids, particularly on the oxidation state of the central ring, flavonoids are themselves subclassified as flavonols, flavones, flavanones, flavanols or flavan-3-ols (catechins and their oligomers: proanthocyanidins), isoflavones, and anthocyanins (Grassi et al., 2010; Chandrasekara and Shahidi, 2010; Forester and Waterhouse, 2009).

Polyphenolic amides are compounds that have N-containing functional substituents. They can be found in two major groups in common foods: capsaicinoids in chili peppers are responsible for the hotness of the chili peppers, with strong antioxidant and anti-inflammatory properties (Whiting et al., 2012), and avenanthramides in oats have also been reported in antioxidant and anticancer activities (Sur et al., 2008; Guo et al., 2010). Besides flavonoids, polyphenolic acids and polyphenolic amides, there are several non-flavonoids polyphenols found in food and with real importance to human health, for example: (a) resveratrol is a phytoalexin found naturally in many common food sources including grapes, mulberries, and peanuts and is reported to have numerous beneficial effects on human health like anticancer properties, antioxidant, anti-inflammatory, anti-aging, and is thought to improve the overall cardiovascular health (Holthoff et al., 2010; Sun, 2010);

(b) lignans are bioactive, non-nutrient, non-caloric phenolic plant compounds that are found in higher concentrations in flax and sesame seeds and in lower concentrations in grains, other seeds, fruits and vegetables, and have demonstrated its antioxidant, anti-inflammatory and cardiovascular protective properties (Yoon and Baek, 2005; Peterson et al., 2010).

POLYPHENOLS OF HONEY

Honey is a nutritious food, with economical importance worldwide, and is the most important primary product of bee keeping – with honeybees *Apis mellifera* L. and stingless bees (Meliponini). Honey has been used by humans since ancient times, both in traditional medicine, for treatment of burns, gastrointestinal problems, asthma, infected wounds, and skin ulcers (Kücük et al., 2007; Tavares et al., 2011), as well as in preserving food by retarding deterioration, rancidity, or discoloration caused by light, heat, and some metals (Meda et al., 2005). It is mainly a supersaturated sugar solution, with more than 95% of its dry mass consisting of sugar, although different valuable nutrients such as vitamins, minerals, enzymes, flavoring organic compounds, free amino acids and numerous volatile compounds constitute minor components (Ayoub et al., 2009; Baroni et al., 2006). However, it is this smaller fraction of the overall composition that is responsible for honey's organoleptic and nutritional properties (Manyi-Loh et al., 2011a).

Honey composition varies due to the differences in plant types, climate and environmental conditions (Kücük et al., 2007). Honey composition is tightly associated to its botanical source and also to the geographical area, because soil and weather determine melliferous flora. Depending on the botanical origin, honey could be classified as: (a) floral, when it is derived from the nectar of flowering plant, or (b) non-floral (honeydew) when it is derived from sweet deposits secreted by living parts of plants or excreted onto them by sap-sucking insects (Manyi-Loh, 2011b). According to the entomological origin, several types of bees produce and store honey in beeswax combs (*Apis cerana*, *Apis dorsata*, *Apis florea*, *Apis mellifera*) (Michener, 2000) or cerumen pots by the great biodiversity of stingless bees (Meliponini) (Camargo

Table 1. Average honey composition.

Compositional parameter	Average (min-max)	
	Apis mellifera[1]	Pot-honey[2]
Water content (g/100 g honey)	17.2	26.7
Sugars	-	-
Fructose (g/100 g honey)	38.2	-
Glucose (g/100 g honey)	31.3	-
Reducing sugars (g/100 g honey)	-	66.0
Sucrose (g/100 g honey)	0.7	2.3
Total sugars (g/100 g honey)	79.7	68.3
Ash (g/100 g honey)	0.2	0.34
Proteins (g/100 g honey)[1], Nitrogen (mg/100 g honey)[2]	30[1]	58.31[2]
Free acidity (g/100 g honey)[1] (meq/kg honey)[2]	0.5[1]	44.8[2]
pH-value	3.9	3.81

Source: Bogdanov et al. (2008) and Souza et al. (2006).

Table 2. Principal flavonoids and phenolic acids in honey.

Group	Compound
Flavonoids	
Flavonols	Quercetin, kaempferol, galangin, fisetin
Flavanones	Pinocembrin, naringin, hesperidin
Flavones	Apigenin, acacetin, chrysin, luteolin
Phenolic acids	
	Caffeic acid, caffeic acid phenethyl ester, cinnamic acid, ellagic acid, gallic acid, protocatechuic acid, syringic acid, *p*-hydroxybenzoic acid, vanillic acid, *p*-coumaric acid, sinapic acid, *p*-methoxybenzoic acid, *p*- methoxycinnamic acid

Source: Tomás-Barberán et al. (1993, 2001), Cushnie and Lamb (2005), Fiorani et al. (2006) and Lianda et al. (2012).

and Pedro, 2007).

Studies have indicated that honey contains about 200 substances, and it is a unique natural concentrated form of sugar available in the world. The overall composition of honey is shown in Table 1. Sugars are the main constituents, comprising about 95% of the honey dry weight. Besides sugars and water, honey contains numerous compounds such as organic acids, proteins, amino acids, minerals, polyphenols, vitamins (ascorbic acid) and aroma compounds (Bogdanov et al., 2008). Particularly interesting are compounds such as polyphenols (phenolic acids, flavonoids and their derivatives), terpenes, steroids, and amino acids, which are considered as an important part of traditional medicine (Kücük et al., 2007; Ahn, 2007).

Honey phenolic compounds (Table 2) act as natural antioxidants and are becoming increasingly popular because of their potential role in contributing to human health. A wide range of phenolic constituents is present in honey, like quercetin, caffeic acids, caffeic acid phenethyl ester (CAPE), acacetin, kaempferol, galangin, chrysin, acacetin, pinocembrin, pinobanksin and apigenin, which have promising effect in the treatment of some chronic diseases. In general, most of the phenolic compounds found in honey are in the form of flavonoids and phenolic acids (Tomás-Barberán et al., 1993, 2001; Cushnie and Lamb, 2005; Fiorani et al., 2006; Lianda et al., 2012). Their concentration depends on various factors, including plant species used by the bees, health of the plant, season, environmental factors, etc. (Kücük et al., 2007). In addition, there is a great variety of enzymes like glucose oxidase and catalase (Viuda-Martos et al., 2008).

Consumption of fruits and vegetables has been inversely associated with a decreased risk of cardiovascular diseases, and other chronic illnesses (Nöthlings et al., 2008) are most likely due to the abundance and variety of bioactive compounds present. As an alternative to pharmaceutical medications, consumption of diets rich in natural bioactive components and their contribution to maintaining or improving health has been a subject of considerable interest to researchers. Dietary intake of certain classes of flavonoids

including flavanones and anthocyanidins, are associated with reduced risk of some chronic diseases (Mink et al., 2007).

Therefore the importance of studying quantity and classes of polyphenols present in honey is because honey can be a functional food and a natural source of this kind of beneficial molecules. For example, the phenolic extracts from two monofloral Cuban honeys for their *in vitro* total antioxidant capacity, phenolic compounds content and free radical scavenging activity, were used to identify 13 phenolic compounds using HPLC-LC/MS with quercetin as the most abundant flavonoid (Alvarez-Suarez et al., 2012). The results also show that both extracts were able to inhibit erythrocytes oxidative damage, and that this may likely be due to their incorporation into cell membranes and their ability to cross it and reach the cytosol. Overall, this study indicates that honey contains relevant antioxidant compounds responsible, at least in part, for its biological activity and that uptake of its flavonoids may provide defense and promote cell functions in erythrocytes.

Classic methods used to quantify flavonoids and polyphenols in honey

The Folin-Ciocalteu method has been used for quantification of polyphenols according to the method described by Slinkard and Singleton (1977). The method is based on the reduction of MoO^{4+} to MoO^{3+} that is detected by color change from yellow to blue, measured at 765 nm. The results were expressed as equivalents of gallic acid or phenol from the calibration curve (Medić-Šarić, 2009). In some cases, another colorimetric method based on Folin reagent, the Folin–Denis method, was used where analysis is based on the reduction of phosphomolybdic and phosphotungstic acids in the presence of phenolic compounds, forming blue complexes that strongly absorb at 620 to 700 nm (Meda, 2005; Sant'Ana et al., 2012).

On the other hand, determination of flavonoid content is very important in honey because most of the phenolic compounds found in honey are in the form of flavonoids (Viuda-Martos et al., 2008). The total flavonoid content is frequently determined by using the aluminum chloride method, with adaptations depending on the sample (Meda et al., 2005). In this method, an aliquot of 2% aluminum chloride in methanol is mixed with the same volume of honey solution, and after 30 min the absorbances are read at 415 nm using a methanol blank. The total flavonoid content is determined by using a standard curve with quercetin (0-0.025 mg/ml) as the standard, and the results are expressed as milligrams of quercetin equivalents (QE)/100 g of honey. However, before determination of polyphenol and flavonoid content, and characterization of type and classes of polyphenols, it is necessary to perform extractive procedures, because honey has a complex chemical profile.

ANTIOXIDANT ACTIVITY OF HONEY

Reactive oxygen species (ROS) are highly reactive molecules that are constantly produced by enzymatic reactions in cells, especially by immune cells in order to sustain their antibacterial and antifungal functions (Hu and Brindle, 2005). In normal physiological conditions, ROS are produced at low levels, which are necessary for maintaining normal cell functions, and the endogenous anti-oxidant defense systems of the body have the capacity to avert any harmful effects. However, several established risk factors for chronic diseases have been linked to excessive generation of ROS, known as a state of oxidative stress, resulting from an imbalance between excessive formation of ROS and/or reactive nitrogen species and limited antioxidant defenses (Maryanovich and Gross, 2012). When ROS are overproduced, they are taken in charge by various enzymatic pathways for inactivation (superoxide dismutase, catalase, cytochromes, etc.) (Victor et al., 2004). Although these enzymatic pathways can be overstepped, ROS accumulate and can react with the different cell molecules such as lipids, proteins, carbohydrates, and nucleic acids. These interactions with the ROS apply an oxidative stress to cells. Some tissues, particularly the brain, are highly exposed to oxidative damages because of their elevated oxygen consumption and the induced generation of large amounts of reactive oxygen species (Migliore and Coppedè, 2004). Oxidative stress has been considered a mechanism involved in the pathogenesis of ischemic heart disease and atherogenesis, in cancer and other chronic diseases, and it also plays a major role in the aging process, principally through many forms of cellular and molecular deterioration such as mitochondrial collapsing, DNA damage, and protein, carbohydrate, and lipid oxidation (Watanabe et al., 2010). Oxidative damage by free radicals has been well investigated within the context of oxidant/antioxidant balance. For instance, in animal models of hiperlipidemia (Küçükgergin et al., 2010; Farah et al., 2012), hypertension (Zhao et al., 2008), are observed elevated levels of vascular superoxide anion production.

Antioxidant activity of honey related to flavonoid and polyphenol contents

Honey, propolis, and royal jelly are functional food with phenolic compounds collected by the bees from the plants where they gather nectar. Apart from sugars, honey contains many minor components with antioxidant activity, among which are amino acids and proteins, carotenes, phenolic compounds and flavonoids, ascorbic acid and organic acids (Erejuwa et al., 2012). It has been proposed that the antioxidant capacity of honey is due mainly to the phenolic compounds and flavonoids they contain, and there is a high correlationship between polyphenols and honey antioxidant capacity (Alzahrani et

al., 2012). This has been demonstrated in honey from different floral, geographic and entomological origins like honeys from Spain (Pérez et al., 2007), Australia (Persano Oddo et al., 2008), Perú (Rodríguez-Malaver et al., 2009), México (Rodríguez et al., 2012), among others. Of course, if possible a synergistic effect is observed on honey polyphenols and the more than 181 compounds that form part of honey.

Different plants cause variations in the type of phenolic compounds and their contents in honey (Blum, 1996). For example, honeys from different countries and plant origin are shown in Table 3. The antioxidant activity is measured by different methods (DPPH named after the reagent 2,2-diphenyl-1-picryhydrazyl, FRAP Ferric Reducing Antioxidant Power, ORAC Oxygen Radical Absorbance Capacity, RSA Radical Scavenging Activity, TEAC Trolox Equivalent Antioxidant Capacity). Flavonoid content is mostly expressed as mg quercetin equivalents (QE) and sometimes as mg catechin equivalents (CE)/100 g honey. The polyphenol content is expressed in mg equivalents gallic acid (GAE)/100 g honey. Honey from northeastern Brazil varied from 10.21 to 108.5 mg gallic acid equivalents (GAE)/100 g honey (Tavares et al., 2011), similarly to flavonoid content of honey from Burkina Faso (with values in the range of 32.59 to 114.75 mg of GAE/100 g honey) (Meda et al., 2005).

Substantial differences were observed in honey from Chile, with total phenolic content varying from 0.0 to 8.83 mg/100 g of honey (Muñoz and Copaja, 2007); honeys of different floral origin from Poland ranged from 21.7 - 75.3 mg GAE/100 g of honey (Socha et al., 2009), whereas honey samples from Slovenia varied between 44.8 and 241 mg GAE/100 of honey (Bertoncelj et al., 2007). Honey from Yemen showed phenol content ranging from 75.13 to 246.21 mg catechin equivalents (CE)/100 g of honey (Al-Mamary et al., 2002). Sant'Ana et al. (2012) quantified total polyphenolic content for 21 monofloral honeys from Rio de Janeiro and Minas Gerais, Brazil, with values between 61.11 and 175.39 mg GAE/100 g. To evaluate their antioxidant activity, three different methods were used. The ferric reducing method showed that honey from the same floral origins had more similar profiles, which made it possible to group the eucalyptus, morrao de candeia, and cambara honey samples from three distinct locations.

Flavonoid contents in honey from Chile (Muñoz and Copaja, 2007) ranged from 0.014 to 13.8 mg QE/100 g of honey. Flavonoid contents in Burkina Faso honey were 0.17 to 8.35 mg QE/100 g of honey, while that for Rio de Janeiro and Minas Gerais (Brazil) ranged between 2.94 and 10.91 mg QE/100 g of honey (Table 3).

Despite the evident relationship that was demonstrated several times between honey bioactivity with polyphenols and flavonoid content, the exact mechanism of action is unknown. Free radical sequestration, hydrogen donation, metallic ion chelation, or their action as substrate for radicals such as superoxide and hydroxyl, interference with propagation reactions, or inhibition of the enzymatic systems involved in initiation reactions have been proposed as steps contributing to antioxidant activity (Maruyama et al., 2010; Al-Waili et al., 2011). Just as proposed for other functional foods, all bioactivities related to honey can be attributed to its antioxidant activity, explained by polyphenol and flavonoid contents. For example, honey inhibits the growth of micro-organisms and fungi, through bacteriostatic and bactericidal effects. The antimicrobial effect of honey is due to different substances like glucose oxidase that produces the antibacterial agent hydrogen peroxide, phenolics and flavonoids, and the low pH (Boukraa, 2008). The antimicrobial activity of honey has been demonstrated in bacteria like *Staphylococcus aureus, Streptococcus mutans, Streptococcus pyogenes*, *Pseudomonas aeruginosa*, etc (Jenkins and Cooper, 2012; Maddocks et al., 2012).

Another important bioactivity of honey is its protection against tumoral development. In this sense, Fauzi et al. (2011) investigated the anticancer potential of Tualang honey - produced by *Apis dorsata*, in human breast (MCF-7 and MDA-MB-231) and cervical (HeLa) cancer cell lines. Also, in the normal breast epithelial cell line, MCF-10A shows that this honey has significant anticancer activity against human breast and cervical cancer cell lines. The same effect is observed with honey consumption in spontaneous mammary carcinoma of CBA mice and in anaplastic colon adenocarcinoma of Y59 rats (Orsolic and Basic, 2004), thereby inhibiting the growth of different bladder cancer cell lines (T24, RT4, 253J and MBT-2) *in vitro*, when administered intralesionally or orally in the MBT-2 bladder cancer implantation mice models (Swellam et al., 2003). These findings indicate that honey activates the immune system, and honey ingestion may be advantageous to prevent cancer and further metastasis. In addition, it is postulated that honey given orally before tumor cell inoculation may have an inhibitory effect on tumor spreading (Othman, 2012).

Finally, the anti-inflammatory properties of honey are attributed to the presence of flavonoids that inhibit the development of inflammation provoked by a variety of agents including pro-inflammatory enzymes and cytokines, low molecular weight compounds such as eicosanoids or the enzymatic degradation of tissues. Kassim et al. (2010) tested the effect of honey methanol extract (HME) and honey ethyl acetate extract (HEAE) of Malaysian honey *in vitro*, and observed nitric oxide production in stimulated macrophages and their effects on tumor necrosis factor-α (TNF) cytotoxicity in L929 cells. The median maximal effective concentrations for *in vitro* nitric oxide inhibition by HEAE and HME were calculated to range between 37.5 and 271.7 µg/mL, respectively. The median maximal effective concentrations for protection from TNF cytotoxicity by HEAE and HME were 168.1 and 235.4 µg/mL, respectively. In another example, Leong et al. (2012)

Table 3. Review of antioxidant activity, flavonoid and polyphenol contents in honey produced by *Apis mellifera* in different countries.

Country of origin (Botanical origin)	Antioxidant activity: DPPH (µmolTE/g) FRAP (µmolTE/g) ORAC (µmolTE/g) RSA (EC_{50}mg.mL) TEAC (µmolTE/g)	Flavonoid content (mg QE[1] or mg CE[2] /100 g honey)	Polyphenol content (mg GAE/100 g honey)	Reference
Algery wild carrot	0.6386 ± 0.05 FRAP	-	503.09 ± 8.29 *	Alzahrani et al. (2012)
Algery unknown	337.77 ± 1.01 FRAP (µM Fe (II)/100 g)	54.23 ± 0.62[2]	459.83 ± 1.92	Khalil et al. (2012)
Brazil multifloral	Honey: 16.62 ± 3.98 RSA Extract: 31.96 ± 18.07 DPPH 172.96 ± 157.32 FRAP 159.65 ± 110.19 TEAC	Honey: 1.53 ± 1.96 Extract: 0.53 ± 0.29	Honey: 58.5 ± 14.78 Extract: 37.91±22.71	Lianda et al. (2012)
Brazil orange blossom	Honey: 40.36 ± 7.58 RSA Extract: 15.22 ± 10.75 DPPH 305.92 ± 158.84 FRAP 217.05 ± 119.68 TEAC	Honey: 0.17± 0.15 Extract: 1.25 ± 2.89	Honey: 40.36 ± 7.58 Extract: 45.67 ± 22.88	Lianda et al. (2012)
Brazil	-	2.94 - 10.91[1]	61.11 - 175.39	Sant'Ana et al. (2012)
Brazil	-	0.25 - 8.38[1]	10.21 - 108.5	Tavares et al. (2011)
Burkina Faso	-	0.17 - 8.35[1]	32.59 - 114.75	Meda et al. (2005)
Chile	0.260 (eq/g) FRAP 1.97 (eq/g) DPPH	-	1093	Mejías and Montenegro (2012)
Chile	-	0.014 - 13.8[1]	0.0 - 8.83	Muñoz and Copaja (2007)
Germany acacia	1.366 ± 0.06 FRAP	-	627.56 ± 44.03*	Alzahrani et al. (2012)
Italy	59.02 ± 1.86 TEAC 66.39 ± 13.57 DPPH 347.01 ± 333.91 FRAP	7.92 ± 5.97[1]	12.06 ± 4.58	Perna et al. (2012)
New Zealand Manuka	1.2106 ± 0.005 FRAP	-	899.9 ± 11.75*	Alzahrani et al. (2012)
Poland	-	-	21.7 - 75.3	Socha et al. (2009)
Saudi Arabia Lavanda	0.2089 ± 0.022 FRAP	-	111.42 ± 3.54*	Alzahrani et al. (2012)

Table 3 Contd.

Southern Africa	10.56 ± 0.7 TEAC 1.74 ± 0.4 DPPH 22.58 ± 2.01 ORAC	30.77 ± 2.2[c]	99.75 ± 6.0	Serem and Bester (2012)
Slovenia	-	-	44.8 - 241	Bertoncelj et al. (2007)
Yemen	-	-	75.13 - 246.21	Al-Mamary et al. (2002)

* Polyphenol contents (mg GAE/kg).

investigated the anti-inflammatory activity of a selection of previously untested indigenous New Zealand (NZ) honeys, showing that several, but not all, New Zealand honey samples exhibited potent, dose-dependent reduction of human neutrophil superoxide production *in vitro,* indicating elating with clinically relevant anti-inflammatory activity. However, further investigation is warranted to identify the active components and mechanisms responsible for these activities and to determine potential applications for anti-inflammatory honeys in the topical treatment of clinical inflammation.

CONCLUSIONS

Honey remais a valuable product in past-present-future cultures. Differences and similarities in their chemical composition of honey affect the bioactive properties. Particularly, the content of flavonoids and polyphenols (including phenolic acids) are related to the antioxidant activity, as reviewed here. Bee flora and bee species vary in tropical and temperate environments. Therefore, raw materials collected and processed by the bees provide important information contained in the honey matrix. Paradoxically, studies on chemical quantifications and bioactivity of honey frequently lack melissopalynological data, or provide imprecise data, and viceversa. Multidisciplinary research teams are essential to improve scientific interpretations, especially in bee plant derived products. A general comment is made on the need to report correct units of flavonoids and polyphenol to build up a sound database for further ventures. As a function of food, honey provides an opportunity to improve the human health, reduce health care costs and support economic development in rural communities.

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