Chapter 11
Honey as Functional Food and Prospects in Natural Honey Production

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11.1 Introduction

Honey is a superfood that has practically existed for as long as recorded human history. Evidence of bee hives and honey have been found in cave paintings in Spain during the 7000 BC, and in Egyptian tombs as old as 2400 BC (The Honey Association n.d.). Aside from being used as food ingredient and natural sweetener, honey was also valued for its healing properties. Today, after over 2600 years, honey continues to be produced by honeybees in bee farms and consumed by humans as functional food because of its antioxidant, anti-inflammatory, anti-microbial, antitumor, and anti-mutagenic effects.

Honey is defined as "*the natural sweet substance produced by honey bees from the nectar of plants or from secretions of living parts of plants or excretions of plant sucking insects on the living parts of plants, which the bees collect, transform by combining with specific substances of their own, deposit, dehydrate, store and leave in the honey comb to ripen and mature.*" (Codex Alimentarius Commission 1999). Honey is made up of glucose and fructose mainly (~95% of dry weight), as well as sucrose, maltose, turanose, and erlose, and oligosaccharides such as raffinose and melezitosein smaller quantities (Bogdanov et al. 2008). It also contains amino acids, proteins, organic acids and enzymes such as diastase, glucose oxidase and invertase, minerals, vitamins, insoluble matter like honey comb debris and pollen. Traces of bacteria, algae and fungi may also be found.

The use of honey as natural sweetener began to decline after the cultivation of sugar cane in Papua New Guinea in 8000 BC and the production of table sugar around 100 AD in India (Deerr 1950). But throughout human history, honey had been celebrated for its folkloric medicinal effects. In 2016, the annual global honey

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C. Egbuna, G. Dable-Tupas (eds.), *Functional Foods and Nutraceuticals*,
https://doi.org/10.1007/978-3-030-42319-3_11

production represented less than 1% of the 2014 total sugar production (Tridge 2019). However, because of the growing preference of consumers for healthier sugar alternatives and functional food, global consumption by the year 2024 is expected to hit 2.8 million tons (Global Industry Analysts, Inc. 2019).

11.2 Classification of Honey and their Distribution

There are 2 major classes of honey based on whether they come from flower nectars (called Blossom or Nectar Honey), or if they chiefly are excretions of plants or plant sucking Hemipterans insect (called Honeydew Honey). The differences in the relative amount of the fructose and glucose is used to determine if the honey is unifloral blossom honey (Bogdanov et al. 2004).The types of minor sugars in blossom honey, however, do not vary since they are products of the enzyme invertase. Between honeydew and blossom honey, greater amounts of oligosaccharides are found in honeydew honey, including melezitose and raffinose that are absent in blossom honey.

There are over 300 types of honey in the world today. Depending on the botanical and geographical origin of the honey, there will be variations in the appearance, taste, and composition of the honey (Bogdanov et al. 2008). Blossom honey types are named based on the plant species honey is derived from. For example, the source of the Manuka honey is the manuka bush (*Leptospermum spp*.) found in Asia and New Zealand, and Heather honey from heather (*Erica spp.* or *Calluna vulgaris*) mainly from Europe and Asia. Clover honey from Europe or Asia contain nectar from *Trifolium spp*. Eucalyptus honey from America is composed of *Eucalyptus* nectar (Bogdanov et al. 2015).

Multifloral blossom honey are commonly labelled as blossom or nectar blend. Honeydew honey types are not as many as blossom honeys, and are named based on where they were taken (e.g. forest honeydew, beach forest honeydew, tree honey, bug honey, or flea honey). Honey may also be named according to the method of its removal from the comb (i.e. extracted honey, pressed honey, drained honey, comb honey, or honey with comb).

11.3 Honey as Functional Food

While the two main purposes of food are to provide nutrition and to give satisfaction to the body, a third purpose of food has emerged after mounting proof coming from scientific researches worldwide. This is functional foods, and it refers to *"foods that have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis at effective levels"* (Hasler 2002).

Honey stands among these functional foods whose natural production has not been significantly modified since its discovery. Honey is a healthier alternative to table sugar because of its lower glycemic index (Atkinson et al. 2008). Honey also contains prebiotics that encourage the growth of probiotic microorganisms, such as lactic acid bacteria. Prebiotics, probiotics, and the secondary metabolites found in honey are responsible for the medicinal properties of honey (Luchese et al. 2017; Olofsson and Vasquez 2008). The details of the health benefits of honey is explained in the following section,

11.4 Health Benefits of Honey

11.4.1 Antiseptic and Antimicrobial

Honey possesses a broad-spectrum antibacterial activity that varies in potency depending on the honey's plant origin (Molan 2006). The hygroscopic nature of honey dehydrates bacteria. It's acidic environment and high sugar concentration deters microbial growth (Simon et al. 2009). The other antimicrobial components of honey are discussed in the next section. Kynurenic acid, an intermediate in tryptophan metabolism, reported in arboreal honey, was also found to have antimicrobial properties (Beretta et al. 2007).

11.4.2 Anti-Diabetic

Diabetics are advised to consume food with low glycemic index. Albeit having a high total carbohydrate content, the average glycemic index of honey is only 55, compared to 100 for glucose, and 65 for sucrose (table sugar) (Atkinson et al. 2008), making it a healthier natural sweetener. The high levels of fructose, and the presence of oligosaccharides like isomaltulose in honey reduces hyperglycemia and prolongs gastric emptying, thus slowing down intestinal absorption in humans (Vaisman et al. 2006; Erejuwa et al. 2012; Kellet et al. 2008; Kashimura and Nagai 2007).

11.4.3 Antioxidant

The antioxidant activity of honey is largely due to the synergistic effects of phenolic phytochemicals such as flavonoids and phenolic acids, and non-phenolic compounds like ascorbic acid, organic acids and amino acids, and the action of enzymes like catalase and glucose oxidase (Sousa et al. 2016; Gorjanovic et al. 2013). The levels of these bioactive substances vary depending on the geographical and botanical origin of honey.

Two classes of phenolic acids in honey have been studied: (1) benzoic acids, and (2) cinnamic acids. For honey flavonoids, 3 classes have also been found:

(1) flavones, (2) flavanones, and (3) flavonols. These phytochemicals contribute to the flavour, color, and the distinctive taste of honey. Phenolic phytochemicals have also been explored as potential markers of the botanical origin of honey (Silva et al. 2012).

11.4.4 Anti-Inflammatory and Wound Healing

For centuries, the topical use of honey on skin wounds have been practiced because it controls wound infection, debrides the wound, produces a clean wound bed with minimal scarring, and reduces inflammation and pain (Dunford et al. 2000; Molan 2006). To date, however, only two honey brands have been approved for therapeutic use (Medihoney™ and Active Manuka Honey).

Bee pollen enzymes, essentials oils, propolis, and secondary metabolites like flavonoids, polyphenols and terpenes were found to contribute to honey's wound healing properties (Azeredo et al. 2003; Viuda-Martos et al. 2008). The mild acidity of honey, and its low levels of hydrogen peroxide also enhance tissue repair and the antibacterial activity of honey (Lusby et al. 2005). Honey can also stimulate the cytokine production of the monocytes, thus, initiating tissue repair (Molan 2006). Chestnut honey, rhododendron honey, and multifloral blossom honey from Turkey were reported to improve histopathological parameters during wound healing (epithelialisation, angiogenesis, macrophages, and fibroplasias) when compared to the control treatment (Nisbet et al. 2010).

11.4.5 Regulation of Blood Pressure and Cardiovascular Function

Honey was found to improve the lipid profile and lower the C-reactive protein (CRP) levels. Honey consumption also lowered homosycteine and the triacylglycerol levels in subjects with hypertriglyceridemia (Al-Waili 2004). The risk factors for cardiovascular diseases, such as obesity, hypertension, smoking, and chronic periodontal disease, are correlated with elevated levels of CRP (Koenig 2003). Thus, the anti-inflammatory activity of honey also relates to its potential cardiovascular function protection.

11.4.6 Anti-Cancer

In a review by Ahmed and Othman (2013), the anti-cancer activity of cancer was organized into: (1) antioxidant activity; (2) anti-inflammatory activity; (3) p53 regulation; (4) cell cycle arrest; (5) immunomodulatory activity; (6) anti-mutagenic activity; (7) estrogen modulation; (8) cyclooxygenase-2 (COX-2) modulation; and (9) tumor necrosis factor (TNF) modulation. While the complete mechanism of honey's anti-cancer activity is not yet fully elucidated, the phenolic constituents of honey have been reported to be the main actors in its anti-cancer activity (Abubakar et al. 2012). But as with the other health benefits of honey consumption or use, the anti-cancer components in honey will vary with the geographic location and the plant sources of honey.

11.5 Known Bioactive Components of Honey

11.5.1 Probiotics

Honey is not microbe-free as it is considered a good source of probiotics, such as acid-loving lactic acid bacteria and yeast. Probiotics are defined as "*live microorganisms that, when administered in adequate amounts, confer a health benefit on the host*" (Sanders 2008). Honey acidification is a by-product of glucose oxidase metabolism. The acidic environment deters the proliferation of many spoilage microbes (Da Silva et al. 2016), naturally preserving the honey.

Lactic acid bacteria (LAB) come from the stomach of honeybees (Olofsson and Vasquez 2008), and from the flower secretions and pollen. Among the LAB symbionts found in fresh honey *Lactobacillus acidophilus, L. apis, L. alvei, L. plantarum, L. insects,* and *L. parabuchneri*, and *Bifidobacterium asteroids* and *B. coryneform*. LAB symbionts contribute to the therapeutic and antibacterial properties in honey.

11.5.2 Prebiotics

A dietary prebiotic is "*a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health*" (Gibson et al. 2010). Examples of prebiotics in honey are non-digestible polysaccharides and oligosaccharides, such as maltulose, maltotriose, turanose, panose, melezitose, raffinose, inulobiose and kestose, that encourage the growth of probiotic microbes (Leite et al. 2000; Mei et al. 2010). The osmotic constitution as well as the composition of honey also protects probiotic bacteria as they pass through the human gastrointestinal tract during digestion (Luchese et al. 2017).

11.5.3 Quercetin

Honeys abundantly contain phenolic compounds which act as natural antioxidants. Quercetin, a flavonol, has been identified as one of the most predictable elements of nectar, honey, pollen, beebread, and propolis, and as a signaling substance responsible for pollen germination stimulation and pollen tube growth (Liao et al. 2017). Studies have determined health benefits of quercetin for bees including increased response for detoxification and immunity genes in honey bees (Mao et al. 2013; Mao et al. 2013). Moreover, polyphenols identified in honeys including quercetin have been reported as "promising pharmaceutical drugs in the treatment of cardiovascular diseases" (Khalil and Sulaiman 2010). Quercetin-detection capability of honey bees, however, still remain a mystery since it is a non-volative compound. Some researchers stated that it may be detectable by gustatory receptors (Kaškonienė et al. 2015).

11.5.4 Hesperitin

Hesperitin is a common bioactive flavonoid which belongs to the chemical class "flavanone", that quickly emerges as an appealing curative agent which covers a broad spectrum of properties including antioxidant, anti-carcinogenic, hypolipidemic, vasoprotective, and other essential therapeutic properties (Chakraborty et al. 2012).

The phenolic profile of honey vary depending on the floral source and geographical location. Honey composition of phenolic compounds were identified as strongly affected by geographical location, while concentrations of phenolic compounds are reliant on the floral source. Studies have shown that geographical location and floral source have a more considerable impact on flavonoid content than on the phenolic acid profile of honey samples. Results have shown that phenolic acid compounds and flavonoids can be utilized as a botanical marker to determine the floral source and geographical origin of honey samples. Consequently, hesperitin was identified as an investigative compound that can be used in determining the floral source of various honey samples, whether it be unifloral or multifloral (Cheung et al. 2019).

11.5.5 Luteolin

Luteolin is one of the most commonly reported flavonoids in honey which has antioxidant, anti-inflammatory, antitumor properties, and has neuroprotective effects against microglia-induced neuronal cell death (Lin et al. 2008; Rahman et al. 2014). Luteolin is listed as a major component of the flavonoid fraction of mānuka honey (Yao et al. 2003). Luteolin was found to be weakly correlated with non-peroxide antibacterial activity of honey and probable marker compounds for mānuka monofloral honey (Chan et al. 2007).

11.5.6 Kaempferol

Kaempferol is a major flavonoid found in several natural products including bee pollen. Kaempferol exhibits numerous pharmacological properties which includes antimicrobial, anti-inflammatory, antioxidant, antitumor, cardioprotective, neuroprotective, and antidiabetic activities (Imran et al. 2019). Different polyphenols have been identified as floral markers in honey. For acacia honey, kaempferol rhamnosides and rhamnosylglucosides have been proposed as markers. Kaempferol was also identified in eucalyptus honey (Istasse et al. 2016).

11.5.7 Galangin

Galangin is another natural flavonoid found in honey, and is known as a marker compound of honey. Galangin has antimicrobial, anti-diabetic, anti-obesity, anti-tumor, anti-inflammatory, anti-mutagenic, anti-clastogenic, anti-oxidative, radical scavenging, and metabolic enzyme modulating activities (Patel et al. 2012; Ma et al. 2019). Similar with other compounds, galangin was found to have a positive effect in the treatment of cardiovascular diseases and aid in the preservation of other protective antioxidants including vitamin E, vitamin C, and other flavonoids (Khalil and Sulaiman 2010).

11.5.8 Naringenin

Naringenin is considered as one of the most important naturally-occurring flavonoid that is extensively seen in different citrus fruits, bergamot, tomatoes, and other fruits (Salehi et al. 2019). Numerous biological activities such as antioxidant, antitumor, antiviral, antibacterial, anti-inflammatory, anti-atherogenic, antiadipogenic and cardioprotective effects have been attributed to naringenin (Alam et al. 2014; Salehi et al. 2019).

Aside from the sources mentioned, naringenin was also found in many types of honey (Afroz et al. 2016). Significant difference in the content of naringenin in relation to origin of honey was identified. High amounts of naringenin were found in linden honey, chestnut honey, and acacia honey, respectively. On the other hand, the minimum content of naringenin was found in mountain honey (Kurtagic et al. 2013).

11.5.9 Isorhamnetin

Isorhamnetin is another flavonol which is present in an individual's daily diet. It has antioxidant, antiviral, anticancer, antimicrobial, and anti inflammatory effects (Settu and Manju 2017). Isorhamnetin was found to be one of the main phenolic compounds found in bee bread, "a fermented mixture of plant pollen, honey, and bee saliva used as food for larvae and for young bees to produce royal jelly" (Sobral et al. 2017). Isorhamnetin was also detected in most honeys including melon, pumpkin, cherry blossom, rhododendron, rosemary lemon, orange, dandelion, maple, and pine tree honey (Petrus et al. 2011). Isorhamnetin was identified as a complementary biomarker for the identification of the floral origin of Argentinean Diplotaxis honeys (Truchado et al. 2010).

11.5.10 Bee Defensin-1

Bee defensin-1 is the only cationic bactericidal compound curretly identified that is naturally present in honey. It was previously isolated from the royal jelly which is the "main source of food for bee queen larvae and was identified in honeybee hemolymph". Bee defensin-1 is released by the worker bees' hypopharyngeal gland into the gathered nectar with carbohydrate-metabolizing enzymes. Presumably, it aids in the protection of the royal jelly, and of honey against microbial spoilage since antimicrobial properties of honey are dependent on the hydrogen peroxide, methylglyoxal and defensin-1 content (Kwakman et al. 2010; Ilyasov et al. 2012).

Bee defensin-1 amount ranges from 0.04 to 5.17 μg/g of honey. Lesser amounts of bee defensin-1 questions the purity of honey. Defensin-1 is found in all tested types of larval jelly and honey, including Manuka honey, although its amount differes significantly (Valachova et al. 2016).

11.6 International Standards for Honey

The Codex Alimentarius Standard for Honey and European Honey Directive have been widely used worldwide as guidelines describing the standard honey quality criteria. The latest revision of the Codex Alimentarius Honey was in 1998(Codex Alimentarius Commission 1999), while the latest revision for the EU Directive for honey was in 2001 (EC 2001). Codex Alimentarius Standard is generally usable for honey trade globally. However, other regional standards like the

European Honey Regulation may also be recognized, especially when there are local quality requirements that cannot be met if the Codex Alimentarius Standard was to be followed. In New Zealand, for instance, the Unique Manuka Factor Honey Association (UMFHA) has a unique trademark UMF®, which set an independent standard to ensure that honey products have been tested for quality and purity before leaving New Zealand (UMFHA 2019). UMFHA's focus is to identify the unique signature compounds of genuine Manuka Honey to protect consumers and the industry.

The draft for the EU honey standard was found to be somehow identical with the Codex standard, except that specifics on contamination, hygiene, and sugar adulteration found in Codex was not included in the EU Directive. Conversely, there are also points contained in the EU standard that are lacking the in the Codex Standard. Examples include the definition of "industrial" or "bakery-honey" and the question of honey pollen. Codex Alimentarius stated that the quality standards set are not compulsory for governments and can be agreed upon. On the other hand, the EU Honey Directive demanded that all commercial retail honeys should abide by their standards.

Table 11.1 summarizes the criteria mentioned in the CL 1998/12-S of the Codex Alimentarius and to the Council Derivative 2001/110/EC of the EU, and the other quality criteria proposed by the International Honey Commission (IHC) (Bogdanov et al. 2015).

11.7 Challenges in Honey Production

The levels of bioactive substances in honey vary depending on its geographical and botanical origin. Thus, proper labelling of honey products must be advocated so that consumers are not misled. The Codex Alimentarius Standard for Honey is generally accepted worldwide for honey trade. In the wake of expected increase in global and local honey trade, however, issues of adulteration and sub-standard honey production must be given importance, and regulations must be in place even in the regional level.

Climate change is an on-going risk to precision apiculture. Comparing the beehive weights in the optimal beekeeping conditions and during drought in the Mediterranean areas in 2017 showed that bee populations, honey reserves, and pollen spectrum was affected greatly (Flores et al. 2019). Another risk to beekeeping is the phenomenon called the Colony Collapse Disorder (CCD), where honey bee stocks dip dramatically due to unknown reasons. Researchers point to parasites, pathogens, pesticides, or immune system disorders as the drivers of CCD (Stokstad 2007).

Table 11.1 Proposed criteria to assess honey quality and standard

Parameter	European Directive 2001/110/EC	Codex Alimentarius CL 1998/12-S	International Honey Commission (Proposed Standard)
Moisture content			
General	≤ 21 g/100 g	≤ 21 g/100 g	
Heather, clover	≤ 23 g/100 g	≤ 23 g/100 g	≤ 21 g/100 g
Industrial or bake-honey	≤ 25 g/100 g	≤ 25 g/100 g	
Apparent reducing sugars content			
Honeys not listed below	≥ 65 g /100 g	≥ 65 g /100 g	
Honeydew honey or blends of honeydew honey and blossom honey	≥ 45 g /100 g	≥ 60 g /100 g	
Xanthorrhoea pr.	≥ 53 g /100 g	≥ 53 g /100 g	
Apparent sucrose content			
Honeys not listed below	≤5 g/100 g	≤ 5 g/100 g	
Robinia, Lavandula, Hedysarum, Trifolium, Citrus, Medicago, Eucalyptus cam., Eucryphia luc. Banksia menz[a] Rosemarinus[b]	≤10 g/100 g	≤ 10 g/100 g	
*Calothamnus san., Eucalyptus scab., Banksia gr., Xanthorrhoeapr., h*oneydew honey and blends of blossom with honeydew honey	–	≤15 g/100 g	
Water-insoluble solids content			
General	≤ 0.1 g/100 g	≤ 0.1 g/100 g	
Pressed honey	≤ 0.5 g/100 g	≤ 0.5 g/100 g	
Mineral content (ash)			
General	≤ 0.6 g/100 g	≤ 0.6 g/100 g	
Honeydew or blends of honeydew and blossom honey or chestnut honey	≤ 1.2 g/100 g	≤ 1.2 g/100 g	
Acidity			
In general	≤ 50 meq/kg	≤ 50 meq/kg	
Baker's honey	≤ 80 meq/kg		
Diastase activity			
After processing and blending (diastase number in Schade scale)			
General	≥ 8	≥ 8	
Honeys with natural low enzyme content	≥ 3	≥ 3	
Hydroxymethylfurfural (HMF) content			
In general, except baker's honey	≤ 40 mg/kg		
After processing and/or blending	≤ 60 mg/kg	≤ 60 mg/kg	
Honeys of declared origin from regions with tropical climate and blends of these honeys	≤ 80 mg/kg		
Sugar content			
Sum of fructose and glucose			
Honeys not listed below		≥ 60 g/100 g	≥ 60 g/100 g

(continued)

Table 11.1 (continued)

Parameter	European Directive 2001/110/EC	Codex Alimentarius CL 1998/12-S	International Honey Commission (Proposed Standard)
Blossom honeys Honeydew honey or blends of honeydew honey and blossom honey		≥ 45 g/100 g	≥ 45 g/100 g
Sucrose			
Honeys not listed below		≤ 5 g/100 g	≤ 5 g/100 g
Alfalfa (*Medicago sativa*), Citrus spp., false Acacia (*Robiniapseudoacacia*), French honeysuckle (*Hedysarum*), Menzies Banksia (*Banksia menziesii*), red gum (*Eucalyptus camaldulensis*), leatherwood (*Eucryphia lucida*), Eucryphia milligani		≤ 10 g/100 g	
Lavender (*Lavandula spp*), borage (*Borago officinalis*)		≤ 15 g/100 g	
Banksia, Citrus, Hedysarum, Medicago, Robinia			≤ 10 g/100 g
Lavandula			≤ 15 g/100 g
Electrical conductivity			
(a) Honey not listed under (b) or (c), and blends of these honeys		≤ 0.8 mS/cm	≤ 0.8 mS/cm
(b) Honeydew and chestnut honey, except the honeys listed below and blends with those		≥ 0.8 mS/cm	≥ 0.8 mS/cm
(c) Strawberry tree (*Arbutus unedo)*, bell heather (*Erica*), Eucalyptus, lime (*Tiliaspp*), Ling heather (*Calluna vulgaris*) Manuka or jelly bush (*Leptospermum*), tea tree (*Melaleuca spp*) (exceptions listed in Codex Alimentarius)			
(d) *Arbutus, Banksia, Erica, Eucalyptus, Eucryphia, Leptospermum, Melalueca, Tilia* (exceptions listed in IHC proposal)			

[a]The European draft refers to honeydew honey and mixtures of honeydew and blossom honey, acacia, *Banksia* and *Citrus* honeys
[b]The IHC proposes also that *Rosemarinus* be included in this list

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