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Review paper

Bioactive compounds in honey: a literature overview

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ABSTRACT

Honey is a natural product used worldwide and has a multiple nutritional and health benefits. From ancient times, honey was used as a natural sweetener and healing agent. The specific composition of honey includes primarily carbohydrates, but organic acids, enzymes, vitamins, proteins, volatile compounds, phenols, flavonoids and minerals as well. These compounds are provenly related to honeys' antioxidant, anti-inflammatory and antimicrobial properties. This paper shows the latest scientific data about bioactive compounds and health benefits of honey.

1. Introduction

From ancient times, honey was not only used as a natural sweetener but also as a healing agent (*Helmi*, 2012). Increased rates of different cancers, autoimmune diseases and chronic non-infective and infective diseases have led to a search for new, reliable, non-synthetic, traditional and natural therapeutic products. Therefore, science is now returning to natural products with new approaches in an endeavour to understand older medicinal applications. In that respect, prevention or therapy of diseases by bee products is defined as a very ancient medical practice and is one of the areas in which bee products are used. Moreover, the use of natural products in the nutritional and/or therapeutic context has been growing.

According to the statistical data reported by the World Health Organisation, up to 80% of the population in some developed countries prefer natural products in primary health care (*WHO*, 2014). Nowadays, natural materials are more acceptable to consumers, and if these alternative approaches are effective, this could reduce the reliance on more synthetic substances (*Slover et al.*, 2009). Furthermore, since modern medicine is undergoing a crisis because of the adverse effects of synthetic drugs on human health and increased anti-microbial resistance, natural alternatives are more discussed. In that context, novel scientific data about health benefits of honey are presented in this paper.

2. Materials and methods

A literature search was conducted to identify recent scientific data about bioactive compounds and health benefits of honey. Scientific online databases including Web of Science, Science Direct and Pub Med were used. The following keywords were used individually and in combination as inclusion criteria for articles to be considered for this review: bee products, honey, health, antibacterial, antioxidant, phenolic compounds, and microorganisms.

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3. Composition of honey

Codex Alimentarius (2001) define honey as 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. Numerous studies from different countries have presented the high nutritional value and health benefits of bee products (honey, bee bread, bee pollen, beeswax, bee toxin, propolis, royal jelly and bee brood). The results of these studies have shown a positive impact on human health (antioxidant, antimicrobial, anti-fungal, anti-inflammatory, etc.), which correlated to the high contents of specific bioactive compounds. The popularity of using natural materials, such as honeys, is due to their potent activities and generally very low toxicity (*Albaridi*, 2019).

3.1. Nutritional value of honey

Different studies show that honeys have a high nutritional and biological value (*Tsavea et al*., 2022; *Ávila et al*., 2022; *Graikou et al*., 2022). Honey is an excellent source of energy, as 100 g of honey supplies about 306 kcal. Similarly, 20 g of honey is the usual quantity per serving or tablespoon that provides about 61.2 kcal, which represents more or less 3% of the energy necessary per day (*Bogdanov et al*., 2008). The main constituents of honey are the carbohydrates that are used for human body energy requirements after being rapidly absorbed into the blood without previous digestion (*Ajibola et al*., 2012). According to chemical composition, honey contains various sugars and other substances, such as organic acids, enzymes, vitamins, proteins, volatile compounds, several bioactive substances (phenols and flavonoids) and minerals.

The main sugars are carbohydrates (60–85%), predominantly fructose and glucose (*Samarghandian et al*. 2017; *Machado De-Melo et al*., 2018). The water content of honey is about 20% and it is related to different factors, such as the botanical and geographical origins of nectar, season of harvesting, intensity of nectar flux, degree of maturation, manipulation by beekeepers during the harvest period, as well as to the extraction, processing and storage conditions (*Ojeda de Rodrıguez et al*. 2004; *Pontara et al*., 2012; *Ciric et al*. 2019; *Ćirić et al*., 2021). Honey's protein content is very low and ranges up to 0.5%. The physicochemical characteristics and quality of honey are defined in different national and EU regulations.

3.2. Antioxidants in honey

The antioxidant activity of different honeys has been already measured using different in vitro methods (*Martinello and Mutinelli*, 2021). The characterization of the polyphenolic profile was carried out mainly to determine which specific compounds might have the strongest effect upon the antioxidant and antimicrobial properties. Twenty compounds were identified in honey samples, eleven of which were flavonoids (sakuranetin dimer, rutin, isorhamnetine 3-O-rutinoside, quercetin 3-O-glucuronide, orientin, vitexin, quercetin, epicatechin, kaempferol, pinobanksin and apigenin), eight were phenolic acids (gallic, neochlorogenic, chlorogenic, protocatechuic, caffeic, sinapic, 3,4-di-O-caffeoylquinic and protocatechuic acid-O-hexoside acids), and one compound belonged to ellagitannins (ellagic acid) (*Sawicki et al*., 2022). Gallic, ellagic, neochlorogenic, chlorogenic, protocatechuic and sinapic acids were detected in honeys in different studies (*Sawick et al*., 2022; *Yucel et al*., 2016; *Habryka et al*., 2021). Also, sakuranetin dimer, caffeic acid and quercetin were detected only in honey. Similar, *Habryka et al*. (2021) found six phenolic acids (ferulic, gallic, p-hydroxybenzoic, caffeic, p-coumaric and protocatechuic acids) and four flavonoids (kaempferol, chrysin, galangin and quercetin) in Polish multifloral honey. Differences in the polyphenolic profiles and contents can be related to the laboratory method of extraction and the sensitivity of the analytical technique. Moreover, the number of compounds detected could be related to the geographic region of honey origin.

In most of the studies, the polyphenolic compounds were measured by the 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and [2,2-di(4-tert-octylphenyl)-1-picrylhydrazyl] (DPPH) assays and the photochemiluminescence (PCL) method. The order of average antioxidant activity for the honey was as follows: ABTS > ACL (lipophilic antioxidants) > ACW (hydrophilic antioxidants) > DPPH. The multifloral honeys were also tested by *Sawicki et al*. (2022) for their ability to scavenge superoxide anion radicals. The higher antioxidative ability of hydrophilic antioxidants was noticed in comparison to the honeys' lipophilic antioxidants. Moreover, the results for honey are consistent with the findings from another study examining multifloral Polish honey (*Wesołowska and Dzugan*, 2017).

Different flavonoids in honey originate from pollen, nectar or propolis (*Khalil et al*., 2012). According to *Bogdanov et al*. (2008), the main flavonoids found in honey are pinocembrin, apigenin, campferol, quercetin, pinobanksin, luteolin, galangin, hesperetin and isorhamnetin. *Khalil et al*. (2011) found the total content of phenolic compounds in Tualang honeys ranged between 26.99 ± 0.13 µg/g and 42.23 ± 0.64 µg/g. *Lianda et al*. (2012) found that multifloral honeys have the highest content of phenolic compounds compared with other honey types. The highest flavonoid content was identified in heather honey (44.5 ±3.2 µg/g) followed by buckwheat honey (41.7 ±2.1 µg/g), lime honey (32.0 ±1.7 µg/g) and rape honey (13.5 ±1.3 µg/g) (*Kaškonienė et al*. 2009). *Cheung et al*. (2019) not detected flavonoids in wolfberry honey, acacia honey and loquat honey. The highest total content of phenolic compounds was found in Manuka honey (250.18 ± 14.39 µg/g). On the other hand, eucalyptus honey has the highest phenolic compounds (41.65 ± 10.35 µg/g) (*Cheung et al*., 2019).

3.3. Antimicrobial compounds in honey

Various components contribute to the antibacterial efficacy of honey: the sugar content, polyphenol compounds, hydrogen peroxide, 1,2-dicarbonyl compounds and bee defensin-1 (*Almasaudi*, 2021). Phenolic compounds are found at high levels in honey and may contribute to its antibacterial activity. *Estevinho et al*. (2008) found that dark honey has a high amount of flavonoids and this has been shown to have a good correlation with its higher antibacterial activity. However, the amount of phenolic acid in honey is influenced by the geographic location and the botanical source of the nectar. The sugar content, polyphenol compounds, hydrogen peroxide, 1,2-dicarbonyl compounds and bee defensin-1 in honey depend on the source of nectar, bee type and honey storage. These components in honey work synergistically, allowing honey to be potent against a variety of microorganisms, including multidrug resistant bacteria, and/or to modulate microorganisms' resistance to antimicrobial agents. The effectiveness and potency of honey against microorganisms depends on the type of honey produced, which is contingent on its botanical origin, the health of the bee, its geographical origin and the processing method.

The natural components of honey have various activities against different microorganisms. Honey has excellent antibacterial efficacy against methicillin-resistant *Staphylococcus aureus* (MRSA) and a variety of *Pseudomonas*, which are often associated with wound and burn infections (*Hazrati et al*. 2010). Interestingly, Manuka honey, which originates from New Zealand, differs from other types of honey in that it contains a high concentration of methylglyoxal, rather than hydrogen peroxide. This compound is considered the main antimicrobial agent in Manuka honey.

Also, honey has been used in the medical treatment of surface wounds, burns and inflammation, and has a synergistic effect when applied with antibiotics (*Samarghandian et al*., 2017). *Chein et al*. (2019) found that the application of antibiotics with honey yielded better antimicrobial potential, and synergistic effects were noted against biofilms.

4. Conclusion

Honey is a natural sweetener, rich in bioactive compounds that have proven health-promoting properties. It has antimicrobial potential, showing a broad spectrum of antibacterial activities against microorganisms. Many important factors contribute to its antimicrobial efficacy, including osmolarity, hydrogen peroxide content, low pH, phenolic acid levels, and flavonoids. Honey has been used in the treatment of surface wounds, burns and inflammation, and has a synergistic effect when applied with antibiotics. The antioxidant and antibacterial activity of honey could partly be due to the presence of enzymes, such as glucose oxidase and catalase, as well as to compounds, such as phenolic acids, flavonoids and organic acids. In the future, more research needs to be conducted to understand the full potential of honey use.

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