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Ana Valéria Brazini
Faculty of Technology of Marilia (Fatec), Av Castro Alves, Marília, São Paulo-Brazil.

José Vitor da Silva
Faculty of Technology of Marilia (Fatec), Av Castro Alves, Marília, São Paulo-Brazil.

Flavia Maria Vasques Farinazzi-Machado
Faculty of Technology of Marilia (Fatec), Av Castro Alves, Marília, São Paulo-Brazil.

Renata Bonini Pardo, Claudia Dorta, Elke Shigematsu, Juliana Audi Giannoni
Faculty of Technology of Marilia (Fatec), Av Castro Alves, Marília, São Paulo-Brazil.

Correspondence:
Flavia Maria Vasques Farinazzi-Machado
Faculty of Technology of Marilia (Fatec), Av Castro Alves, Marília, São Paulo-Brazil.

Benefits of honey for human health and the environmental importance of bees

Ana Valéria Brazini, José Vitor da Silva, Flavia Maria Vasques Farinazzi-Machado, Renata Bonini Pardo, Claudia Dorta, Elke Shigematsu, Juliana Audi Giannoni

Abstract
The aim of this study was to gather information about the beneficial effects of honey on human health and the importance of bees in environmental preservation. Through a descriptive exploratory study and research in full scientific articles, it was observed that honey has been used for thousands of years as food and for therapeutic purposes. Scientific studies have demonstrated the beneficial effects of using honey in experimental and human models, in view of its anti-inflammatory, antioxidant, healing, antimicrobial and anticancer properties. Such effects are attributed to the expressive presence of phenolic and flavonoid compounds, whose concentrations are directly influenced by the origin of the flora, seasonal factors, and bee species, with the highest levels found in stingless honey bees. The environmental importance of bees is reflected in the ecosystem service performed by these insects as pollinating agents, since they are responsible for the production of food and livelihoods and have a significant role in linking wild ecosystems to agricultural production systems.

Keywords: Therapeutic properties, Phenolic compounds, Antioxidants, Stingless bees, Pollination.

1. Introduction

Honey is a natural product produced by bees; it is a nutritious compound derived from the nectar of flowers. When nectar is ingested by bees, it is synthesized by digestive enzymes inside their digestive tract and stored in combs inside the hives, serving as food for both the developing larvae and the adult insects of the colony. This food has been used by humans since prehistoric times [1, 2].

There are records of the use of honey by the Hindus as early as 6.000 B.C., and by the Sumerians as early as 5.000 B.C. Some inscriptions in the pyramids of Egypt show a creation of bees in 2.400 B.C., being considered the first beekeepers. The use of honey in the treatment of wounds and ulcers is described in the Smith papyri from 1.700 B.C. The Teutons (Germanic peoples), in 200 B.C., used mead, a fermented honey-based drink, to celebrate their weddings, and there are also several citations in the Bible about the consumption of this food [3, 4].

In general, honey has a viscous texture with a sweet taste. Its taste, acidity, color and smell may vary according to the flowering, the environmental conditions, and the bee species [5].

Honey contains combinations of several elements. It contains sugars such as fructose (about 42%), glucose, sucrose and maltose; vitamin A, vitamins C, H, PP and B Complex, in addition to containing minerals such as calcium, copper, chlorine, manganese, iron, sulfur, potassium, silica, sodium, boron and phosphorus, in addition to proteins [6, 7, 8].

The presence of phenolic and flavonoid compounds, secondary metabolites from honey plants, make honey a functional food with expressive metabolic and physiological effects beneficial to health [9, 10]. The concentrations and types of these components in each type of honey are directly influenced by the origin of the flora, seasonal factors and bee species [11, 12]. Therapeutic activities have been attributed to honey and its products, they are described in the literature, including antibacterial, anti-inflammatory, depurative, emollient, energetic, healing, immunostimulant and antioxidant activities [13, 14, 15].

In addition to the importance of honey products in food and human health, bees are usually the most essential insects, acting as pollinators of native and cultivated plants, playing an indispensable role in the conservation of the ecosystems where they live; in the economic production of different cultures; in the evolutionary adaptation of plants and maintenance of wild plant populations [16, 17]. The aim of this study was to gather information about the beneficial effects of honey on human health and the importance of bees in environmental preservation.

2. Material and Methods

This article is a descriptive exploratory study. This is a qualitative study of scientific literature review, carried out by searching and reading full articles, in the following databases: Scholar Google, Scielo and PubMed. The articles were selected using the descriptions: "honeybee"," environmental preservation", "anti-inflammatory", "antioxidant", "wound healing", "antibacterial", "phenolic compounds", "stingless bees", "pollination", in a combined way two by two. In addition, a time interval of 10 years (2013 to 2023) was recommended.

3. Results & Discussion

Antimicrobial Properties

Among the many properties of honey is its ability as an antimicrobial agent. According to Molan [18], honey, as it is a supersaturated solution of sugars and has low water activity, does not offer favorable conditions for the growth of bacteria, in addition to having a natural acidity that inhibits the action of several pathogens.

According to Silva [19], when bees secrete honey, they excrete glucose oxidase enzymes, which when in the presence of oxygen and water are capable of converting glucose ($C_6H_{12}O_6$) into gluconic acid ($C_6H_{12}O_7$) and hydrogen peroxide (H_2O_2), which have a strong antioxidant action and attack the envelope of certain microorganisms.

In a study by Azevedo [20], the application of geopropolis from bee *Plebeia aff. flavocincta* to control the growth of *Staphylococcus aureus* and *Enterococcus faecalis* proved to be effective, considering that these microorganisms did not grow on the surface where geopropolis was dripped. In addition, the use of honey proved to be effective in combating the growth of Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) microorganisms, in a study conducted by Caldas [21].

In addition to its antimicrobial activities, honey has recently been studied for its positive association with the human intestinal microbiota, playing an essential role in the prevention and treatment of chronic diseases, due to the presence of phenolic compounds that promote a greater balance between pathogenic microorganisms and the beneficial population of the intestinal microbiome [22, 23].

Healing Effects

Wound healing can be influenced by factors such as pathophysiological and exogenous ones. Wound infections have an increased risk when there are favorable conditions for the growth of bacteria, the most frequent being *S. aureus* and Pseudomonas auruginosa, this one is present in chronic diseases, delaying healing and decreasing the success of skin grafts in wounds [24].

In the scientific literature, honey is mentioned for its healing properties, in view of its antibacterial and anti-inflammatory activity, through which it maintains moisture in the wound due to its high viscosity, forming a barrier, preventing infections, being effective in healing of various types of lesions, especially in burns, facilitating debridement [25]. Honey also has adhesive characteristics, aiding in the fixation of skin grafts, improving the healing of surgical and septic wounds [26, 27].

Reports of studies in rabbits treated with topical use of honey in cavitary wounds showed less edema and necrosis, fewer polymorphonuclear and mononuclear cell infiltrations, better wound contraction and epithelialization, and lower concentrations of glycosaminoglycans and proteoglycans; honey stimulated collagen synthesis with the formation of new tissue, in addition to the development of new blood vessels [24].

Various plant-derived compounds and organic compounds from bees, which act directly on the immune system, the so-called immunomodulators, can help in the healing process. According to some studies, honey acts directly on the main skin cells, keratinocytes and fibroblasts, having the ability to regenerate their cells [28], in view of its low pH and high free acidity [29]. Topical application of *Melipona subnitida* honey in infected wounds of Wistar rats stimulated greater synthesis of collagen, leukocytes, fibroblasts and cytokines (especially TNF), reducing healing time, in a study conducted by Alves et al. [25].

Honey is also being included in treatments such as pityriasis, a skin disease characterized by the appearance of spots on the skin, mycosis, seborrhea, diaper dermatitis, psoriasis and anal fissures [28].

Anti-inflammatory Effects

Inflammation is a common underlying cause of many disorders, initiating numerous pathogenic changes in metabolic pathways, tissue damage, and even necrosis and apoptosis. Inflammatory diseases are diagnosed after an increase in inflammatory cytokines such as interleukins (IL)-1β, IL-6 and tumor necrosis factor-α (TNF-α) [30].

Honey and its polyphenolic compounds such as pinocembrin, luteolin, galangin, chrysin and quercetin (3,3',4',5,7-pentahydroxyflavanone) showed anti-inflammatory, immunomodulatory, antiproliferative and antimetastatic properties, demonstrating induction of cell apoptosis and antioxidant activity in many types of cancer, in a review by Afrin et al. [31]. According to Borsato et al. [32] stingless bee honey extract can reduce the production of reactive oxygen species, leukocyte migration and edema, contributing to the anti-inflammatory impact on tissues. The antioxidant effect of honey prevents activation of signaling pathways sensitive to oxidative stress such as NF-κB (nuclear factor kappa beta) and MAPK (mitogen-activated protein kinase), it also reduces the production of inflammatory factors IL-6, TNF -α and IFN-γ [33].

Also, in a study by Kowalska et al. [34] it was demonstrated that the use of bee products encapsulated with arabinoxylans isolated from rye bran could significantly improve the inflammatory response in macrophages of the RAW 264.7 cell line, treated with lipopolysaccharide (LPS), decreasing the secretion of IL-6, TNF -α and nitric oxide (NO).

Studies have also revealed that honey can be used in the prophylaxis and treatment of oral mucositis, an acute inflammation of the mucous membranes of the oral cavity, in individuals undergoing radiotherapy and chemotherapy

[35, 36]. It has also been suggested by the scientific literature that, due to its anti-inflammatory potential, honey from stingless bees may help reduce the severity of pulmonary manifestations, which characterize *severe acute respiratory syndrome*, in COVID-19 infections [37, 38].

Antioxidant Properties

The mechanisms implicated in the antioxidant activity of honey involve glutathione reductase (GR), vitamin C (Vit. C), beta-carotene, uric acid, hydrogen donation, metal ion chelation (MIC) or free radical scavenging (FRR). In addition, honey reduces reactive oxygen species (ROS) and stimulates biomolecules (nucleic acids, proteins, carbohydrates, lipids) [39].

In a study by Al-Waili [40], the oral administration of honey dissolved in water (1.2 g/kg of body weight) in men and women for a period of two weeks, promoted an increase in the plasmatic levels of beta-carotene (3 %), glutathione reductase (7%), vitamin C (47%) and uric acid (12%). It increased the percentage of monocytes by 50% and slightly increased the percentages of lymphocytes and eosinophils. A decrease in AST (aspartate aminotransferase) and ALT (alanine aminotransferase) liver enzymes of 22% and 18%, respectively, was also observed, as well as a reduction in levels of creatine kinase, lactic acid dehydrogenase and IgE (immunoglobulin E).

Honey's antioxidant capacity varies according to its floral origin, that is, its botanical source, possibly due to differences in the amounts of secondary metabolites and enzyme activities [41]. Darker honey has more antioxidants than lighter honey [42].

Stingless bee honey contains a higher level of phenolic acids and flavonoids than honey produced by *Apis mellifera* [20]. Duarte et al. [43] identified the presence of high concentrations of polyphenol compounds (106.01 ± 9.85 mg GAE/100 g) in honey extracted from stingless bees cultivated in the state of Alagoas, northern Brazil.

Anticancer Properties

In addition to its numerous benefits, such as healing and antioxidant properties, studies also indicate that honey has anticancer properties. It works by preventing the proliferation of cancer cells.

According to Teyssier [28], these anticancer characteristics may involve different processes, such as increasing apoptosis of cancer cells through depolarization of the mitochondrial membrane, inhibition of cyclooxygenase-2 by different compounds, as well as the release of H_2O_2 in amounts that are cytotoxic.

Mohammed et al. [44] studied the anticancer effects of honey samples taken from Acacia varieties, on human cancer cell lines HCT116 (colon), MCF7 (breast) and HepG2 (liver). High-altitude acacia honey had significantly more effective anticancer activity against HCT116 and MCF7 cells compared to low-altitude honey, possibly due to higher concentrations of total flavonoid compounds (10.63 ± 0.53 mg quercetin equivalent [QE]/100 g) in its composition.

In an *in vitro* study conducted by Ahmad et al. [45] it was observed that honey from stingless bees, produced locally in a region of Malaysia, significantly inhibited cell proliferation of a lineage of human malignant glioma (U-87 MG), characterized by its aggressive growth, rapid progression, and poor prognosis. The results obtained, according to the authors, were dependent on time and dose, considering that the inhibition of 50% of cell viability (IC50) for U-87 MG cells was obtained with 10% of treatment with honey.

Environmental Importance

In addition to the various health benefits attributed to honey produced by bees and which are scientifically proven, the ecosystem service constantly performed by these insects as pollinating agents, responsible to produce food and livelihoods, and for their expressive performance in linking wild ecosystems to agricultural production systems is considered invaluable and precious [46, 47].

Bees are the main "crossing" agents of the environment, as they are attracted by the sweet substances of vegetables, carrying pollen from flowering plants in their hair, which is extremely important for the development of their hive, being their main source of proteins, and by ensuring the development of their family, bees perpetuate the plant species [48].

The interaction between bees and plants ensured success in cross-pollination for plants, which constitutes an important evolutionary adaptation of them, increasing the vigor of species, enabling new combinations of hereditary factors, ensuring important genetic variation for the development of species, and increasing the fruit and seed production [49].

The presence of bees indicates environmental quality, that is, the environmental health of existing ecosystems [50].

The production of many foods depends on the pollination process. According to Klein et. al [47], about 35% of the world's food depends on pollinating agents, among which bees, specifically, act in the fertilization of about 70% of the plant species that are cultivated in the world, being responsible for the pollination of agricultural and natural ecosystems, in addition to the preservation and diversification of the flora [51, 52, 53]. According to a study developed by Giannini et al. [54], among 141 traditional Brazilian crops, at least 85 depend on pollinating insects, the vast majority represented by bees, which also contribute to increasing the production, weight and number of seeds in the fruits.

Studies indicate that Apis mellifera L. (Hymenoptera: Apidae) bees have been the most used worldwide for pollination of cultivated plants. However, Garibaldi et al. [55] point out that pollination services in agricultural areas do not depend only on the species of domesticated bees, but also on the populations of wild bees that are present in different environments. Thus, the bees of the Meliponini group (stingless) generally belong to the genera Trigona (Irapuá, Arapuá), Melipona (Munduri, Rajada, Guarupu, Mandaçaia, Uruçu Amarelo, Jandaíra), Plebeia (Mirim guaçu) among others [56].

Advances in human interventions on the environment such as agriculture and the insertion of pesticides in the agricultural environment; the expressive deforestation; removal of vegetation cover as a source of energy and incorporation into agriculture and livestock and the process of urbanization have caused important environmental impacts, generating greater fragility and vulnerability of the environment, compromising biodiversity, and causing significant consequences for the communities of organisms that make up the ecosystem, including pollinating agents. The number of these agents ends up decreasing due to the scarcity of sufficient resources to feed themselves and form

their nests [50].

During the celebrations of World Bee Day in 2022, celebrated on May 20, the Food and Agriculture Organization of the United Nations (FAO), warned about the decline of pollination services in many parts of the world. In a speech given by FAO Director-General, Qu Dongyu highlighted that "The number of bees, pollinators and many insects is decreasing due to unsustainable agricultural practices, pesticides, pests and pathogens, habitat destruction and climate crisis." Bees and other pollinators play a vital role in maintaining Earth's ecosystems. They are critical to food production and livelihoods and directly link wild ecosystems to agricultural production systems [46].

4. Conclusions

Honey is considered a product empirically and traditionally very explored and consumed by the oldest populations, highly marketed as food, having its therapeutic properties, such as anti-inflammatory, antioxidant, microbial, healing, anticancer, among others, widely recorded by the scientific literature. Currently, a closer look has turned to the protection and management of many species of bees, revealing the importance of these insects, both to produce honey as a functional food, as well as for the maintenance of biological diversity, environmental preservation and to ensure food production worldwide.

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