

Review Article

Bioactive compounds and therapeutic benefits of honey

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Abstract

Natural sweetener honey has been valued for generations for its delectable flavor and therapeutic benefits. This mini-review examines the various medicinal advantages of the bioactive substances present in honey. Although sugars are the main component of honey, it also contains a variety of

secondary metabolites, including phenolic chemicals, flavonoids, enzymes, and peptides. The antioxidant, anti-inflammatory, antibacterial and wound-healing effects of honey are a result of these bioactive substances. Traditional medicine has used honey to cure a variety of illnesses, and modern scientific investigations have offered strong evidence in favor of honey's therapeutic potential. In order to highlight honey's promising potential as a natural medicine, this article provides an overview of the present level of knowledge on its bioactive chemicals and their applications in human health.

Key words

Honey, Composition, Bioactive compounds, Therapeutic benefits.

Introduction

Honey, a sticky, sweet liquid made by honeybees from flower nectar, has played a significant role in human history for thousands of years. Honey has long been praised for its therapeutic qualities in many cultures around the world, while being mostly known for its gastronomic delights. Honey has a wide range of bioactive chemicals in its complex chemical makeup, which is what gives it its therapeutic potential. In order to shed light on the scientific justifications that have supported honey's use as a natural treatment, this mini-review attempts to give an overview of the bioactive chemicals that are present in honey and their related therapeutic advantages.

The floral source, place of origin, and techniques of processing all have a significant impact on the composition of honey. Despite this, the majority of the dry weight of honey is made up of carbohydrates, namely glucose and fructose [1]. However, honey's diverse bioactive components, such as phenolic compounds, flavonoids, enzymes, peptides, organic acids, and volatile chemicals - distinguish it from simple sugar syrup [2-4]. The antioxidant, anti-inflammatory, anti-bacterial, and wound-healing effects of honey are all attributed to its secondary metabolites [5-7].

Ancient civilizations like the Egyptians, Greeks, and Chinese used honey in traditional medicine because of its alleged therapeutic properties [7]. Scientific research over the last few decades has gotten more and more interested in figuring out honey's medicinal potential. Its effectiveness in

treating wounds [8], antibacterial activity against a variety of infections [7], and anti-inflammatory benefits [5] have all been the subject of numerous research.

The goal of this mini-review is to compile the most recent information on the bioactive components in honey and the various therapeutic uses for them. We want to present a complete view on honey's potential as a natural cure in contemporary healthcare by combining existing research findings.

Therapeutic history of honey

Evidence from Stone Age artwork reveals that 8000 years ago was when diseases were first treated with bee products like honey. The use of honey as a medication dates back thousands of years, as evidenced by ancient scrolls, tablets, and books such the Sumerian clay tablets (6200 BC), Egyptian papyri (1900-1250 BC), Veda (Hindu literature), Holy Koran, Bible, and Hippocrates (460-357 BC) [9-11]. The therapeutic potential and activity of honey were clearly described in the Qur'an [12].

The Quran refers to honey as a food that is healing. There are numerous Hadith references that support the benefits of honey for health. For instance, the Prophet Muhammad (peace be upon him) stated in a Hadith recorded in Sahih Al-Bukhari that "healing is in three things: a gulp of honey, cupping, and branding with fire (cauterising)." The Prophet Muhammad (peace be upon him) expressly acknowledged the curative value of honey. Additionally, according to a Hadith from Tirmidhi, he recommended

believers to "make use of the two remedies: honey and the Quran." This prescription included using honey to treat a variety of health problems, such as sore throats and coughs. In a Hadith from IbnMajah, the Prophet Muhammad (peace be upon him) stated that honey found use as a topical therapy for wounds, burns, and even cosmetic purposes, demonstrating its adaptability in improving health and well-being within the context of Tibb e Nabvi.

Composition of honey

A remarkable and broad-ranging natural product, honey has a complex composition that comes from the plant sources that honeybees visit to gather nectar. The composition of honey can vary greatly, reflecting the variety of nectar types available, with about 300 recognized kinds [13]. Honey's main ingredients are primarily carbohydrates, which make up 95–97% of its dry weight. Notably, fructose and glucose are the two monosaccharides that predominate, playing crucial roles in both the nutritional value and the physical characteristics of honey. Honey contains a wide range of bioactive components that complement its carbohydrate composition. Proteins, vitamins, amino acids, minerals, and organic acids are a few of these that collectively add to the food's nutritional worth. In addition, honey contains a variety of secondary metabolites, including as anthraquinones, polyphenols, reducing chemicals, alkaloids, glycosides, cardiac glycosides, and flavonoids [14-16]. These substances enhance honey's chemical diversity in addition to the existence of numerous disaccharides, trisaccharides, and oligosaccharides. Several sugars are generated as honey ripens and matures, enhancing its carbohydrate composition. The main organic acid in the mixture is gluconic acid, which is produced when glucose is oxidized. Acetic, formic, and citric acids are also present in very small levels. Together, these organic acids give honey its distinctive acidic quality and keep its pH between 3.2 and 4.5 [17].

The nine necessary amino acids and the majority of the non-essential amino acids, with the exception of asparagine and glutamine, are both present in honey. In honey, proline appears as the main amino acid [18]. Protein in honey is largely made up of enzymes, such as diastase, invertases, glucose oxidase, catalase, and acid phosphatase [19]. Water-soluble vitamins are present in honey, however their amounts are modest and fall short of the daily requirements. Notably, the water-soluble vitamin found in honey most frequently is vitamin C. The variety of minerals found in honey includes important trace elements like silicon, rubidium, vanadium, zirconium, lithium, and strontium as well as key minerals like phosphorus, sodium, calcium, potassium, sulphur, and magnesium. However, as a pollutant, honey may occasionally include minute quantities of heavy metals like lead, cadmium, and arsenic [20].

The roughly 600 volatile chemicals in honey are thought to be responsible for its unique scent and potential medicinal benefits [21]. The chemical classes represented by these volatile substances—which are present in relatively small amounts—include aldehydes, alcohols, hydrocarbons, ketones, acid esters, benzene derivatives, pyran, terpenes, norisoprenoids, sulphur, furan, and cyclic compounds. Honey's complex and varied makeup emphasises how important it is as a natural substance with both culinary and possible health-promoting characteristics.

One of the most important bioactive components abundantly present in honey are flavonoids and polyphenols, which are known for their strong antioxidant capabilities [22, 23]. The existence of approximately thirty different polyphenols has recently come to light in honey, with levels and types varying greatly depending on the floral source, climate, and geographic location. Galangin, quercetin, kaempferol, luteolin, and isorhamnetin are a few bioactive substances that are consistently present in different honey kinds [24]. However, other substances, such as

naringenin and hesperetin, are exclusive to certain kinds of honey.

Numerous studies have been conducted on the various components of honey, indicating its capacity to have a variety of positive impacts. Both antibacterial activity, which prevents the growth of germs, and antioxidant capabilities, which fight oxidative stress and cellular damage, is included in these actions. Honey also exhibits anti-inflammatory and anti-proliferative qualities, and it has demonstrated great potential in the fields of cancer and metastasis therapy. Honey's beneficial and diverse significance as a natural product with a variety of health-promoting benefits is highlighted by the bioactive chemicals that make up honey.

Therapeutic benefits of honey

Antimicrobial activity

Due to its powerful antimicrobial properties, honey has drawn a lot of attention. Numerous studies have shown that it has inhibitory effects on a variety of bacterial species [25]. Notably, honey-derived alcohol extracts have shown inhibitory effects on a variety of bacterial strains, including aerobes and anaerobes as well as both Gram-positive and Gram-negative bacteria. What makes honey unique is its capacity to exert potent antimicrobial effects on both pathogenic and non-pathogenic microorganisms, including yeasts and fungi. Surprisingly, honey's effectiveness endures even against strains that have become resistant to numerous antibiotics. It's important to note that depending on the dose used, honey's antibacterial activity might take on different forms. Bacteriostatic effects, which prevent bacterial growth and replication, may be seen at lower doses while bactericidal effects, which successfully eradicate bacteria, may be seen at greater concentrations. This diversity in antimicrobial action shows honey's significance in medicinal and therapeutic applications and highlights its potential as a significant natural resource in battling bacterial infections [26].

Antioxidant activity

Despite its long history of use in domestic and medicinal settings, honey's antioxidant capabilities have only recently attracted major attention [27]. As the need for antioxidants in diet grows, honey is becoming more and more well-liked as a natural source of these beneficial substances. Cellular damage and disruption of genetic structures are results of oxidative stress, which is caused by an imbalance between the body's natural defence mechanisms and the generation of free radicals. The most prevalent antioxidants in honey are phenols, which include substances like quercetin, hesperetin, and chrysin. Additionally, honey has melanoidins, which are Maillard products that help increase its antioxidant ability [28]. A prominent phenolic substance found in honey called quercetin directly interacts with cellular transcription factors and efficiently inhibits their activity. This inhibition counteracts the biological consequences of free radicals by outpacing the phosphorylation and activation processes. Quercetin has also been demonstrated to decrease the levels of protein expression in human fibrosarcoma cells and to promote apoptosis, or programmed cell death, in human osteosarcoma cells. These results highlight honey's potential therapeutic significance as an antioxidant source and its capacity to protect against oxidative stress-related health problems [29].

Immunomodulatory and anti-inflammatory activity

Chronic inflammation damages tissues, which can obstruct tissue repair and slow down healing. According to recent research, honey has been shown to be able to lessen inflammatory reactions in animal models, cell cultures, and clinical trials [30, 31]. Honey's ability to reduce inflammation is mostly related to the flavonoid chemicals in its phenolic content [32]. By inhibiting the pro-inflammatory actions of enzymes like cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), these phenolic and flavonoid substances are of critical importance [33]. Moreover, it has been

discovered that honey and its components control the expression of a number of proteins, including iNOS, ornithine decarboxylase, tyrosine kinase, and COX-2. The synthesis of immune-related molecules such as tumour necrosis factor alpha, interleukin-1 beta (IL-1), and IL-6 has been demonstrated to be stimulated by various types of honey. Additionally, honey boosts the production of essential immune cells during primary and secondary immune responses in tissue culture, including T and B lymphocytes, antibodies, eosinophils, neutrophils, monocytes, and natural killer cells [34]. The formation of short-chain fatty acids (SCFA) during honey's gradual absorption in the body is another possible mechanism by which it modifies the immune response. It is conceivable that ingestion of honey will result in the synthesis of these advantageous fermentation products because SCFAs have been shown to have immunomodulatory effects [35]. In addition, honey includes nigerooligosaccharides, a type of sugar that has been shown to have immunopotentiating properties. Other non-sugar honey components also contribute to its capacity to affect the immune system; therefore the immunomodulatory effects of honey are not simply attributable to its sugar content. These results highlight the multiple benefits of honey for immunological function and its potential as a natural immunomodulatory [36, 37].

Wound healing activity

Patients may suffer negative consequences from the emergence of wound infections, including worsened pain, discomfort, and inconvenience. In severe circumstances, infections from wounds can progress to illnesses that are deadly or life-threatening [38]. Additionally, wound infections impede the body's normal healing process, lengthen hospital stays, and raise treatment costs, including those for medications, bandages, and staff time. The complex process of wound healing is impacted by both exogenous factors, such as the presence of microbes, and endogenous factors related to the patient's physiology [39]. When local circumstances foster

an environment that is conducive to bacterial invasion and multiplication, the risk of wound infection increases. In this situation, honey shines out as a typical natural cure that has been used for centuries to treat wounds. The healing qualities of honey help wounds heal more quickly by encouraging regeneration tissue growth and epithelization while reducing or preventing scarring [40, 41]. Additionally, honey's capacity to control prostaglandins and nitric oxide, both of which are essential to the healing process, is linked to its effectiveness in wound healing. It's significant that honey has an impeccable safety record for usage in wound care. Honey has not shown allergic reactions or negative side effects when administered on mucosal membranes in body cavities or applied externally as dressings. Honey is significant as a natural and successful option in the treatment of different types of wounds because of its safety as well as its extraordinary wound-healing abilities, which give patients a faster and less arduous healing process.

Anti-cancer activity

Cancer cells are well known for their unchecked proliferation and resistance to apoptosis, a normal mechanism of programmed cell death [42]. Chemicals that cause cancer cells to undergo apoptosis are frequently used in conventional cancer treatments. Honey has proven to be a wonderful natural compound capable of encouraging apoptosis in a variety of cancer cell types by influencing the depolarization of the mitochondrial membrane [43]. The high phenolic content of honey is thought to be responsible for its ability to induce apoptosis in human colon cancer cell lines by activating caspase 3 and cleaving poly (ADP-ribose) polymerase (PARP). Additionally, honey controls the expression of proteins that are both pro- and anti-apoptotic in colon cancer cells, encouraging apoptosis [44]. Critical apoptotic regulators like p53, caspase 3, and the proapoptotic protein Bax are stimulated while the expression of the anti-apoptotic protein Bcl2 is down regulated. Additionally connected to

honey's apoptotic effects is the production of reactive oxygen species (ROS), which triggers p53. In turn, p53 promotes and inhibits apoptosis by regulating the production of proteins including Bcl-2 and Bax. In tumor tissues of experimental animals, studies have shown that oral administration of honey increases the expression of the pro-apoptotic protein Bax and decreases the expression of the anti-apoptotic protein Bcl-2. It's interesting to note that honey can induce apoptosis when administered intravenously as well as orally. For instance, it has been demonstrated that manuka honey causes cancer cell types to undergo apoptosis by activating caspase 9, which then activates caspase-3, the executor protein of apoptosis. DNA fragmentation, PARP activation, and Bcl-2 expression down regulation are all components of this process [45]. In addition to conventional chemotherapeutic drugs, which also depend on inducing apoptosis for their effectiveness, honey's capacity to trigger apoptosis makes it a promising natural material with potential anti-cancer capabilities. This study highlights honey's diverse medicinal potential for the treatment of cancer.

Conclusion

In conclusion, honey offers a wide range of therapeutic advantages in addition to being a delicious natural sweetener and a rich source of bioactive chemicals. While its anti-inflammatory and antibacterial characteristics make it an invaluable tool in addressing a variety of medical ailments, its antioxidant capabilities can aid in the fight against oxidative stress. The well-established benefits of honey for tissue regeneration and wound healing also raise the bar for its medicinal potential. The significance of taking into account honey as a natural cure in the field of complementary and alternative medicine is emphasized by this mini-review. While much has been learned about its bioactive components and therapeutic uses, more study is necessary to fully understand it and uncover any advantages that haven't yet been identified. Honey is a time-honored, multidimensional gift from nature with

the potential to improve our well-being and provide unique therapeutic interventions, which is important as we continue to look for sustainable and natural solutions to health challenges.

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