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Biological Activity and Health Promoting Properties of Honey: A Comprehensive Review

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Abstract: Since ancient times, honey has been highly esteemed and cherished as a natural product. It is not only recognised as a nutritious food, but also as an effective remedy for a variety of health ailments in traditional medicine. Honey's therapeutic characteristics have been used to cure eye illnesses, bronchial asthma, throat infections, TB, tiredness, hepatitis, and a variety of other ailments. It is also utilised as a dietary supplement. Honey has antioxidant, antibacterial, anti-inflammatory, antiproliferative, anticancer, and antimetastatic compounds. Numerous studies have demonstrated that honey can help regulate and treat wounds, diabetes, cancer, asthma, cardiovascular, neurological, and gastrointestinal problems. Honey contains phytochemicals, anti-inflammatory compounds, antibacterial agents, and antioxidants that aid in disease of medical treatment. The primary bioactive compounds contained in honey are flavonoids and polyphenols, both of which act as antioxidants. The use of honey in the management of different medical states, such as diabetes mellitus, pulmonary, gastrointestinal, cardiovascular, and nervous system problems, is supported by modern scientific literature. Because of its antioxidant characteristics, honey is especially effective in cancer treatment. Given all of these advantages, honey can be regarded as a natural therapeutic agent for a wide range of medical applications.

Keywords: Honey, Medical properties, Antioxidant, Biological activity, Antibacterial, Anticancer

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Introduction

Apiculture is the practise of keeping honeybees healthy and utilising their products for various reasons. Honey, bee bread, bee venom, bee pollen, propolis, and royal jelly are examples of these

products. There has been a surge of interest in the use of bee products in both traditional and modern medicine in recent years. As a result, numerous studies are being carried out to investigate their health advantages and pharmacological qualities. This has resulted in the creation of nutraceuticals and functional foods derived from these products. Diet that is not only nutritional but also offers additional health benefits as compared to conventional diet is referred to as functional food. These advantages can contribute to improved general health, happiness, and a reduction in chronic disorders (Mohan *et al.*, 1999). Bee products have been known for their medicinal benefits since ancient times in Egypt, Greece, and China. The myriad benefits of these products have been documented in several holy writings, including the Vedas, the Bible, and the Quran (Crittenden *et al.*, 2011). The use of honeybee products for their medicinal characteristics has a long history, although it has declined with the emergence of functional foods and pharmaceutical preparations (Münstedt *et al.*, 2009). However, there is a revived interest in these goods as society returns to traditional nutrition and embraces natural treatment. This revival is fuelled by significant and scientific research that substantiates the good effects of bee products on human health (Martinello *et al.*, 2021).

Honey is widely produced in countries all over the world and is important not only as a nutritious food source but also as a great medicine. Its functional and nutritional characteristics contribute to its status as an energy-supplying food. Furthermore, honey is well-known for its diverse biological, physiological, and pharmacological properties. The most common bee product is honey, which is produced by *Apis mellifera* bees. It is derived from plant nectar, secretions of living plant parts, or secretions of insects that eat these parts (Papa *et al.*, 2022). Honey is often employed as a sugar substitute in different culinary applications such as beverages, desserts, and entrees due to its high sugar content ranging from 80-95% (Bogdanov *et al.*, 2008). Honey is prized for its nutritional qualities as well as its sweet taste. It contains necessary amino acids as well as bioactive ingredients such as vitamins, phenols, flavonoids, fatty acids, and organic acids. These components contribute to its beneficial effects on health and determine its effectiveness as a dietary supplement. Honey has been used to prevent and treat a variety of ailments, including cardiovascular disease, cancer, and diabetes. It is also used to treat wounds, care for the mouth, and treat skin ailments (Jull *et al.*, 2015). Honey is also immunomodulatory, anticancer, anti-hypertensive, anti-allergic, and prebiotic (Fakhrildin *et al.*, 2014). It has been demonstrated to help people with hormonal imbalances and infertility. Honey is used in cosmetics to moisturise and repair the skin. Its fruit acids contribute to its exfoliating function, while flavonoids protect the skin from sun exposure.

A comprehensive literature search was done to investigate the efficiency of honey in the treatment of illnesses. For this, several web databases were used, including Web of Science, ScienceDirect, and PubMed. The search was restricted to recent articles that discussed how well honey can be used to treat diseases. As inclusion criteria for relevant publications, a mix of keywords, including "honey antioxidant", "anti-inflammatory", "antibacterial", "antidiabetic", "apoptotic", "respiratory", and "gastrointestinal" were employed both singly and collectively to ensure a thorough assessment.

Chemical composition of Honey:

Honey is a natural sweet material made by bees from floral nectar. Its chemical composition varies based on factors such as the type of flowers from which bees collect nectar and the region in which it is created. Honey, on the other hand, is often composed of the following components:

- *Carbs*: Honey is mostly composed of carbs, namely glucose and fructose. These simple sugars provide the pleasant taste while also providing energy.

- *Water*: Honey contains various levels of water, ranging between 17 and 20%. Honey's consistency and shelf life are affected by its water content.
- *Organic acids*: Honey contains gluconic acid, acetic acid, formic acid, and citric acid, among other organic acids. These acids contribute to honey's taste and acidity.
- *Enzymes*: During the honey-making process, bees add enzymes to the nectar. Enzymes like invertase and amylase aid in the breakdown of complex carbohydrates into simpler ones.
- *Amino acids*: Honey includes trace levels of amino acids, which are protein building blocks. Varied types of honey have varied amino acid compositions.
- *Vitamins and minerals*: Trace amounts of vitamins and minerals such as vitamin C, calcium, potassium, and iron can be found in honey. The amounts, however, are normally low and can vary depending on the floral source.
- *Polyphenols*: Honey includes polyphenols, which are antioxidants that contribute to its possible health advantages. These chemicals are obtained from flowers and give honey its distinctive colour. While honey is a natural substance, its composition can be modified by a variety of causes, therefore the chemical makeup of different samples may differ.

Bioactive compounds of honey:

Honey contains trace amounts of bioactive components such as phenolic acid, flavonoid, and -tocopherol. Honey ingredients such as phenolic acids, flavonoids, ascorbic acid, proteins, carotenoids, and particular enzymes such as glucose oxidase and catalase have been shown to provide health advantages (Moniruzzaman *et al*., 2012). Honey contains roughly thirty different forms of polyphenols, according to recent study. These polyphenols' abundance and levels can vary based on factors such as floral source, climate, and geographical conditions. Some beneficial chemicals, such as galangin, quercetin, kaempferol, luteolin, and isorhamnetin, are present in all types of honey, whilst others, such as naringenin and hesperetin, are found only in specific varieties. The main phenolic and flavonoid compounds found in honey include gallic acid, syringic acid, ellagic acid, benzoic acid, cinnamic acid, chlorogenic acid, caffeic acid, isorhamnetin, ferulic acids, myricetin, chrysin, coumaric acid, apigenin, quercetin, kaempferol, hesperetin (Nurul Syazana *et al*., 2012), galangin, catechin, luteolin, and naringenin. According to Khalil *et al.* (2011), these substances have been demonstrated to possess a range of advantageous qualities, including antioxidant, antibacterial, anti-inflammatory, antiproliferative, anticancer, and antimetastatic activities.

Biological activities of honey:

Antioxidant activity:

Honey works as an antioxidant by preventing the production of free radicals, which are frequently aided by metal ions like copper and iron. Flavonoids and other polyphenols, which help stop the production of free radicals, can potentially capture these metal ions when they combine with honey's other ingredients (Yuksel *et al.*, 2011). Bee honey's power to inhibit oxidative processes and scavenge free radicals is what gives it its antioxidant properties in the human body. Since oxygen free radicals have a role in many aspects of inflammation, it is thought that honey's anti-inflammatory effects are partially a result of its antioxidant activity. Honey's antioxidant concentration can still be helpful even when it does not directly reduce the inflammatory process by limiting the amount of damage that would otherwise happen. Honey naturally contains a variety of substances, including peptides, ascorbic acid, phenolic acids (*such as ferulic, ellagic, caffeic, and p-coumaric acids*), tocopherols, catalase, superoxide dismutase, and reduced glutathione. Flavonoids, Maillard reaction products, and phenolic acids are also present. According to Tahir *et al.* (2011), these ingredients combine to have an antioxidant effect.

Anti-inflammatory activity:

Significant levels of phenolic chemicals are present in bee honey, which contribute to its anti-inflammatory qualities. Inducible nitric oxide synthase (iNOS), cyclooxygenase-1, and cyclooxygenase-2 (COX-1 and COX-2) are responsible for suppressing the pro-inflammatory effects of these phenolic and flavonoid chemicals (Viuda-Martos *et al.*, 2008). Additionally, the content of prostaglandins, such as prostaglandin E2 (PGE2), thromboxane B2 (in the plasma of healthy individuals), and prostaglandin F2 (PGF2á), decreases when diluted bee honey is consumed. In an inflammatory colitis model, honey has interestingly demonstrated efficacy comparable to prednisolone therapy. Honey provides a natural anti-inflammatory action without significant downsides, in contrast to corticosteroids and NSAIDs, which frequently have negative side effects (Nooh *et al.*, 2011).

Antimicrobial activity:

The enzymatic glucose oxidation process and certain physical features of honey are the major components that contribute to its antibacterial effect. Honey's high osmotic pressure and low water content, low pH and acidic environment, low protein content, high carbon-to-nitrogen ratio, low redox potential due to the abundance of reducing sugars, and viscosity that inhibits the presence of dissolved oxygen and other chemical agents are all factors that demonstrate its antimicrobial activity. Honey does not support yeast and bacterial development due to its low water content and acidic environment, as well as the presence of glucose oxidase and hydrogen peroxide. Honey's antibacterial effect is not solely attributed to peroxidase, as terpenes, pinocembrin, benzyl alcohol, syringic acid, methyl syringate, 2-hydroxy-3-phenylpropionic acid, 2-hydroxybenzoic acid, 3,4,5-trimethoxybenzoic acid, and 1,4-dihydroxybenzene have all been identified.

Honey has been used as a traditional treatment for microbial diseases since ancient times (Molan *et al.*, 1992). Manuka honey, derived from the plant *Leptospermum scoparium*, has been proven to be effective against a variety of human diseases including *Staphylococcus aureus*, *Enterobacter aerogenes*, *Escherichia coli* (*E. coli*), and *Salmonella typhimurium* (Almasaudi *et al.*, 2013). It has also been shown in studies to be effective against antibiotic-resistant strains such as methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), and *Streptococci* (Mundo *et al*., 2004). Newly found bee honey variations, on the other hand, may offer advantages or parallels to manuka honey in terms of better antibacterial characteristics, local availability, and increased selectivity against medically relevant organisms (Alvarez-Suarez *et al.*, 2014). When compared to *S. aureus*, coagulase-negative *Staphylococci* were found to be similarly vulnerable to bee honey with equivalent antibacterial activity. *Pseudomonas aeruginosa* and *Enterococcus* species, on the other hand, were shown to be less sensitive (Fahim *et al.*, 2014).

Medicinal properties of honey:

Honey and Gastrointestinal (*GI*) *Disorder*:

Infection with *Helicobacter pylori* can cause gastritis, as well as gastric and duodenal ulcers. However, standard treatments for *H. pylori* eradication are ineffective, therefore researchers are looking for alternatives. Graham *et al.* (2014) studied honey as a potential source of novel chemicals that could efficiently tackle this virus. A laboratory study found that a 20% solution of honey had a biocidal effect on *H. pylori* bacteria, which are known to cause gastritis. Interestingly, the honey solution suppressed several strains of H. pylori that were resistant to other antimicrobial treatments (Kim *et al.*, 2017). The gastrointestinal tract (GIT) is home to a plethora of beneficial microorganisms that play an important role in GI health. Bifidobacteria is one such microbe that largely contributes to the maintenance of healthy gut health. It has been suggested that eating probiotic-rich meals can boost the population of bifidobacteria in the GI tract. Furthermore, the presence of prebiotics can boost the biological

activities and growth of this bacteria. Natural honey includes considerable amounts of prebiotics, according to scientific investigations (Abeshu *et al.*, 2016). *In vitro* and *in vivo* studies have shown that honey is a beneficial dietary supplement that promotes the growth of lactobacillus and bifidobacteria while improving their probiotic efficiency in the GI tract (Shamala *et al.*, 2000). Prebiotic components of honey, such as inulin, oligofructose, and oligosaccharides, have been demonstrated in laboratory studies to boost the population of *Lactobacillus acidophilus* and *L. plantarum* by 10 to 100 times, which is extremely advantageous to the gut microbiota.

Honey and Paediatric Care:

Honey has been shown to improve paediatric treatment, notably in the management of skin injury surrounding stomas such as ileostomy and colostomy. It promotes the healing process of the damaged skin by boosting epidermalization [Aminu *et al.,* 2000]. Furthermore, honey can help treat paediatric dermatitis caused by excessive use of diapers and napkins, as well as illnesses like eczema and psoriasis. In clinical research, a mixture of honey, beeswax, and olive oil was found to be well tolerated by individuals with psoriasis or atopic dermatitis, resulting in considerable improvements. Honey includes nitric oxide metabolites, which can help prevent the occurrence of psoriasis (Al-Waili *et al.*, 2003).

Anticancer activity:

Tumour necrosis factor (TNF), a signalling molecule, plays crucial roles in a number of biological processes, including the beginning, growth, and advancement of cancer cells. Honey has exhibited anticancer effects in experiments carried out *in vitro* and *in vivo* utilising mice models by successfully restraining the growth of various bladder cancer cell lines (T24, RT4, 253J, and MBT-2). In mouse models implanted with MBT-2 bladder cancer cells, honey produced beneficial effects when given orally or intravenously. According to Imth *et al.* (2014), some proteins included in royal jelly honey, notably apalbumin-1 and apalbumin-2, have been demonstrated to induce macrophages to release cytokines including interleukin-1 (IL-1), interleukin-6 (IL-6), and TNF-. Additionally, it has been discovered that a variety of honeys, including manuka, jelly bush, and pasture honey, can produce TNF-, interleukin-1 (IL-1), and IL-6 at a very low concentration of 1% weight/volume (Tanks *et al.*, 2001). Recent research has demonstrated that honey has strong antimutagenic capabilities, which raises the possibility that it may be able to prevent cancer (Saxena *et al.*, 2012). Honey was found to trigger a particular reaction known as the SOS response in tests employing *E. coli* cells exposed to UV or radiation. The SOS response is a route for repair that occasionally results in mutagenicity. The research discovered that honey, especially in genes like umuC, recA, and umuD, efficiently suppressed the alterations linked to this pathway. These results confirm honey's significant antimutagenic effect and its potential as an anticarcinogenic agent.

Honey and Liver and pancreatic diseases:

Honey has been shown to offer numerous benefits for the liver system, including pain relief, regulating liver processes, and toxin neutralisation. Complications in the liver system are frequently caused by oxidative damage, however honey contains antioxidant capabilities that may protect against liver damage. One investigation on rats with paracetamol-induced liver damage found that honey's antioxidant and hepatoprotective properties aided in the reduction of liver damage (Wang *et al.*, 2015). One unique feature of honey is its 1:1 fructose-to-glucose ratio, which can assist manage blood sugar levels. This is especially advantageous for people with fatty liver disease because it supports appropriate glycogen storage in liver cells. Inadequate glycogen storage in the liver causes the production of stress hormones, which slows glucose metabolism over time. This poor glucose metabolism eventually leads to insulin resistance, which is a major contributor to the development

of fatty liver disease. Another study discovered significant reductions in blood glucose levels after using tualang honey. Overall, these data imply that honey can help with blood sugar management, which is important for those with fatty liver disease (Erejuwa *et al*., 2011).

Antidiabetic activity:

The most frequent types of diabetes in humans are type 1 and type 2 diabetes. Type 1 diabetes develops when the immune system destroys insulin, whereas type 2 diabetes, which is more common and genetically determined, can be caused by a variety of reasons. Although the actual aetiology of diabetes is unknown, the disease's development is complicated by interactions between environmental, societal, and genetic variables. Current diabetes medications have drawbacks such as high cost and restricted availability. In the management of diabetes, some patients have turned to nutritional supplements, herbal remedies, and natural items such as honey (Alam *et al.*, 2014).

Natural honey's fructose concentration and fructose/glucose ratio can range from 21 to 43% and 0.4-1.6 or higher, respectively. Although fructose is the sweetest naturally occurring sweetener, it has a lower glycemic index (GI) of 19 when compared to the GI of 100 for glucose and 60 for sucrose. Although the actual mechanism underlying honey's hypoglycemic effect is uncertain, multiple investigations have verified this effect. Fructose has been shown in animal studies to lower blood glucose levels (Bobiş *et al.*, 2018). This decrease could be attributed to variables such as reduced meal consumption, slower intestinal absorption, and a longer stomach emptying time. Fructose stimulates glucokinase in hepatocytes, which is required for glucose assimilation and storage as glycogen in to liver. In contrast to fructose, glucose promotes fructose absorption and aids in its hepatic effects by facilitating delivery to the liver. The pancreas is important in diabetes because it produces insulin and glucagon. The antioxidant compounds in honey can protect the pancreas from oxidative stress and damage, which may contribute to its hypoglycemic impact. In normal rats, eating either fructose or a combination of fructose and sucrose enhances insulin response and glucose homeostasis compared to rats eating only glucose. Honey's hypoglycemic impact has been established in a variety of animal models, including the production of type 1 and type 2 diabetes with suitable dosages of alloxan and streptozotocin.

Honey and asthma:

Honey has long been used to alleviate inflammation, coughs, and fevers in traditional medicine. Honey has also been found to help lessen asthma symptoms and prevent the development of asthma. Oral honey consumption has been shown in animal tests to effectively treat chronic bronchitis and bronchial asthma (Bâcvarov *et al.*, 1970). A study also found that honey therapy lowered airway inflammation and delayed the onset of asthma. Honey inhalation has also been shown to successfully prevent excessive mucus formation. However, further research is needed to completely understand the mechanisms underlying honey's capacity to relieve asthma symptoms.

Honey and Wound healing:

Honey is a well-known and ancient wound-healing treatment that has been utilised by humans for generations. When other therapies have failed, honey has been discovered to be beneficial in aiding wound healing even in the presence of sophisticated drugs. Due to its antibacterial, antiviral, anti-inflammatory, and antioxidant capabilities, experimental research has provided more data supporting the use of honey in wound healing (Murosak *et al.*, 2002). Honey promotes wound healing by encouraging leukocytes, a kind of white blood cell, to release cytokines. This sets off a chain of actions that leads to tissue healing. Furthermore, honey stimulates the immune system to fight infection. It has been discovered to increase B- and T-lymphocyte proliferation as well as the activity of phagocytes, which are immune

cells that ingest and eliminate infections. Honey also stimulates the production of antibodies, which strengthens the body's defences against illnesses. There is plenty of evidence to suggest that honey can be used to manage and treat acute wounds, as well as mild to moderate superficial and partial thickness burns. Although some studies have shown that honey can help with wound healing and leg ulcers, additional research is needed to reinforce the existing data and completely comprehend the breadth of honey's therapeutic advantages.

Conclusion

There is currently sufficient data to advocate the use of honey in the treatment of certain medical conditions. Several investigations have proven that honey has antibacterial, anti-inflammatory, apoptotic, and antioxidant characteristics that contribute to its therapeutic qualities. More research, however, is required to fully examine honey's potential in all areas of therapeutic practise. This comprehensive study seeks to offer practitioners with substantial data supporting the medicinal use of honey. While several studies have looked into the efficacy of honey for medical purposes, further research is needed to cover all of honey's medicinal properties.

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