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Honey: A Bioactive Resource for Diversified Therapeutic Use in Traditional Medicine

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Abstract:
Honey, a natural bioactive resource is obtained from *Apis mellifera*. It has been cherished as a natural product known for its dietary supplement and an effective remedy in traditional medicine to creation of nutraceuticals and functional foods in modern medicine of present generations. Apiculture is the practice of rearing honeybees, keeping them healthy and utilizing products like honey, bee pollen, bee bread and royal jelly for various purposes. The myriad benefits of natural products obtained from honeybees has been mentioned in the inscriptions and documents of several holy books like the Vedas, the Bible, and the Quran. and Bible. Bee products are known for their therapeutic use since ancient times in Egypt, Greece, and China. In India honeybee rearing is one of the traditional practices of indigenous community of ethnic tribes. It is a rich source of bioactive secondary metabolites like flavonoids, polyphenols, organic acids, vitamins, and minerals and thus contributes to its effectiveness in dietary supplement both as food and medicine. It also acts as an immunomodulator, anticancer, anti-inflammatory, antioxidant source and hence helps in curing various diseases. Due to its therapeutic characteristics, honey can be used to cure bronchial asthma, cough, TB, hepatitis, GI disorders and a variety of other ailments. Research investigations have proven that honey can also help in wound healing and in the treatment of ulcers. It is used in cosmetics to repair the skin by acting as an exfoliating agent and moisturizer in anti-tanning sunscreen lotions. The present research article highlights the comprehensive study on the efficacy of honey as a bioresource for diversified therapeutic use in traditional medicine.

Keywords: Honey, Bioactive compounds, therapeutic uses, traditional medicine

Introduction:

Honey 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 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. Apiculture is the one of the traditional age old practise of rearing honeybees healthy and utilising their products for medicinal. reasons. There has been a surge of interest in usage of honey bee products in both traditional and modern medicine in recent years. Bee products have been known for their medicinal benefits since ancient times in Egypt, Greece, and China. 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).

Documentation of myriad benefits of the bee products dates back in holy inscriptions like the Vedas, the Bible, and the Quran (Crittenden *et al.*, 2011). Honey, bee bread, bee venom, bee pollen, propolis, and royal jelly are few bee products. 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). 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).

The most common bee product, honey is found to be employed as a sugar substitute in different culinary applications like beverages, desserts, and entrees due to its high sugar content ranging from 80-95% (Bogdanov *et al.*, 2008). Presence of necessary amino acids as well as bioactive ingredients such as vitamins, phenols, flavonoids, fatty acids, and organic acids contribute to its beneficial effects on health and determine its efficacy 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 acts as an immunomodulator, anticancer, anti-hypertensive, anti-allergic, and prebiotic (Fakhrildin *et al*., 2014). It has been demonstrated to help people with hormonal imbalances and infertility. Honey acts as a skin ailment and hence used in cosmetic industry to moisturise and repair the skin. The acidic content of honey 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. As inclusion criteria for relevant publications, a mix of keywords, including "honey antioxidant", "antiinflammatory", "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. Factors like the type of flowers from which bees collect nectar and the region in which it is created results in slight variations in its chemical composition. Honey, on the other hand, is often composed of the following components:

Type of Component	**Activity**
Carbohydrates (Glucose and Fructose)	Provide sweet taste and energy
Water (17-20%)	Maintains Consistency and Shelf life
Organic acids (Gluconic acid, acetic acid, formic acid and citric acid)	Maintains acidic nature and contributes to its taste
Enzymes (Invertase and Amylase)	Enzymatic activity to catabolise complex sugars into simple sugars
Vitamins (Vitamin C) and Minerals (Calcium (Ca), Potassium(K) and Iron (Fe))	Differ based on the floral source and found in minute quantities
Polyphenols	Act as antioxidants and gives a distinctive colour to honey

Honey as a bioactive resource:

Honey contains trace amounts of bioactive components such as phenolic acid, flavonoid, and tocopherol. In addition to it ascorbic acid, proteins, carotenoids, and particular enzymes such as glucose oxidase and catalase have been shown to provide health advantages (Moniruzzaman *et al*., 2012). Abundancy levels of polyphenols depend on factors like 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.

Bioactive Compound with Molecular Formula	**Nature of the activity**	**Type of Disease/Disorder**
Apigenin $C_{15}H_{10}O_5$	Anti-inflammatory Antimutagenic	Cardiovascular diseases treatment
Quercetin-3-O-rutinoside (rutin) $C_{27}H_{30}O_{16}$	Anti-inflammatory Antiproliferative Antitumor	
Caffeic acid $C_9H_8O_4$	Anti-inflammatory effects Anticancer Antidiabetic	
Catechin $C_{15}H_{14}O_6$	Antidiabetic Anti-inflammatory	
Gallic acid $C_7H_6O_5$	Antioxidant Anti-inflammatory Antimutagenic Anticancer	
Chrysin $C_{15}H_{10}O_4$	Anticancer	Improves cognitive deficits and brain damage effect
Cinnamic acid $C_9H_8O_2$	Antimicrobial	
p-Coumaric acid $C_9H_8O_3$	Anticancer activity	

***Biological activities of honey*:**

***Antioxidant activity*:** Honey acts as an antioxidant by preventing the production of free radicals, which are frequently aided by metal ions like copper and iron. Presence of flavonoids and other polyphenols help in stopping the production of free radicals by capturing these metal ions when they combine with honey's other ingredients (Yuksel *et al.*, 2011). Their capability to inhibit oxidative processes and scavenge free radicals help in serving as an antioxidant in the human body. Since oxygen free radicals play a major role in aspects of inflammation, it is thought that honey's anti-inflammatory effects are partially a result of its antioxidant activity. The antioxidant concentration can not only help in reducing the inflammatory process but also limits 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*:** Presence of significant levels of phenolic chemicals in bee honey, contribute to its anti-inflammatory qualities. Inducible nitric oxide synthase (iNOS), cyclooxygenase-1, and cyclooxygenase-2 (COX-1 and COX-2) are mainly 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. High osmotic pressure and low water content, acidic environment (low pH), low protein content, high C/N, low redox potential due to the abundance of reducing sugars, and viscosity that inhibits the presence of dissolved oxygen and other chemical agents are the factors that demonstrate its antimicrobial activity. Honey does not support yeast and bacterial development due to its low water content and acidic environment and 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).

List of Microorganisms found to be sensitive to Manuka Honey

Gram Positive Bacteria	*Streptococcus pyogenes* *Staphylococcus aureus* *Enterococcus faecalis* *Actinomyces viscous* *Bacillus cereus*
Gram Negative bacteria	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella typhi* *Neisseria meningitides* *Proteus vulgaris*

***Medicinal properties of honey*:** *Honey and Gastrointestinal* (*GI*) *Disorder*: Gastrointestinal tract (GIT) serves as a home to a plethora of beneficial microorganisms that play an important role in GI health.

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 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. *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.

***Anticancer and Antimutagenic activity*:** Tumour necrosis factor (TNF), a signalling molecule, plays crucial roles in several 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). 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.

***Antidiabetic activity*:** Type 1 and Type 2 diabetes are the most frequent types of diabetes in humans. 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. 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 into liver. In contrast to fructose, glucose promotes fructose absorption and aids in its hepatic effects by facilitating delivery to the liver. Pancreas produces insulin an glucagon and hence plays an important role in diabetic disorder. The antioxidant compounds in honey can protect the pancreas from oxidative stress and damage, which may contribute to its

hypoglycemic impact. 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.

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. Moreresearch, 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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