



doi: <https://doi.org/10.20546/ijcrar.2021.903.003>

## Biological and Therapeutic Effects of Honey: An Overview

Prem Jose Vazhacharickal<sup>1\*</sup>, K. S. Jagadish<sup>2</sup> and G. Eswarappa<sup>2</sup>

<sup>1</sup>Department of Biotechnology, Mar Augusthinose College, Ramapuram, Kerala-686576, India

<sup>2</sup>Department of Apiculture, University of Agricultural Sciences, GKVK, Bangalore, Karnataka-560065, India

\*Corresponding author

### Abstract

Honey is a very sweet, viscous syrup produced by the honey bees as well as stingless bees which is probably the first natural sweetener ever discovered, widely used as a nutritious food supplement and medicinal agent. The physical, chemical and nutritive properties of honey fluctuate based on the floral preferences, floral sources, climatic conditions and geographic features. The potential health benefits of honey, such as microbial inhibition, wound healing, and its effects on other diseases, are described. Honey exhibits antimicrobial, antioxidant, anti-inflammatory, anticancer, antihyperlipidemic, and cardioprotective properties. Due to these properties, it is used in the treatment of eye disorders, gastrointestinal tract diseases, neurological disorders, fertility disorders and wound healing activity. This review paper mainly focus on the biological and therapeutic effects of honey.

### Article Info

Accepted: 15 February 2021

Available Online: 20 March 2021

### Keywords

Antibacterial activity; Food supplement; Honey bees; antihyperlipidemic; Wound healing.

### Introduction

Honey is a natural sweetener used widely across the world from ancient times. It is widely used for various applications including clinical and contains 200 distinct chemical compounds. Honey is viscous in nature and contains fructose and glucose (80-85%), water (15-17%), ash (0.2%), proteins and amino acids (0.1-0.4%) with trace amounts of enzymes, vitamins and phenolic compounds. Honey composition varies depending on the plant sources from which bees collect nectar.

In general all honey across the world contain similar types of phenolics acids, flavonoids, antioxidants with synergic action of components. The physical and chemical properties of honey fluctuate based on the floral preferences and sources. In addition to floral

sources, climatic conditions and geographic features influence physical, chemical and nutritive properties of honey.

The major biological properties of honey includes antioxidant, anti-inflammatory, anti-bacterial, antiviral, anti-ulcer, antihyperlipidemic, antidiabetic and anticancer properties (Erejuwa *et al.*, 2010; Kishore *et al.*, 2011; Viuda-Martos *et al.*, 2008). Honey lowers cardiovascular risks and shows ameliorative effect on plasma glucose, plasma insulin, cholesterol, triglycerides, blood lipids, C-reactive proteins and homocysteine. Honey is proven to improve memory and learning process including enhanced morphology of memory-related brain areas, increased levels of brain-derived neurotrophic factor, reduced brain oxidative stress, increased acetylcholine concentration. The aim of

this review is to summarize information on the traditional and clinical uses of honey to augment various biological activities and to treat diseases.

### Chemical constituents of honey

Around 200 compounds are present in honey which mainly comprises of water, sugars, vitamins, enzymes, amino acids and minerals. Sugars dominate 95-99% of honey's dry matter with fructose as the most prevalent (32-38% of total sugar). In addition to fructose and glucose other disaccharides and oligosaccharides including maltose, maltotriose and panose. In addition to this various organic acids, minerals and trace elements such as calcium, potassium, sodium, magnesium, phosphorous, sulphur, iron, zinc, copper and manganese.

Various vitamins, including ascorbic acid (Vitamin C), thiamine (Vitamin B1), pantothenic acid (Vitamin B5), riboflavin (Vitamin B2), nicotinic acid (Vitamin B3), pyridoxine (Vitamin B6), biotin (Vitamin B8), folic acid (Vitamin B9) and cyanocobalamin (Vitamin B12), are present (Ciulu *et al.*, 2011). Enzymes and proteins are minor constituents, with the enzymes playing a vital role in various activities, including antimicrobial activity and facilitating calcium absorption (Ariefdjohan *et al.*, 2008). The antioxidant capacity of honey depends on total phenolic compounds and the presence of flavonoids which has an important role in reducing oxidative stress. A variety of flavonoids and terpenoids have been reported in various honeys. In manuka honey, pinocembrin (1), chrysin (2), pinobanksin (3), 8-methoxykaempferol (4), luteolin (5), isorhamnetin (6), galangin (7), kaempferol, sakuranetin (8), quercetin and magniferolic acid (9) and 3 $\beta$ -hydroxy-24-methylenecycloartan-26-oic acid (10) have been identified (Ahmed and Othman, 2013). The various physicochemical properties and therapeutic efficacies of honey are depicted in Fig. 2 and Fig. 4.

### Traditional uses of honey

Honey is widely used in traditional medicines across the globe for ages. Due to antioxidants present in the honey, it is used as hepatoprotective, cardioprotective agent and prevents gastrointestinal ailments. Ancient Chinese, Egyptians, Greeks, Assyrian, Romans and Indians used honey to treat wounds, and diseases of intestine. Honey exerts known antibacterial effects against several microorganisms, including *Escherichia coli*, *Shigella* spp., *Helicobacter pylori* and *Salmonella* spp. (Al Somal *et al.*, 1994; McGovern *et al.*, 1999). Honey has anti-

inflammatory properties and shows anticancer activities against breast, cervical, prostate and osteosarcoma. Honey is also traditionally used as a diabetic and hypolipidemic agent. In India, Lotus honey has been traditionally used to treat eye infections and other diseases (Pasupuleti *et al.*, 2017).

### Antimicrobial activity

The stingless bee honey possesses good antimicrobial activity against bacterium *S. aureus*, *Bacillus cereus* (Gram positive bacteria) and *Pseudomonas aeruginosa* (Gram negative bacteria), as well as against yeasts such as *Candida albicans* and *Saccharomyces cerevisiae* (DeMera and Angert, 2004). Tualang honey from Malaysia was also reported to have significant antimicrobial and wound healing activities (Bergman *et al.*, 1983; Efem, 1988). Both Tualang and Manuka honey were effective against *Stenotrophomonas maltophilia* (Tan *et al.*, 2009). However, Tualang honey had a lower MIC (11.25%) against *Acinetobacter baumannii* compared with manuka honey (12.5%).

### Antioxidant activities

The honey has been reported to have good antioxidant activity and this property varies depending on the type or geographic origin of the honey. Radical scavenging activity of Tualang honey bees is high, and had the highest antioxidant activity with other types of honey. The antioxidant activity, as indicated by several tests especially the 1,1-diphenyl-2-picrylhydrazil (DPPH) and FRAP assay (Henderson *et al.*, 2015), ORAC assay (The Oxygen Radical Absorbance Capacity), ABTS [2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt assay, TEAC (Trolox-equivalent antioxidant capacity) assay and ascorbic acid content assay (Bashkaran *et al.*, 2011; Erejuwa *et al.*, 2012; Ferreira *et al.*, 2009; Khalil *et al.*, 2012; Khalil *et al.*, 2015; Moniruzzaman *et al.*, 2012; Moniruzzaman *et al.*, 2013; Moniruzzaman *et al.*, 2014). Flavonoids and polyphenols in honey is mainly responsible for the antioxidant activity.

### Anti-inflammatory activity

Some honey (*Melipona marginata*) has unique physicochemical properties and distinctive flavour and shows anti-inflammatory effects on skin. The production of various inflammatory cytokines has been assessed by exposing human monocytes to Manuka honey (Tonks *et al.*, 2003). Honey stimulated the production of

inflammatory cytokines interleukin-1 $\beta$  (IL-1  $\beta$ ) and IL-6 as well as tumor necrosis factor-alpha (TNF-alpha).

### Eye diseases

Honey also plays an important role in treating chemically induced cataracts. Honey from the stingless bee *Meliponafavosa favosa* exhibited activity against sodium selenite-induced cataracts in Wistar rats. Meliponini honey has been used as an eyedropper to treat eyesight problems especially glaucoma and cataract.

### Gastrointestinal tract diseases

Another important medicinal use of honey is in the treatment of gastrointestinal tract diseases and stomach disorders. Most honey preparations have shown beneficial effects in dyspepsia and in the treatment of periodontal diseases. Honey has beneficial effects in children with gastroenteritis and diarrhoea.

### Neurological disorders

Oxidative stress is one of the major causes of neuro inflammation, which leads to neuronal apoptosis and death. Honey have significant activity against chronic cerebral hypoperfusion, which is one of several factors contributing to Alzheimer's disease. Honey can improve memory, prevent dementia and other cognitive diseases and increase proliferation of neurons in hippocampal regions.

### Effects on fertility

Honey has beneficial effects on fertility as well as in regulating the hormones related to fertility. Honey consumption ameliorated altered levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone. Stress plays a vital role in many diseases, disorders and dysfunctions leading to poor reproductive capacity. Administration of honey can reduce stress and smoke induced reproductive toxicity.

### Antidiabetic activity

The honey shows antihyperglycemic effects and significantly reduce blood glucose levels. Honey can be used as a good alternative to sucrose as a natural sweetener for diabetic patients. Long term usage of honey reduce weight and reduce blood sugar levels.

### Anticancer activity

The efficacy of honey on various types of cancers have shown that honey has debriding potential and stimulates angiogenic action. Numerous studies shows the effect of honey against cancerous cells regarding their stability, viability and even metastasis showed significant anti-angiogenic effects (Fauzi *et al.*, 2011).

Honey is effective against various cancers especially oral, bladder (Swellam *et al.*, 2003), cervical (Fauzi *et al.*, 2011), liver(Baig and Attique, 2014), bone and breast (Fauzi *et al.*, 2011) cancers. Honey protects non-cancerous cells from the adverse effects of tamoxifen through a DNA repair mechanism and improve post radiation symptoms. Honey also reduce inflammation and odor from the wounds in the oral cavity.

### Cholesterol and lipid-lowering effects in cardiovascular diseases

Cardiovascular diseases (CVDs) constitute a serious challenge for modern medicine; certain factors, such as oxidative stress, hypertension, hypercholesterolemia, inflammatory factors, and diabetes play particularly significant roles in their development (Olas,2020).

Honey is very effective in reducing cholesterol levels in hyperlipidemic conditions. Continues usage of honey reduces lipid levels and shows effects on fasting blood glucose (FBG), body weights, low-density lipoprotein cholesterol (LDL-C), total cholesterol, high-density lipoprotein cholesterol (HDL-C), triacylglycerol, and C-reactive protein (CRP). The oral administration of honey reduces LDL, triacylglycerols and cholesterol in overweight patients while HDL-C levels were elevated.

These results suggests that honey consumption has health benefits of glycemic control and improvement of lipid profile leading to a reduced risk of cardiovascular diseases.

### Wound healing activity

Honey has excellent wound healing activity, improve granulation tissue thickness and open wound size by topical application. Honey ameliorates granulation tissue thickness, epithelialization and oedema around wounds. Honey heals the wound rapidly and act as an antiseptic and antimicrobial agent.

**Fig.1** Description of the different honeybees identified in Bengaluru a) Rockbees; *Apis dorsata* b) *Apis florea* comb showing the brood; c) *Apis florea* brood showing honey storage area; d) *Apis dorsata* worker bee e) *Apis florea* worker bee f) *Apis cerana* colony showing brood and stored honey and pollen g) *Apis mellifera* collecting pollen and nectar.



Fig.2 Schematic representation of the therapeutic effects of honey (Adapted from Rao *et al.*, 2016)

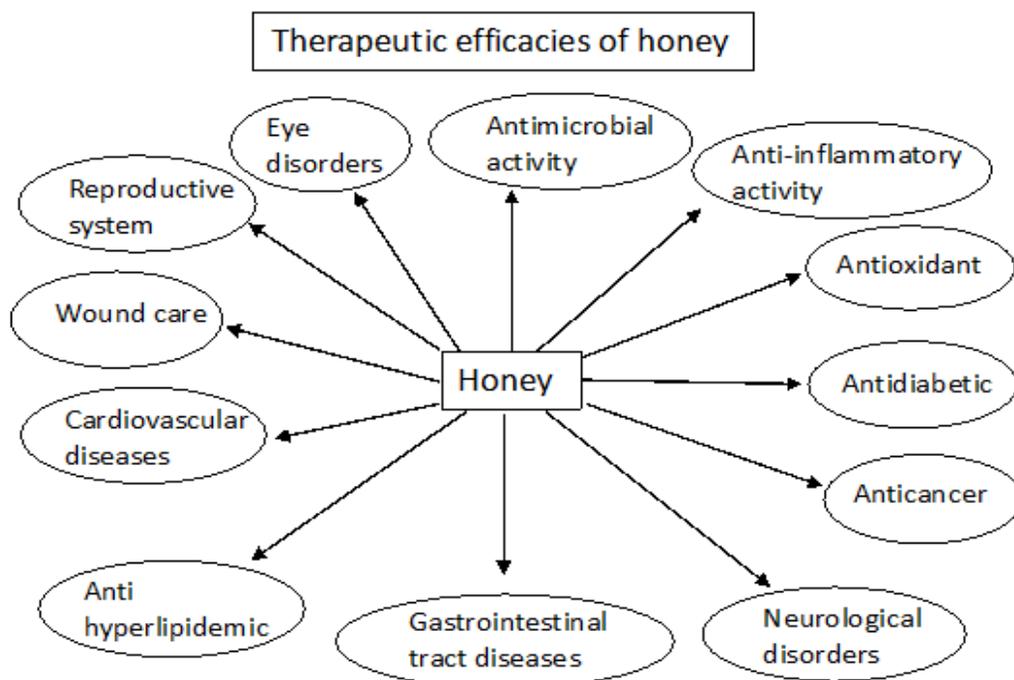


Fig.3 Flavonoids and terpenoids found in honey; pinocembrin (1), chrysin (2), pinobanksin (3), 8-methoxykaempferol (4), luteolin (5), isorham-netin (6), galangin (7), kaempferol, sakuranetin (8), quercetin and magniferolic acid (9) and 3β-hydroxy-24-methylenecycloartan-26-oic acid (10) have been identified. Adapted from Rao *et al.*, 2016.

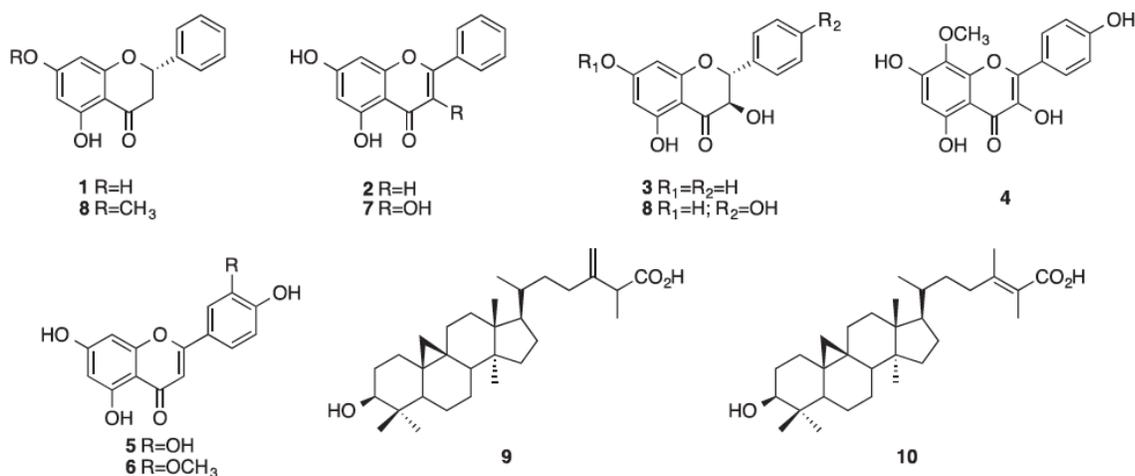
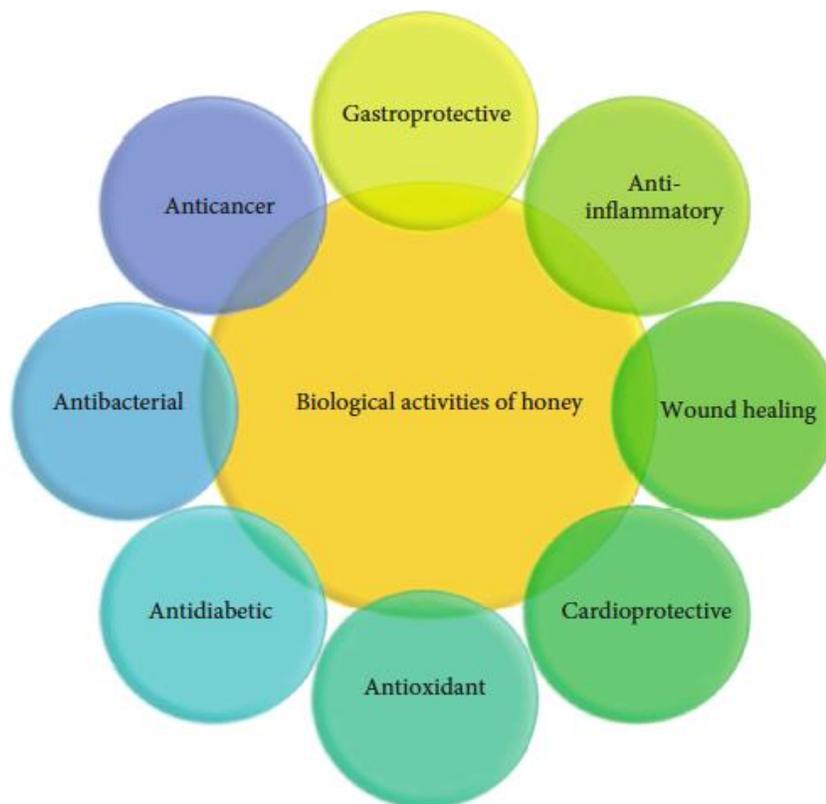


Fig.4 Various types of biological activities of honey products. Adapted from Pasupuleti *et al.*, 2017.



Honey possesses numerous biological, biochemical and physiological activities in animals as well as in humans. The efficacy of these properties depends on the types of phenolic compounds present in the honey.

Honey has been investigated for their antimicrobial, anticancer, antidiabetic, anti-hypercholesterolemic, anti-inflammatory, antioxidant, and wound healing properties. Research should be conducted further for evaluation of the many potential biological and pharmacological activities of stingless bee honey, including the treatment of diabetes, metabolic and neurological disorders, cancer, cardiovascular-disease-related complications and hyper-cholesterolemia and in wound healing.

#### Acknowledgment

This outlook study will not be possible by the encouragement and support from Dr. K. B. Umesh, Dr. Andreas Buerkert, Dr. Prasanna Kumar P. S, Dr. Veerabhadrapa Bellundagi, Dr. Hamsa K. R and Dr. Catrin Westphal.

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**How to cite this article:**

Prem Jose Vazhacharickal, K. S. Jagadish and Eswarappa, G. 2021. Biological and Therapeutic Effects of Honey: An Overview. *Int.J.Curr.Res.Aca.Rev.* 9(03), 23-30.  
doi: <https://doi.org/10.20546/ijcrar.2021.903.003>