

Antimicrobial and Antioxidant Activities of Honey

Irum Naureen^a, Aisha Saleem^{b*}, Hafsa Iqbal^c, Fatima Aslam^d, Sadia Jamal^e
Aqsa Sattar^f, Muhammad Zahid^g

^aAssistant Professor, School of Zoology, Minhaj University Lahore, Pakistan

^{b,c,d,e,f,g}M. Phil Researcher, School of Zoology, Minhaj University Lahore, Pakistan.

^aEmail: dr.irimnaureen@mul.edu.pk, ^bEmail: aishasaleem160@gmail.com, ^cEmail:

hafsaranjha23@gmail.com, ^dEmail: Fatimaaslam01101998@gmail.com, ^eEmail:

sadiajmaldogar123@gmail.com, ^fEmail: sattaraqsa902@gmail.com, ^gEmail: mzahid1111@gmail.com

Abstract

Honey a super saturated concentrated solution with complex constituents has been used as therapeutic agent since ancient times. Natural products have been used as a substitute for various conventional treatments and drug discoveries. They have properties of honey including antioxidant, antibacterial, and anti-inflammatory, anti-cancerous. The advent of antibiotics in Modern Western Medicine has made the use of honey in the treatment of infectious diseases abandoned wound healing. Hence, this review exposes why honey remains the best antibiotic and its potency as an antioxidant, antibacterial, and anti-inflammatory. Honey possesses some vital components such as Methylglyoxal, Bee defensin-1, Hydrogen peroxide, osmotic effect and phenolic compounds. Honey also possesses properties that inhibit the formation of bio films. These made honey more powerful because it prevents the formation of antibiotic-resistant bacteria while conventional antibiotic fail because they only target the essential growth processes of bacteria and this allows bacteria to build up resistance over time.

Keywords: Honey; Antibacterial; antioxidant properties; Antibiotics; Wounds and burns.

1. Introduction

Honey, the only sweetening material that can be stored and used exactly as produced in nature. No refining or processing is necessary before enjoying this. Honey is the sweet, viscous substance elaborated by the honeybee from the nectar of plants. This simple definition excludes honeydew honey, which is produced by the bee from honeydew excreted by various plant-sucking insects. The combs are constructed by the bees from wax they secrete, the production of which requires about 8–10 times its weight in honey [1]. As produced, it is highly variable, particularly in color, flavor, moisture content, and sugar composition, indeed in nearly every constituent.

* Corresponding author.

As agricultural practices and crops change, the value of areas for beekeeping or the quality, type, and amount of honey produced will be influenced. Honey is characterized by its color and floral type [2]. The antioxidant activity of honey is very much dependent on the botanical origin where the bee was reared. A group of naturally blended honeys is available on a consistent basis such as, fall flowers, alfalfa, sweet clover, and mixed flowers from various specified areas [3]. Manuka honey has had major importance due to its broad antibacterial efficacy. Manuka honey is derived from *Leptosperm sp.* originating in New Zealand [4].

This unifloral honey has been used in the pharmaceutical industry for the treatment of a variety of diseases and has been reverted to medical-grade honey [5]. The antibacterial activity of honey is attributed to its osmolarity, H_2O_2 content, low pH, phenolic acids levels, and flavonoids. Phytochemical factors, such as tetracycline, fatty acids, peroxides, ascorbic acid, amylase, terpenes, phenols, benzoic acid and benzyl alcohols, are factors that make honey active against pathogenic bacteria and produce either bacteriostatic or bactericidal efficacy [6].

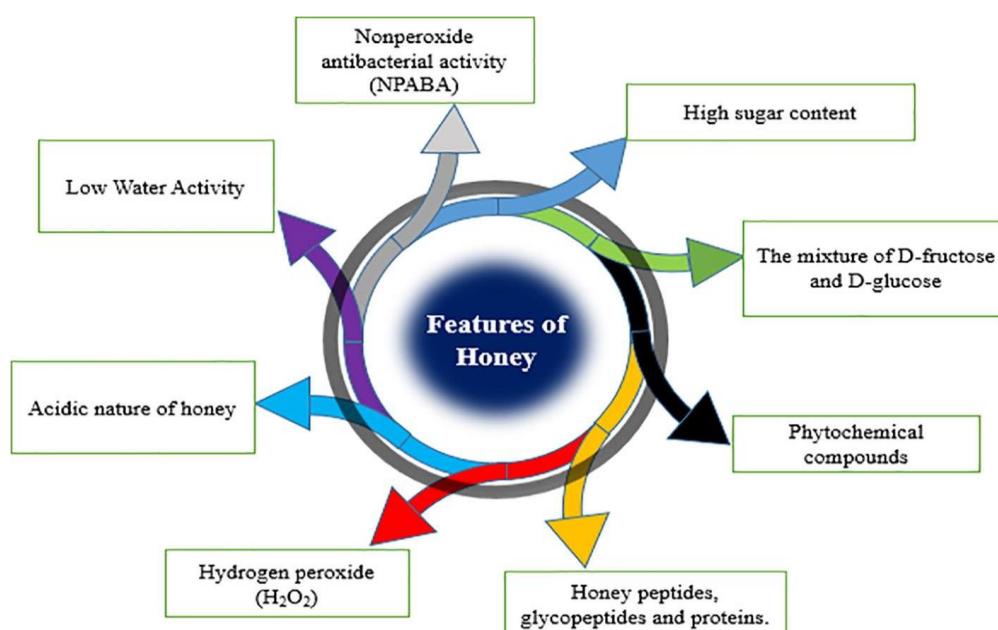


Figure 01: Schematic diagram showing the parameters that contribute to the antimicrobial potential of honey [7].

2. Composition of Honey

Honey is a mixture of sugars and carbohydrates. It is mainly fructose and glucose and remaining sugars are maltose, sucrose, and other complex carbohydrates. Composition and properties like aroma, color, and flavor and antioxidant nature of honey depends on Flowers, Honey bee species, Geographic regions, Weather and climate, Processing/storage [8]. Honey begins with nectar but Honey is a viscous and has low water content, nectar is about 80% water. Honey is a flavorful and sweet product which is consumed over years due to its high nutritional values and benefits on health. Honey is a complex food substance contains 181 substances such as sugars, moisture, vitamins, minerals, enzymes, flavonoids and 5-hydroxymethylfurfural (HMF). The main constitutions of honey are glucose, fructose, sucrose, proteins, and moisture [9].

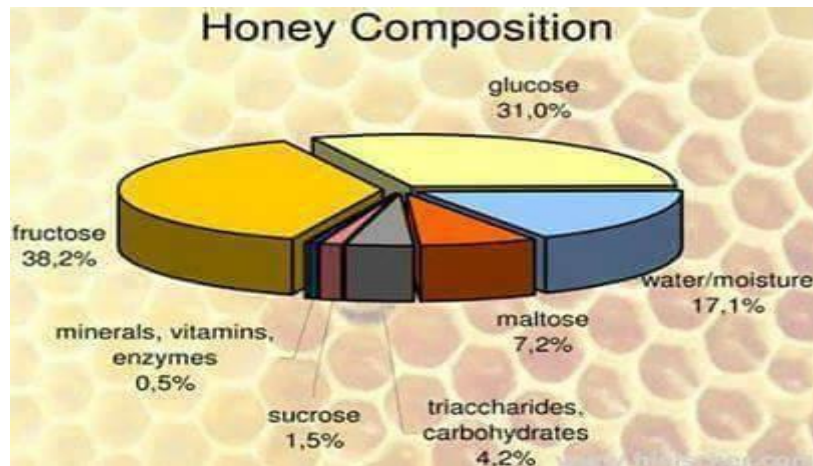


Figure 02: composition of honey natural 'inhibine' [10]

2.1 Forms of Honey

Honey is a saturated or supersaturated sugar solution produced by social bees and some other social insects. Bees and insects gather nectar or honeydew from the flower of living plants and process by the addition of enzymes into honey, then store as a food for use in dearth periods [11].



Figure 02: Different forms of honey [12].

Despite the contributions of few other insects honey is chiefly produced by the bees which are social insects with a perennial life cycle. The bees are mainly classified into different groups which include all honey bees (*Apis* spp.), stingless bees (*Melipona* and *Trigona* spp.) as well as Nectarina wasps in South America and several species of honey ants, especially *Melophorus inflatus* in Australia. There are other social wasps and bumblebees (*Bombus* spp.) with annual life cycles which produce honey, but only very little [13].

2.2 According to QURAN

In the Holy Quran, Allah Almighty declared the special ability of honey. It is used to heal and cure diseases. Allah Almighty said “And your Lord revealed to the bee: Make hives in the mountains and the trees in what they build. Then eat all the fruits and walk in the ways of your lord submissively. There comes forth from their bellies, a beverage of many colors, in which there is healing for mankind. Verily in this, sign for those who give thought.” (Surah AlNahal: verses 68 and 69). Honey has been praised in Islam as well as other religions and cultures including the Ayverda and ancient Chinese cultures for many centuries. The importance of honey for 24 Muslims nutrition and therapy is evidenced in their two main references Quran and Sunnah.

3. Antimicrobial Activity and Mechanism action

Antimicrobial identified that inhibine was a 1, 2-dicarbonyl compound in the form of methylglyoxal, a potent antimicrobial, found mainly in Manuka honey [14]. Honey bee which derived protein, bee defensin-1, as a potential antimicrobial component within honey [15]. Honey contains multiple components that act synergistically, enhancing its potency as an antimicrobial. Key factors contributing to its antimicrobial effects, these were high sugar content, low pH, hydrogen peroxide, polyphenolic compounds and the identification of an inhibine [16, 17].

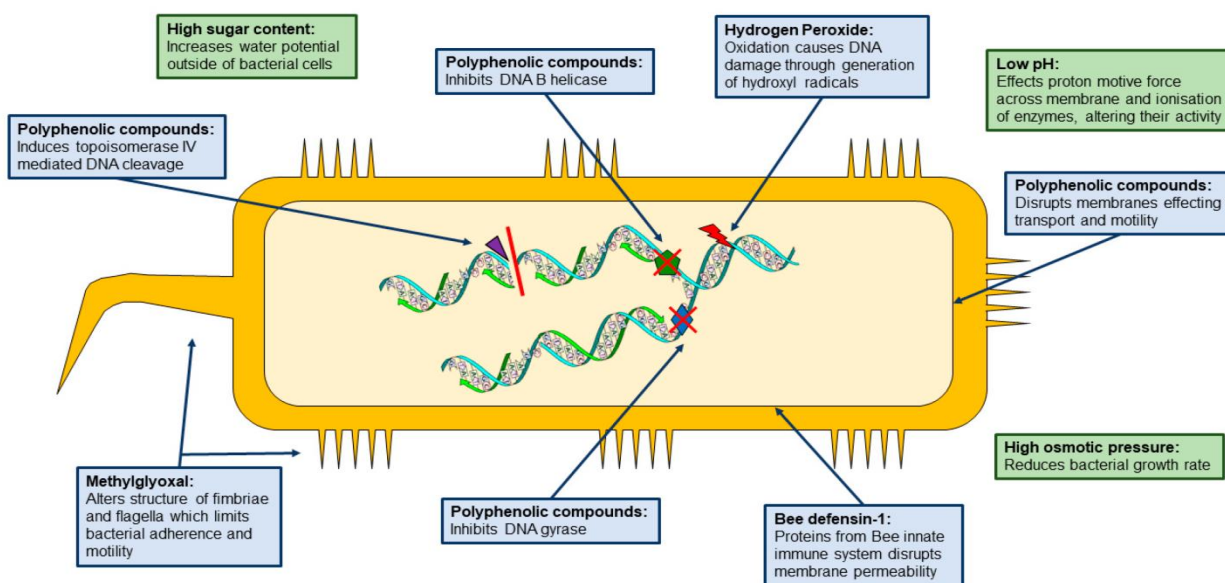


Figure 03: the main constituents attributed to honey’s antimicrobial activity and their mechanism of action.

Direct inhibitory factors affect cellular mechanisms (blue), indirect inhibitory factors have a wider ranging effect on the bacterial cell (green) [18].

3.1 Use of Different Species of Bees for honey

Bees of different *Apis spp* produce natural honey which is composition of sugar solutions. *Apis dorsata*, *Apis cerana*, *Apis florae* and *Apis andreniformis*, these are the four *Apis* species found in Indian sub continents.

From Europe, the *Apis Mellifera* bees are widely used in honey farms on large scales for natural honey production [19, 20]. Around the world, natural honey has been used as an effective medicine since ancient times. The ancient Egyptians, Assyrians, Chinese, Greeks and Romans employed honey for wounds and diseases of the gut [21]. Investigations have shown that a wide range of trace elements are present in honey, including Al, Ba, Bi, Co, Cr, Mo, Ni, Pb, Sn, Ti, as well as minerals (Ca, Cu, Fe, K, Na, Mg, Mn, Zn) among them, the main mineral element is potassium while copper presents in lowest amount [22]. Vitamins such as thiamin (B1), riboflavin (B2), pyridoxine (B6), and ascorbic acid (C) have also been reported but their amount is very small in honey [23].

3.2. Honey by *APIS SPP*

The latter complex compounds do not breakdown easily under heat or light treatment and provide some types of honey with antibacterial activities even after these honeys were exposed to the mentioned factors, which usually destroy enzymes. The typical honey investigated by most researchers is produced by *Apis* spp. This honey is undoubtedly the most widely and massively collected and used by people for different purposes [24]



Figure 04: Honey bees (*Apis* sp.) on a honeycomb, queen bee at centre [25].

3.3. Honey by Stingless bees

But regionally, especially in the tropics and subtropics, there are other honeys made by different bee species, which are sometimes collected in substantial quantities. One group of bees that produces a considerable amount of honey and hence can be used in beekeeping is the stingless bees [26, 28].



Figure 05: Honey of Stingless Bees [27].

4. Therapeutical Properties of Honey

Honey is one of the most effective natural products used for wound healing, such as antimicrobial, antioxidant,

anti inflammatory and cardio protective properties; the treatment of eye disorders, gastrointestinal tract diseases and wound healing activity are described. In vitro research describes beneficial effect(s) of honey on human platelets and blood coagulation proteins [28].

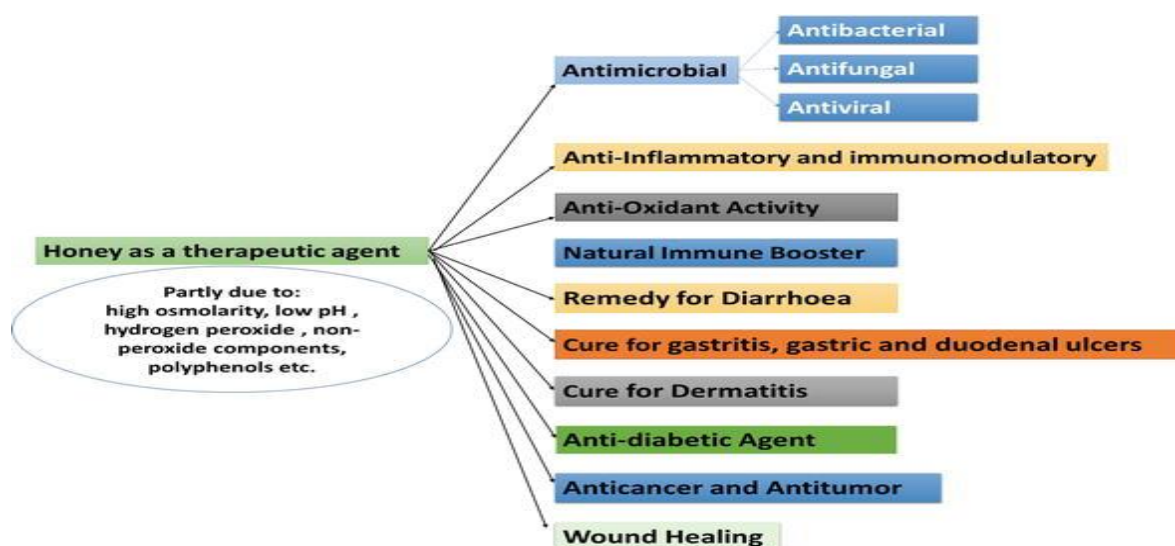


Figure 04: Therapeutical Properties of Honey [29].

4.1 Antioxidant and Antibiotic properties

Honey has an antioxidant property which may be enzymatic (catalase, glucose etc) and non-enzymatic (Amino acids, ascorbic acids, carotenoids etc). [30] The amounts of antioxidants are depending upon honey variety and floral sources. Antibiotics used for the treatment of infections caused by organisms that are sensitive to them such as bacteria or fungi [31]. A Spectrophotometric assay is used to determine the water soluble antioxidant capacity of 19 samples of honey from 14 different floral sources.

It shows that honey has a great variation in chemical nature according to multiple floral sources [26]. Antioxidant constituents were positively correlated with water as well as honey color. Manuka honey has high antioxidant properties than others such as Polish honeys. Manuka MGO-250 and MGO-400 with honeydew, shows high antimicrobial effect against bacteria. Honey has a significant antioxidant content measured as the capacity of honey to free radicals. This antioxidant activity may be at least partly responsible for the anti-inflammatory action of honey [32]. The imbalance between free radical production and the antioxidant defense system which leads to an excess of oxidation is known as oxidative stress [33]. Natural honey is rich with antioxidants from different sources including Vitamin C, monophenolics, flavonoids, and polyphenolics.

A wide range of antioxidants are present in various types of honey which includes monophenolics such as 4-hydroxybenzoic and 4-hydroxycinnamic acids predominate in different honey. The success in the re-establishment of honey in recent medicines led to plenty of investigations in the antioxidant properties of honey and their application in food industry [27]. Antioxidants, which act as preservatives because of their antioxidative activity included both enzymatic (e.g., catalase and glucose oxidase) and nonenzymatic (e.g.,

organic acids, Maillard reaction products, amino acids, proteins, flavonoids, phenolics, α -tocopherol, and ascorbic acid) substances [28]. The flavonoids content reaches about **0.5%** in pollen, **10%** in propolis and about **6 mg/kg** in honey. If honey can slow or stop the growth of spoilage organisms or food pathogens then its incorporation into 98 foods as a preservative can be explored. Due to its antimicrobial properties, honey may serve as a natural food preservative [28].

4.2 Wound healing properties of honey

Honey from different sources has been used for a wide spectrum of wounds. Presently a blend of jelly bush and the Manuka honey (Med honey) is first which certified and medically licensed for the wound care in the many European countries [29]. Honey is beneficial also re-growth of tissues, angiogenesis and fibroblast growth to produce collagen fibers and the replace of connective tissue. Honey facilitates formation of new skin by encouraging the re growth of the epithelial cells over healed wounds and prevents scar and keloid formation also eliminates the necessity of skin grafting [30]. The floral source of the honey belongs to the family of *Leptospermum* trees which gives nectar from manuka and Jelly bush flowers [31]. Honey also used for the treatment of respiratory diseases. Honey can be used as a substitute for glucose in solution with electrolytes. The use of honey on severe affected infections clear wound in a very particular manner. Many types of honey have been studied for antimicrobial activity [32].

4.3. Antibacterial Activity of Manuka Honey

Antibacterial activity of honey is mainly due to the acidity, high osmotic pressure, volatile compounds, flavonoids and polyphenolic acids. Moreover, enzymes like glucose oxidase and catalase are also responsible for the antibacterial potential of honey [33]. The strong antibacterial activity of manuka honey is due to the presence of the antibacterial substance methylglyoxal. The antifungal activity of honey against *Candida albicans* has been reported in many studies. Phenolic compounds are amongst the most important groups of compounds occurring in plants, and are found to exhibit ant carcinogenic, anti-inflammatory, anti-atherogenic, antithrombotic, immune modulating and analgesic activities and which may exert these functions as antioxidants [34]. Hydrogen peroxide plays very important role regarding antimicrobial properties of honey. It is produced by glucose oxidase in enzymatic oxidation of glucose. It was previously reported that the highest level of hydrogen peroxide was formed in **30%** water solutions after **24 h** of incubation at room temperature. It can be seen that the antibacterial properties depend on the honey type and bacterial strain [35].

4.4. Phenolic activities of honey

The flavonoids present in honey are categorized into **three classes** with similar structure: **flavonols, flavones and flavanones**. These are contributed significantly to honey color, taste and flavor and also have been beneficial for health effects. Diastase numbers (DN), hydroxymethylfurfural (HMF), proline and sucrose are usually used as indicators of the ripeness and quality of honey [36]. In terms of antimicrobial and antioxidant activity because of differences in levels of peroxide production and non-peroxide factors, a comparative study has been conducted to establish the antibacterial and antioxidant potency of four varieties of honey from

different botanical and geographical origins [37].



Figure 04: Phenolic Compounds in Honey and Their Associated Health Benefits [38].

4.5. Anti-inflammatory Activities

The anti-inflammatory effects of honey have been demonstrated in histological studies of wounds in animals where there was no Infection involved. Honey acts as a potential anti-inflammatory agent. Inflammation is a sign of response to infection or injury but when excessive or prolonged, it can prevent healing or even cause advance damage. Honey's anti-inflammatory activity have been found in a clinical trial to prevent partial thickness burns from converting to full-thickness burns which would have needed plastic surgery, a characteristic of burns, where there is much inflammation[39]. However, the pharmaceutical ones have serious limitations: corticosteroids suppress tissue growth and suppress the immune response and the non-steroidal anti-inflammatory drugs are harmful to cells, especially in the stomach but honey has an anti-inflammatory action free from adverse side effects. Forest honey (*honeydew*), poly-floral honey and mono floral *acacia* honey [40]. The poly-floral honey from central Serbia is characterized by a lower content of metals, except the content of Mn and Ni, compared to the honey from other regions of Serbia. The level of organic acids in honey is relatively low and about **18** organic acids have been detected Most of the acidity present in honey is added by honey bees [41].

4.6. Antibiotic Properties

It has been demonstrated in many studies that honey has antibacterial effects, attributed to its high osmolarity, low pH, hydrogen peroxide content, and content of other, uncharacterized compounds The low water activity of honey is inhibitory to the growth of the majority of bacteria, but this is not the only explanation for its antimicrobial activity. Honey is mildly acidic, with a pH between **3.2** and **4.5**. The low pH alone is inhibitory to many pathogenic bacteria. It could be sufficient to exert an inhibitory effect. When consumed orally, the honey would be so diluted by body fluids that any effect of low pH is likely to be lost [42]. The primary amino acid is

proline, contributing **50-85%** of the total amino acids. Gluconic acid, the predominant honey, is the product of glucose oxidation, presenting at 50-fold higher levels than other acids [43].

5. Uses of Honey

Although honey has been used as a medicine since ancient times, its effectiveness as a remedy has been revealed to be due to its antibacterial activity only a century ago. [44] The antibacterial activities of honey were considered to be owing to the high osmolality of honey whereby water is drawn away from microorganisms, reducing their ability to survive. Honey is acidic with a pH value between 3.2 and 4.9 which inhibits growth of many pathogens whose optimal pH of growth is not acidic [45].

Table 1

Uses of Honey	References
❖ Honey has been used to treat wounds, burns, sores and boils. Manuka honey can enhance wound healing, amplify the regeneration of tissue and even decrease pain in patients suffering from burns.	[44 , 46]
❖ Promote Oral Health	[47]
❖ Soothe a Sore Throat	[48]
❖ Help Prevent Gastric Ulcers	[49]
❖ Improve Digestive Symptoms	[50, 51]
❖ Reduce Heart Disease Risk by Impacting Cholesterol Levels	[52]
❖ Specific Proteins May Lower Blood Pressure	[47]
❖ Regulates Blood Sugar by Reducing Oxidative Stress and Inflammation	[53]
❖ Improved memory and reduced symptoms of depression	[54, 55]

6. Conclusion

Honey prevents the formation of antibiotic-resistant bacteria because of its effectiveness on multiple levels. Conventional antibiotics fail because they have only targeted the essential growth processes of bacteria and hence allow bacteria to build up resistance over times. Honey has a potent activity against bacteria and fungi. This means that honey can be expected treatment for diabetic foot ulcers brought about by microorganisms. The low pH (3.5-4.5) of honey restrains *Staphylococcus aureus* development. It invigorates the bactericidal activity of macrophages in injuries and furthermore smothers the creation of provocative cells at the injury site. This may invigorate the creation of the pro-inflammatory cytokine, permitting to happen and animating the multiplication of fibroblast and epithelial cells. The movement of the revolutionary (DPPH) shifted fundamentally among most examples of honey.

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