



CRITICAL REVIEW: ANTIOXIDANT PROPERTIES AND ANTIBIOTIC MECHANISM OF HONEY AGAINST INFECTIOUS DISEASES

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ABSTRACT

The advent of antibiotics in modern western medicine has made the use of honey in the treatment of infectious diseases abandoned. 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 biofilms. These made honey more powerful because it prevents the formation of antibiotic-resistant bacteria while conventional antibiotics fail because they only target the essential growth processes of bacteria and this allows bacteria to build up resistance over time.

Keywords: Honey, Antibiotic, Antioxidant, Anti-Inflammatory

1. INTRODUCTION

Honey is a sweet and flavourful product that has been consumed over the years for its high nutritional values and beneficial effects on human health. Honey has been reported [1] to contain about 181 substances including sugars, proteins, moisture, vitamins, minerals, 5-hydroxymethylfurfural (HMF), enzymes, flavonoids, phenolic acids and volatile compounds. Honey contains moisture, glucose, fructose, sucrose, minerals and proteins as the main constituents [2, 3]. Reports indicate that honey has an antioxidant property. These antioxidant properties of honey may be enzymatic (catalase, glucose oxidase and peroxidase) and non-enzymatic substances (ascorbic acid, α -tocopherol, carotenoids, amino acids, proteins, Maillard reaction products, flavonoids and phenolic acids) [4-6]. The amount of antioxidants present dependent largely on the variety honey and floral sources.

Antibiotics are substances produced by or derived from microorganisms that destroys or inhibits the growth of other microorganisms. Antibiotics are used to treat infections caused by organisms that are sensitive to them usually bacteria or fungi [7]. For all antibiotic classes including the major last resort drugs, resistance is increasing worldwide [8, 9] and even more alarming, very few new antibiotics are being developed. The potent activity of honey against antibiotic-resistant bacteria [10-12] resulted in renewed interest for its application. Honey has been approved for clinical application. This review gives an

overview of the current knowledge on honey, its antioxidant, antibiotic and mechanism of action against bacteria.

2. ESSENTIAL COSTITUTUENTS IN HONEY

Hydrogen peroxide: Hydrogen peroxide (H_2O_2) is one of the main elements of honey considered when looking into antibacterial activity. Its production is the result of the enzyme glucose oxidase produced by bees; this enzyme uses glucose and oxygen to create gluconic acid and H_2O_2 , and is activated when honey is diluted [13]. Glucose oxidase is affected by heat and light and is inhibited by catalase. Catalase can be present in flower pollen and in the tissues of the body. [14] have speculated that the presence of catalase in wound tissue may have an inhibitory effect on hydrogen peroxide production by honey, making non-peroxide activity an important factor in a clinical setting. Some honeys exhibit activity in the presence of catalase that cannot be explained solely by their high sugar content. Many honeys are kept in the dark and at room temperature prior to experimentation to prevent the degradation of glucose oxidase and the loss of hydrogen peroxide.

High Osmolarity: High osmolarity is also considered an important factor as it inhibits bacterial growth by drawing moisture from the environment and dehydrating the microorganisms. This means that an artificial honey made to the same concentration of sugar (80% w/v) [15] as real honey does exhibit some antibacterial activity, but this is often lower than that of the honeys it is being compared to.

pH: pH is a likely factor in undiluted honey, as most honeys are naturally acidic (pH 3.2-4.5) and this will inhibit the activity of many microorganisms. When honey is diluted this pH changes and may become more neutral, but activity is still observed, so it is not thought to be a central factor.

Methylglyoxal: Methylglyoxal (MGO) is a protein-glycating agent and has been found in medical honeys and is thought to be responsible for the non-peroxide activity observed in some honeys [16]. Its activity in diabetic ulcers has been questioned on the grounds of safety issues, due to the production of advanced glycation end products; which cause health complications in diabetes.

Bee Defensin-1: Bee Defensin-1 was found in Revamil honey [15] and was shown to contribute towards the anti-bacterial activity against some bacterial species.

Propolis: This is a resinous structural component of the hive composed of floral elements, such as tree sap. It can have anti-microbial activity which some honeys may be exposed to it [17].

The Honey's Micro Flora: This has been implied in the activity of honey [18] tested bacterial isolates from American honeys and manuka to determine if they produced anti-microbial agents, and found that a majority did, with one of the manuka samples having the highest isolate activity. [15] gradually removed/inhibited the MGO, H_2O_2 , Bee defensin-

land altered pH to see what was responsible for the broad spectrum antibacterial activity, in Revamil. They found that different bacteria were sensitive to different components, e.g. the neutralisation of MGO alone reduced the activity against *Escherichia coli* and *Pseudomonas aeruginosa*, and the neutralisation of H₂O₂ reduced activity against all tested organisms except *Bacillus subtilis*. When MGO, H₂O₂, and Bee defensin-1 activity were removed, and the pH was adjusted to pH7, the honey had the same activity as the artificial honey.

3. ANTIOXIDANT POTENTIALS OF HONEY

Honey has been found to have a significant antioxidant content [19], measured as the capacity of honey to scavenge free radicals. The antioxidant activity of honey has also been demonstrated as inhibition of chemiluminescence in a xanthine-xanthine oxidase-luminol system that works via generation of superoxide radicals [20]. This antioxidant activity may be at least partly what is responsible for the anti-inflammatory action of honey, as oxygen free radicals are involved in various aspects of inflammation, such as further recruitment of leucocytes that initiate further inflammation [21, 22]. The application of antioxidants to burns has been shown to reduce inflammation [23]. But even if the antioxidants in honey do not directly suppress the inflammatory process they can be expected, by scavenging free radicals, to reduce the amount of damage that would otherwise have resulted from these.

Honey inhibit the formation of free radicals, a potential to exert antioxidant activity. Superoxide formed during inflammation is unreactive, this is then converted to hydrogen peroxide a much less reactive peroxide radical generated [24]. Formation of the oxidant peroxide radical is then catalysed by metal ions (e.g.; iron and copper). Sequestration of these metal ions in complexes with organic molecules is an important antioxidant defence system [25]. Flavonoids and other polyphenols, common constituents of honey, will do this [26].

4. ANTIBACTERIAL POTENTIAL OF HONEY

Honey has an antibacterial activity of therapeutic importance, especially in situations where the body's immune response is insufficient to clear infection. Bacteria often produce protein digesting enzymes, which can be very destructive to tissues [27] and can destroy the protein growth factors that are produced by the body to stimulate the regeneration of damaged tissues in the healing process [28]. Furthermore, some bacteria produce toxins that kill tissue cells [29]. Additional damage is often caused by bacteria carrying antigens that stimulate a prolonged inflammatory immune response which gives excessive production of free radicals that are very damaging to tissues [30]. Bacteria in wounds can also consume oxygen and thus make the level of oxygen available to the wound tissues drop to a point where tissue growth is impaired [31]. Consequences associated with bacterial infection devoid of administering honey to clear infection include: non-healing of wounds; increase in size of wounds and development of ulcers and abscesses; failure of skin grafts; inflammation, causing swelling and pain.

Reports indicated shows that not all honeys are likely to have the same therapeutic effect due to the variety of antibacterial activity possessed by honey. Physicians in past millennia were aware of this, at least from practical experience and specified particular types of honey may be used to treat particular ailments. Dioscorides (c. 50 AD) stated that a pale yellow honey from Attica was the best, being 'good for all rotten and hollow ulcers' [32]. Aristotle (384-322 BC) discussing differences in honeys, referred to pale honey being good as a salve for sore eyes and wounds [33]. There is a similar awareness in present-day folk medicine: the strawberry tree (*Arbutus unedo*) honey of Sardinia is valued for its therapeutic properties [34] in India, lotus (*Nelumbium sceciosum*) honey is said to be a panacea for eye diseases [35]; honey from the Jirdin valley of Yemen is highly valued in Dubai for its therapeutic properties; and manuka honey in New Zealand has a long standing reputation for its antiseptic properties.

5. HONEY'S POTENTIAL AS AN IMMUNE SYSTEM BOOSTER

One way through which honey clears infection is by stimulating the body's immune system to fight infection. Honey has been reported to stimulates B-lymphocytes and T-Lymphocytes in cell culture to multiply, and activates neutrophils [36]. It has also been reported that it stimulates monocytes in cell culture to release the cytokines TNF-a,1 and IL-6, the cell 'messengers' that activate facets of the immune response to infection.

Honey is also known to provides a supply of glucose which is vital for the respiratory burst in macrophages that produces hydrogen peroxide, the bacterial destroying activity [37]. It furthermore provides substrates for glycolysis a major mechanism for energy production in the macrophages and thus allows them to function in damaged tissues and exudates where oxygen supply is limited [37]. The acidity of honey may also assist in the bacteria-destroying action of macrophages, as an acid pH inside the phagocytotic vacuole is involved in killing ingested bacteria [37].

6. ANTI-INFLAMMATORY POTENTIAL OF HONEY

It has been observed clinically that when honey is applied to wounds it visibly reduces inflammation [38]. It has also been observed to reduce oedema around wounds [12, 39, 40] and exudation from wounds [12, 41, 42] both of which result from inflammation. Pain is another feature of inflammation and honey has been observed to be soothing when applied to wounds [43, 44]. A histological study of biopsy samples from wounds has also shown that there are fewer of the leu-cocytes associated with inflammation present in the wound tissues [38]. What is responsible for these observations is a direct anti-inflammatory effect, not a secondary effect resulting from the antibacterial action removing inflammation causing bacteria: the anti-inflammatory effects of honey have been demonstrated in histological studies of wounds in animals where there was no Infection involved [45-47]; A direct

demonstration of the anti-inflammatory properties of honey, where honey decreased the stiffness of inflamed wrist joints of guinea pigs has also been reported [48].

Honey acts as a potential anti-inflammatory an important therapeutics as the result of inflammation may be major. 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 [38], a characteristic of burns, where there is much inflammation. The free radicals formed in inflammation are also involved in stimulating the activity of the Fibroblasts [49] which is the basis of the body's repair process, normally triggered by the inflammation that follows injury. These cells enables the production of connective tissues including the collagen fibres of scar tissue and in prolonged inflammation their over-stimulation will lead to proud flesh and fibrosis an excessive production of collagen fibres [50]. The reduction in keloids and scarring that is a feature of the dressing of wounds with honey [41, 51, 52] and the cosmetically good results obtained [53], are probably due to the anti-inflammatory action of honey. However, the pharmaceutical ones have serious limitations: corticosteroids suppress tissue growth and suppress the immune response [54] and the non-steroidal anti-inflammatory drugs are harmful to cells, especially in the stomach [55] But honey has an anti-inflammatory action free from adverse side effects.

7. HONEY: AN EXCEPTIONAL ANTIBIOTIC

Lead author [56]; presented the findings at the 247th National Meeting of American Chemical Society. She reported that the ability of honey to fight infection lies in its multiple levels; this makes it difficult for bacteria to develop resistance. She also reported, Honey uses a combination of weapons including polyphenols, hydrogen peroxide and an osmotic effect. It uses multiple modalities to kill bacteria and hence an ambidextrous fighter.

The first fighting method employed is its osmosis effect. This effect is exerted from honey's high sugar concentration. During the process, water is drawn from the bacteria cells, causing dehydration and subsequent death.

Honey destroys the modes of bacterial communication. It possesses properties that stop the formation of biofilms. These slimy biofilms are bacteria communities which harbour diseases. In a process called Quorum Sensing, honey breaks up bacterial communication by keeping these biofilms from congregating. Breaking this process stops bacterial communicating and hence expanding their viability. Without this communication mode the bacteria cannot release the toxins that increase their ability to cause diseases. She said, the ability of honey to disrupt the quorum sensing leads to the virulent behavior of bacteria is weakened, rendering the bacteria more susceptible to conventional antibiotics.

It can be concluded that honey is so powerful for destroying bacteria that it should be the first mode of treatment when treating a bacterial illness. Doctors are advised to

prescribe honey first, since it attacks bacteria from multiple angles. Honey prevents the formation of antibiotic-resistant bacteria because of its effectiveness in fighting on multiple levels. Conventional antibiotic fail because they only target the essential growth processes of bacteria and hence allow bacteria to build up resistance over time thereby destroying the essential bacteria in their alimentary canal.

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