### Honey – A remedy rediscovered and its therapeutic utility

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#### Abstract

Honey is a common household product with many medicinal uses described in traditional medicine. Modern system of medicine is also finding the honey efficacious in various medical and surgical conditions. Antimicrobial, antioxidant and wound healing properties of honey are being evaluated with successful outcome. Prevention and treatment of various infections due to a wide variety of organisms and promoting surgical wound healing are some of the areas where honey is making its mark.

Key words: Honey: wound healing.

Honey is a popular sweetener and a common household product used throughout the world. Popularity comes not only of its being a natural sweetener but also many benefits, proven or unproven are associated with it.

Apitherapy or therapy with bee products like honey is an age-old tradition. Human use of honey is traced to some 8000 years ago as depicted by stone age paintings. Different traditional systems of medicine have elaborated the role of honey as medicinal product. Sumerian clay tablets (6200 BC), Egyptian papyri (1900-1250 BC): Vedas (5000 years); holy Koran, Bible and Hippocratic methods (460-357 BC) have described the uses of honey. The latter described its use for baldness, contraception, wound healing, laxative action, cough and sore throat, eye diseases, topical antisepsis, prevention and treatment of scars.

In the twentieth century the use of honey as having good antimicrobial properties and aiding wound healing have been reported. The Russians used it in World War I to prevent wound infection and to accelerate wound healing. The Germans combined cod liver oil and honey to it to treat ulcers, burns, fistulas and boils.

#### **Composition of honey**

Bees are the natural source for producing honey and depending upon the geographical areas, different varieties of plants are used to prepare honey.<sup>1</sup> Nutritional values and profiles vary accordingly and can thus influence the value of a specific honey for medicinal or health promoting purpose.

Calories	300
Water	17.1 gm
Total Carbohydrates	82.40 gm
Fructose	38.50 gm
Glucose	31.0 gm
Maltose	7.2 gm
Sucrose	1.5 gm
Others	4.0 gm
Dietary	0.2 gm
Total proteins	0.3 gm
Total fat	00
Total cholesterol	00
Fat soluble vitamins	`0'
pH range	3.4 - 6.1 (usually 3.9)
Acids	0.017 - 1.17%
Water content	16% - 18.3%

On an average, the composition of honey per 100 g is:

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Dr.Bikash Medhi, Assistant Professor, Department of Pharmacology, PGIMER, Chandigarh. It also contains proteins (proline the maximum) vitamins and minerals. Honey has good quantities of antioxidants<sup>2</sup>, both with enzymatic and non-enzymatic activities. Depending on their source varying concentrations of catalase, flavonoids, ascorbic acid and alkaloids are present. In general, the darker the honey, more is the antioxidant activity. Higher water content also has higher antioxidant activity.

#### Enzymes

A variety of enzymes are present in honey like oxidase, invertase, amylase, catalase etc. The enzyme glucose oxidase, produces hydrogen peroxide (which provides antimicrobial properties) along with gluconic acid from glucose which helps in calcium absorption. Invertase converts sucrose to fructose and glucose. Dextrin and maltose are produced from long starch chains by the activity of enzyme amylase. Catalase helps in producing oxygen and water from hydrogen peroxide.

## Possible mechanisms of antimicrobial activity of honey

1. Low Water Activity: Honey, a supersaturated sugar solution, with water activity (AW) of 0.56 - 0.62 does not support the growth of bacteria which, in most of the cases, required AW = 0.94 - 0.99.

2. Acidity: Usual pH range of most of the pathogens is around 4.0 - 4.5. Honey with an average value of 3.9 does not support the growth of bacteria. Dilutions with body fluids will raise the pH and may lessen this antimicrobial activity.

3. *Glucose Oxidase*: Glucose oxidase, is an enzyme that forms honey from nectar. In the process, there is formation of gluconic acid and hydrogen peroxide. These by products preserve and sterilize honey during the ripening process. Dilution of honey results in 2500-50,000 times increase in enzyme activity and a slow release antiseptic that is non-damaging to skin.

4. Small contributions in antibacterial activity comes from the presence of non-peroxides flavonoids<sup>3</sup> (like pinocembrin), benzylalcohol, terpenes, etc. This non-peroxide activity is found to be maximum in manuka honey.

#### Infections found sensitive to honey

Manifold pathogens that are found to be sensitive to antinfective properties of honey.<sup>4</sup> Variable results favour for its activity against Bacillus anthracis, Corvnebacterium *diptheriae*, Haemophilus pneumoniae. influenzae, Klebsiella Listeria monocytogenes, *Mycobacterium* tuberculosis, Pasteurella *multicoda*, Proteus species,

Pseudomonas aeruginosa, Salmonella diarrhoea, Salmonella typhi, Serratia marcescens, Shigella dysentery, Staphylococcus aureus, Streptococcus faecalis, Streptococcus mutans, Streptococcus pneumoniae, Streptococcus pyogenes and Vibrio cholerae.

#### **Antioxidant Activity**

Honey is a naturally occurring powerful antioxidant with antioxidant status varying with the floral source<sup>5</sup> and positively correlated to dark colour and water content. It may serve as a potential source of dietary antioxidant and studies are undergoing to confirm the same.

# Clinical conditions found responsive to treatment with Honey

#### Wound healing

One of the most studied and most effective use of honey is found in healing of wounds.<sup>6</sup> Nearly all types of wounds like abrasion, abscess, amputation, bed sores / decubitus ulcers, burns, chill blains, burst abdominal wound, cervical ulcers, cracked nipples, diabetic ulcers, fistulas, leprosy ulcers, traumatic ulcers, septic wounds, malignant ulcers, varicose ulcers, sickle cell ulcers, surgical wound or wounds to abdominal wall and perineum are found to be responsive to honey therapy.

Application of honey as wound dressing leads to stimulation of healing process and rapidly clears the infection. Honey has cleansing action of wounds, stimulates tissue regeneration, reduces inflammation and honey impregnated pads act as non adhesive tissue dressing.<sup>7</sup>

The exact molecular mechanism of wound healing using honey is yet to be elucidated. However, several recommendations are made regarding appropriate wound dressing with honey. Type of wound and degree of severity will effect efficacy. Selected honey should be used in sufficient quantities so that it remains there if diluted with wound exudates. It should cover and extend beyond the wound margins. Better results occur when applied on dressing than on wound. All the cavities should be adequately filled with honey and occlusive dressing applied to prevent oozing from the wound.<sup>8</sup>

In one of cases of below knee amputation in a young boy, which was heavily infected with *Pseudomonas* and *Staphylococcus aureus* and non responsive to conventional treatment, application of sterilized active manuka honey dressing pads led to complete healing in ten weeks.<sup>9</sup> Similar results are found with burns. Honey dressing speeds up healing process, sterilizes wound, reduces pain with enhanced formation of granulation tissue, lessens inflammation and scarring, has an advantage of easy dressing change and a lower cost of therapy.<sup>10</sup>

Studies in Fournier's gangrene showed rapid improvement with decreased edema and discharge, rapid regeneration and little or no scarring, effective wound debridement and a decrease in mortality.<sup>11</sup> Honey is used successfully for treating ulcerations following radical surgery for carcinoma of the breast and varicose veins. It is also used following radical surgery for carcinoma of vulva resulting in infection free wound with minimal wound debridement and hospital stay.<sup>12</sup> Healing within two weeks is observed for cases of wound disruption following caesarian section by using honey.<sup>4</sup> Similar efficacy is observed in bed sores and decubitus ulcers.<sup>13</sup>

In a study treatment of 59 patients having recalcitrant wounds and ulcers of varied etiologies like Fournier's gangrene, burns, cancrum oris, diabetic ulcers, traumatic ulcers, decubitus ulcers, sickle cell ulcers and tropical ulcers, which have been treated with conventional treatments (such as Eusol, dressing with acriflavine, sofra-tulle, or cicatrin or systematic and topical antibiotics) for "sufficiently long time" (1 month to 2 years) and not improved. Treatment of these cases with honey showed remarkably encouraging results<sup>7</sup>. Similar results are found in other studies with beneficial therapeutic effects of honey.

Clinical trials are also conducted comparing honey dressing in burns with amniotic membrane dressing, silver sulfadiazine dressing and boiled potato peel dressing. Honey dressing showed improvement in these cases as better and showed early healing with lesser degree of contracture and scarring.

#### Advantages of honey as wound dressing

Honey provides a moist healing environment and prevents bacterial growth even when wounds are heavily infected. It is an effective means of quickly rendering heavily infected wounds sterile and inhibiting the growth of antibiotic resistant strains of bacteria. Viscosity of honey further acts as a barrier against wound infection. It provides glucose to leucocytes, which is essential for respiratory burst to produce hydrogen peroxide leading to antibacterial activity of macrophages. The acidity of honey further aids in antibacterial activity.<sup>7</sup> Presence of wide range of amino acids, vitamins and trace elements also have direct nutrient effect on regenerating tissues. Osmotic outflow after the application of honey assists in lifting dirt and debris from the bed of the wound. The dressing thus is non-sticky and enables pain free change. Some people have however even experienced pain or discomfort. This may be because of naked nerve endings coming in contact with acidity of honey. Honey dressing has economic advantages to the patient. Rapid healing reduces hospital stay and dressing material and surgical costs. Domociliary care is possible alongwith rapid return to work with its use. Different animal studies in partial and full thickness wounds, burns on different animal models have shown advantage of using honey as wound dressing compared to conventional treatment.

Honey has also shown antimycobacterial effect. Standard L-J media containing different concentrations of honey was prepared. Bacilli from positive cultures and from positive smears of the affected patients were inoculated on each of the prepared plates. Growth of mycobacteria was inhibited at honey concentrations of 10% and 20% but not at 5%, 2.5% or 1% concentration.<sup>14</sup>

Potential use of honey as anticariogenic agent is being evaluated and studies have till now yielded some positive. Benefits also have been seen in tooth extraction pain and infection or caries due to radiation-induced xerostomia.<sup>15,16</sup>

#### Gastro intestinal Tract

Diarrhoea and gastroenteritis are found to resolve quickly with honey.  $^{17,18}$  At 5% (v/v) concentration, honey decreased the duration of diarrhoea in cases of bacterial gastroenteritis as compared to group using sugar in replacement fluid. No change was seen in viral gastroenteritis. In rehydration fluid, honey adds potassium and water uptake, without increasing sodium uptake. It also helps to repair the damaged intestinal mucosa, stimulates the growth of new tissues and work as an anti-inflammatory agent.

H. Pylori is found to be sensitive to honey with a median level of antibacterial activity due to the presence of hydrogen peroxide at a 20% concentration.<sup>19</sup> Non peroxide antibacterial activity at a concentration of 5% as in manuka honey is equally good. This may lead to antiulcer property of honey. Other possible mechanisms that may help to protect and heal gastric mucosa are stimulation of blood supply, anti-inflammatory activity and stimulation of growth of new epithelial cells. Honey can act as both bacteriostatic and bactericidal depending on the concentration used. 4-8% pasture honey and 5-11% manuka honey were bacteriostatic whereas bactericidal activity was achieved at 5-10% and 8-15% (v/v) concentrations, respectively. In contrast, artificial honey (sugar solution which mimics

composition of honey) was bacteriostatic only (at 20-30%) and not bactericidal.

#### Fungal infections

Candidiasis, caused by *Candida albicans*, may respond to honey.<sup>20</sup> Cutaneous and superficial mycoses like ringworm and athletes foot are found to be responsive to honey. This responsiveness is partly due to the inhibition of fungal growth and partly to inhibition of bacterial infection. Mastitis in cattle may respond to honey and can be a good alternative to antibiotics.

#### **Ophthalmology and Honey**

Honey is used worldwide for the treatment of various ophthalmological conditions like blepharitis, keratitis, conjunctivitis, corneal injuries and chemical and thermal burns to eyes. In one of the study, with topical application of honey as ointment, in 102 patients with non responsive eye disorders, improvement was seen in 85% patients and in remaining 15% there was no disease progression. Transient and stinging sensation were noted shortly after applying honey. Application of honey in infective conjunctivitis reduced redness, swelling, pus discharge and time to bacterial eradication.<sup>4,20</sup>

#### Honey and Carbohydrate Metabolism

Honey is a natural mixture of fructose-glucose along with some oligosaccharides, proteins, vitamins and minerals. Studies are conducted that demonstrated honey as an effective carbohydrate source for athletes before and after resistance training and during endurance exercise.

#### Honey and Diabetes

In one of the clinical trial of type I and type II diabetes the use of honey was associated with significantly lower glycaemic index than with glucose or sucrose in normal as well as type I diabetes. Type II diabetics had values similar for honey, glucose and sucrose. Honey compared with dextrose caused a significantly lower rise in plasma glucose levels in diabetic subjects. It also caused reduction of blood lipids, homocysteine levels and CRP (C reactive protein) levels in normal and hyperlipidemic subjects.<sup>21</sup>

#### As food preservative and prebiotic

Hydrogen peroxide and non peroxide components such as antioxidants are found to inhibit growth of *Shigella, Listeria monocytogenes,* and *Staphylococcus aureus* helping in food preservation. *Clostridium botulinum* however may be present in small amounts in honey. It is also found to lower bacterial counts in poultry and fish products. It has a good potential to be used as a natural source of antioxidants to reduce negative effects of polyphenol oxidase browning in fruit and vegetable processing.<sup>5</sup>

A prebiotic is a non-digestable dietary supplement that modifies the balance of the intestinal microflora stimulating the growth and activity of the beneficial organisms and suppressing potentially deleterious bacteria. Honey is found to be a suitable sweetener in fermented milk products without inhibiting the growth of common bacteria like Streptococcus thermophilus, Lactobacillus acidophilus, Lactobacillus delbruekii and Bifidobacterium bifidum which are important for maintaining the health of gastrointestinal tract. Honey also increased and supported the growth of bifidobacterium<sup>22</sup> which is mainly due to the presence of a variety of oligosaccharides. 23

#### Adverse effects

Honey is relatively free of adverse effects. Topical application of honey may lead to transient stinging sensation. Otherwise it is described in different forms as soothing, relieving pain, to be non-irritating and a painless dressing change.

Allergy to honey is rare, but there could be an allergic reaction to either pollen or bee proteins in honey. Excessive application of honey may lead to dehydration of tissues which can however be restored by saline packs. Theoretical risk of rise in blood glucose levels may always be there when applied to large open wound in diabetics.

Risk of wound botulism, due to presence of spores of clostridia, can be minimized by gamma irradiation which will kill the spores of clostridia without any loss of antibacterial activity.<sup>24</sup>

#### Conclusion

The age-old remedy of honey is being rediscovered in modern system of medicine. With more properly conducted clinical trials and better availability of pure preparation of honey, it may be possible to use honey as a place in therapeutics.

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