Recent advances of honey in modern medicines: A review

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Abstract
Honey is used frequently due to its nourishing and healing values. China, Turkey, Argentina, Ukraine, and United States are the main honey producing countries. The most imperative component of honey is carbohydrates. It is present in the form of monosaccharide, fructose and glucose. It plays a vital role as an antioxidant, anti-bacterial and anti-inflammatory agent. This amazing rich golden fluid is much better alternative to sugar. It is an instantaneous energy booster and is used in skin care, hair care and various health linked aspects. The role of honey has been accredited in literature and there is considerable evidence in support of its antioxidant and antiseptic nature, cough avoidance, fertility and wound healing characteristics. However, its use has been controversially deliberated and has not been sound acknowledged in the modern medicine. So the present review is to explore and highlight the role of honey in modern medicine.

Keywords: Anti-inflammatory, Anti-bacterial, Antioxidant, Honey, Modern medicine

Introduction
Rearing of honey bees is not new. Honey has been consumed in human civilizations since its emergence. It is a good business for farmers as well as industrialist. Initially 5-10 honey bee colonies can be a better option to start this occupation. Beehive boxes should be opened at the place where they can be kept permanently. The total production of honey is more than 1.20 MT per annum (Bogdanov et al. 2008) [9]. The sweetness of honey is due to existence of monosaccharide, glucose, fructose and disaccharides, maltose, iso-maltose, turanose and sucrose constituents. Furthermore, honey includes amino acids, traces of vitamin B, vitamin C, niacin, folic acid, minerals, zinc, iron, and many antioxidants (David, 2007 and Fatimah et al. 2013) [14, 17]. Noori et al. (2014) [36] also confirmed that honey is frequently used as an anti-bacterial, anti-inflammatory and anti-oxidant agent.

Castes in Honeybee
In one box three kinds of bees are there viz; one female Queen Bee, many female worker bees and a few male drones. There is only one queen per colony and its role is to lays eggs throughout its life. Worker bees are supposed to collect pollens and nectar from flora and fauna. Drones have primarily no work to do, their function is only to mate with queen and are debarred from the hive during the cool months when primary focus of bees, is warmness and food protection. Drones have big eyes. They do not protect and sting trespasser because absence of a stinger. The worker bee’s crowd around the queen bee at the middle of the cluster and move to keep the center warm till the queen recommends lying. The worker bees turn around the cluster from the outside to the inside so that no bee is too cold. In one colony there could be 60,000 worker bees. Their duties may be different upon bee age in the subsequent order (commencing by cleaning out their cell after ingestion through capped brood cell): feeding offspring, receiving of nectar, hive cleaning and guard duty. A Queen which is getting older may leave the hive with half of the workers and take off to establish a new hive leaving a daughter queen behind. If she is no longer producing workable bees, the colony may sting and kill her. A substitute queen can be added or colony creates new queen by continuous feeding diet of royal jelly to larvae.

Major Significance
Honey is extremely appreciated by consumers for health reassuring features. Correspondingly, the application of honey has been controversially conferred in the literature, whether management with honey bee product is safe or not particularly for metabolically cooperated persons. It is strongly supposed that honey is a chief source of development and vitality. The health encouraging features of honey produce are largely due to the existence of several
metabolites including folic acid, niacin, thiamine, biotin, phytosterols, tocopherol, polyphenols, besides presence of different enzymes and co-enzymes. The encouraging confirmations on the anti-fungicidal, anti-bacterial, anti-oxidant, liver-protective are frequently available in the literature. Mainly honey is a cherished supplement for health of people (Denisow and Denisow-Pietrzyk, 2016) [15]. Modern advances in research, literature emphasized that honey has prospective biological accomplishments with encouraging sound health related properties (Muhammad et al. 2016) [35]. Bees are supposed to converse through many special chemicals, as is common in insects, but also using specific behaviors such as dance pattern that suggests ideas about the quality and variety of resources in the environment, and where these resources are situated. The details of the signaling being used differ from species to species i.e., the two smaller species, Apis andreniformis and A. florea, dance on outside colony, which is horizontal and worker bees dance in the actual compact track of the resource. Similarly, Apis mellifera carnica use their antenna asymmetrically for societal connections with a brawny lateral preference to use their right antennae. It is important to regularly examine the amount of honey in the hive because if it is gone, the colony will have nothing to eat. This malnourishment can check movement of honey bees to an area where plants are providing nectar or by feeding them table sugar or solution made with sugar. Sugar left over in comb must be taken out with the next honey extraction.

**Honey Types**

Depending upon several floral sources honey has almost 320 different varieties. The flavor, appearance, color and aroma of a particular type of honey depends on the several liquid sources of the flowers and fauna etc. visited by honey bees. Various types of honey are analogous in terms of season in which it is produced, prevailing temperature, rainfall and weather changes. The colour of honey ranges from light brown to dark brown. It depends on the fact that from where bees have collected it. Some common types of honey are described below-

i. **Manuka honey**- is a normal healing agent and works as an antibiotic for wounds.

ii. **Acacia honey**- is helpful in cleansing of liver and digestive tract.

iii. **Buckwheat honey**- darker in color and is full of antioxidants

iv. **Neem honey**- is helpful in high blood pressure and diabetes.

**Biological bioactive compounds**

Honey has numerous vital biological bioactive complexes including vitamins A (in form of Retinol), Vitamin B1 (Thiamine), Vitamin B2 (Riboflavin), Vitamin B6, Vitamin C (Ascorbic acid), Vitamin E (Tocopherol), Vitamin K (Anti-Haemorrhagic), Niacin, Panthenolic acid and fatty acids, phenolics, hydroxybenzoic acid, octadecanoic acid, cinnamic acid, flavonoids and ethyl ester (Bogdanov et al. 2008 and Muhammad et al. 2015) [9, 34]. Honey also contains apigenin, pinocebmbrin, acacetin and acids like absicic and ferulic (Marghitas et al. 2010 and Muhammad et al. 2014) [31, 33]. Likewise, many amino acids of physiological importance are cysteine, arginine, proline, aspartic acid and glutamic acid (Qamer et al. 2007) [40]. It comprises several flavonoid, ascorbic acid, amino acid phenolic, protein and carotenoid contents according to their weather conditions and topographical situations (Alvarez-Suarez et al. 2010) [3]. The existence of dynamic compounds affords better perceptive of the potential biological role of the honey.

**Antioxidant properties**

The word “oxidative stress” describes the poor balance between free of charge radicals and antioxidant defensive action (Bogdanov et al. 2008) [9]. Antioxidant is a component that can prevent the oxidation of supplementary molecules. Oxidation is a biochemical reaction that produces free radicals for chain reaction that may impair the cells and eventually the physiological purposes. Antioxidant such as vitamin C (Ascorbic Acid) dismisses the chain reactions to defend the body against free radicals. For constancy the oxidative state, human body sustains complex organizations of overlying antioxidants. The food comprising antioxidants have been supposed to advance the health. The literature recommends that honey comprises powerful anti-oxidative agents. As an antioxidant property honey with phenolic compounds, has abundant preventive properties in contradiction of several clinical situations such as provocative disorders, cancer, coronary artery diseases, aging and neurological worsening (Kishore et al. 2011) [27]. Constituents like polyphenols and phenolic acids established in honey diverge according to the geographical condition; for example, flavanol kaempferol components can be found in rosemary honey and quercetin component in sunflower honey (Akan and Garip, 2011) [2]. Alvarez-Suarez et al. (2012) [4] resolute role of phenolics from monofloral honeys on humanoid Red Blood Cells (RBCs) membranes in contradiction of oxidative impairment. The consequences shows that honey makes RBCs oxidative impairment most perhaps due to its adjustment into cell membrane and competence to enter and arrive at cytosol. Honey comprises suitable antioxidants which are accountable for beneficial action, rise in RBCs functions and defense.

**Antimicrobial action**

In recent medicine the healing use of honey necessitates that it must display reliable and standardized antimicrobial action. Pharmacological and biological researchers need to recognize the floral classes which give anti-microbial physiognomies. Low pH of Honey and more osmolarity united through the enzymatic assembly of hydrogen peroxide applies an anti-microbial outcome (Bang et al. 2003) [7]. The use of honey in wound bandage is becoming popular in modern medical science because of its anti-microbial activities (Ismail et al. 2015) [22]. Moreover, some particular types of honey displays broad-spectrum antimicrobial property contrary to antibiotic resilient bacteria and pathogens (Blair et al. 2009, Cooper et al. 2002a, Cooper et al. 2002b and French et al. 2005) [8, 12, 13]. Floral sources are accountable for alterations in the kind and level of anti-microbial action of honey (Brady et al. 2004) [10]. The nature of honey is mainly based on the ecological conditions and geographical locality of the flora and fauna (Price and Morgan, 2006) [39].

Julie et al. (2011) [24] found that honey displays a wide-ranging antibacterial activity with a recognized potential therapeutic use. This anti-bacterial action is mainly due to hydrogen peroxide molded by the bee-derived enzyme glucose oxidase. Antibacterial activity is mostly dependent on honey’s peroxide activity and non-peroxide reactions. Mohd et al. (2013) [32] reported that honey has antibacterial influence consequential from overall and non-peroxide actions. There is evidence in literature that honey has broad spectrum action against gram+ve and –ve bacteria(Katrina and Calvin, 2014) [26].
Wound Healing Properties in Honey

The therapeutic importance of honey has also been described in scientific literatures. The healing character of honey is primarily due to its antibacterial action, sustaining a moist wound ailment and it has more viscosity that helps to offer a protective barrier against the infection (Manisha and Shyampada, 2011 and Hananeh et al. 2015) [30, 21]. Honey has been recognized for its consequence on the healing progression and with manifold constructive effects on wound (Jull et al. 2013) [22]. Honey is supposed to improve blood circulation and healing growth in affected area. In research literature, high attention is given to honey in the area of wound healing (Cooper and Jenkin, 2009 and Gethin and Cowman, 2009) [11, 12] especially the burn area (Jull et al. 2013) [23]. Honey is very effective on several kinds of wounds where other wound healing agents are ineffective (Ligouri and Peters, 2010) [28]. Honey reduces the risk of contamination in wounds (Wilkinson et al. 2011) [81]. In addition, honey plays an important role in the adherence of skin grafts, anti-inflammatory affects and has antibacterial properties with higher healing gradation. Honey meaningfully decreases the infection degree on the 5th day of the injury (wound), and lessens pain and hospital stay duration. Furthermore, honey has durable glue like characteristics for skin graft obsession with least graft shrinkage and honey dressing improves the healing process of the medical/surgical wounds (Goharshehnsan et al. 2016) [20].

Honey in Glycemic Index

The influence of carbohydrate nutrient on health has been controversially disputed particularly to understand about the reaction that how carbohydrates diet converts into the blood glucose. Presently, the significance of carbohydrate is normally established as glycemic index (GI). Carbohydrates with least amount and highest GI suggest high/low blood glucose respectively. It is established fact that uni-floral honeys have changeable fructose component and ratios of fructose/glucose (Persano and Piro, 2004) [38]. The GI concept declares to forecast the role of carbohydrates in both metabolic and endothelial linked disorders (Ludwig, 2000) [29]. Smaller GI honeys are more appreciated in comparison to high GI. The diet with low GI offers recompense with respect to metabolic including diabetes mellitus and in coronary blood vessel heart ailment (Jenkins et al. 2002) [23]. The intake of honey with a low GI, such as acacia honey have physiological beneficial effects and may be used among patients with endocrine activity impaired diseases (Peretti et al. 1994 and Al-Waili, 2003) [37, 5].

Honey in Fertility

Egyptians demonstrated that honey is helpful in cases where fertility is problem. Furthermore, many civilizations by tradition are consuming honey for improvement of vitality among males. It has been described that there are quite a lot of causes of infertility and probable medicines. In vision of rich content of vitamins, calcium, iron, other minerals, amino acids and immune-improving properties, abundant remarks are available in literature that honey bee pollen are thought to advance egg quality and fertility along with productiveness. Honey has been recommended in males with problems of impotence (weakness) and in females with problems associated to infertility as well as unpredictable ovulation. For sterile or sub-fertile male, a drink of honey added in warm milk is supposed to improve substantial amount of sperm count. Honey is being rich in vitamin B, helpful in the production of testosterone. Erection or impotence problem can be solved with honey’s high content of nitric oxide – a chemical component involved in vasodilatation, it can improve erection. It has been revealed that 100 grams of honey is adequate to rise nitric oxide levels in blood by up to 50%. Complementary medicine traditions suppose that honey advances sperm quality in men and strengthens the ovaries and uterus in women. In recent reports researchers described that the supplementation of honey to cry protectant solution results in improvement of sperm worth (Fakhridin and Alsaadi, 2014) [16]. Attia et al. (2011) [6] conducted experiment on male rabbits and fed them with bee pollen. They found experienced enhanced fertility and semen quality. Researchers have shown that the couples having problem in conceiving in normal way can apply honey which has shown enhanced fertility (Abdelhafiz and Mohammed, 2008) [11].

Honey as a Natural Remedy

Honey can be further used as a natural remedy in curing several discomforts, if consumed appropriately.

a. Gastro esophageal reflex
b. Infantile gastroenteritis
c. Improve digestion
d. Relieve nausea (with ginger & lemon juice)
e. Acne cure (addition of baking soda)
f. Exfoliator
g. In diabetes as a substitute of sugar

Common Problems in Honey bees

1. Varroa Mites

It can be observed with naked eyes as a red or brown spot on body of bee. These are carriers of many viruses that are harmful to bees. These mites are normally not a trouble for a robustly growing hive. When growth of colony population is lowered in groundwork for winter or due to poor late summer feed, the mite population expansion can pass the bees and can does harm. Often a colony will depart as a group, but leaving no inhabitants behind if such conditions succeed. Mechanical controls include give up of drone brood (varroa mites are supposed to attracted to the drone brood), crushed sugar dusting (which promotes cleaning behavior and remove some mites also), screened bottom boards brood stoppage and perhaps, trim of the brood cell volume.

2. Hive Beetle

Hives infest comb by beetle larvae will drive out bee colonies. To control this, the best solution is to stop hive beetle and prevention of ants climbing into the hive. The lifecycle of this beetle take pputation in the earth on the outer side of hive. Many pesticides are presently used to control the small hive beetle.

3. Wax Moths

They feed on the wax. Damage of the comb will infect the honey and kill bee larvae. Damaged comb may be worn out and is restored by the bees. Wax moths are not major problem as in winter they do not survive. The problem becomes serious if the colony is weak. These moths can be controlled by application of Bacillus thuringiensis spores.

4. Chalk Brood

Chalk brood mummies are found at entrance of the bee hive. It is normally visible for the duration of wet springs. Hives with chalk brood can normally be improved by increasing the aeration in the hive.

5. Chronic Bee Paralysis Virus

Pattern 1 – Strange wavering of the wings and body. Affected bees cannot fly and frequently creep on the ground (in large
numbers). The bees group together on the top bars of the hive. They may have swollen abdomens due to enlargement of the honey sac. The wings are incompletely extended or displaced. **Pattern 2** - Affected bees are incapable of flying and are without hairs. They emerge as dark and smaller. They have a comparatively wide abdomen. They are often eaten by older bees in the hive due to hairlessness. They are forbidden to enter into hive by the guard bees. They then become unable to fly and shortly die.

**Tribulations of Pesticide in Apiculture**

Bees are vulnerable to many of the chemical compounds used for crop spraying. Many of these pesticides are known to be noxious for bees. Since the bees look for their food up to several miles from the hive, areas being sprayed by farmers or they may accumulate pollen from polluted flowers. Carbamate group poisons, such as carbaryl, can be dangerous since toxicity can take as long as 48 hours to become apparent (Ismail et al. 2015). Organophosphates group insecticides are very lethal to kill honey bee in treated areas. Pesticide losses may be relatively easy to recognize (large and sudden numbers of dead bees) or rather difficult, particularly if the loss results from a regular increase of pesticide mass brought. Quick-acting pesticides may divest the hive of its foragers, killing them in the field. Insecticides that are fatal to bees have label guidelines, defending the bees from poisoning. To act in accordance with the label, applicators should know where and when honey bees feed and residual activity duration of the pesticide. Some pesticide authorities advocate that notice of spraying be sent to beekeepers in that area, so they can close up the entrances to their bee hives and keep the bees inside until the pesticide effect gets reduced. This however does not answer all problems related with spraying and the label information should be followed regardless of doing the same. Beekeeper notification does not offer any safeguard to bees, if the beekeeper cannot have the right to use them, or to wild native or uncultivated honey bees. Therefore, beekeeper warning as the sole security procedure does not really guard all the pollinators of the area, and is in effect, a circumventing of the label necessities. Pesticide losses are a main cause in pollinator reduction.

**Pesticides harmful for bees**

1. Orthene (Acephate group)
2. Seven (Carbaryl group)
3. Diazinon (Spectracide etc.)
4. Bayer systemic pesticides (like Imidacloprid)
5. Ambush, Pounce (Permethrin etc.)
6. Crossfire (Resmethrin)

These pesticides can hurt bees in moist condition, but aren’t harmful when dry, so if you use with care, can be safe:

1. Spinosad (insecticidal property)
2. Pyrethrum (insecticidal property)
3. Neem oil (with insecticidal and fungicidal properties)

**Bee Friendly Pesticides/Insecticides**

1. Sulfur (with fungicidal property)
2. Serenade (with biological fungicide property)
3. Insecticidal soaps
4. Petroleum-based oil behavior
5. B.T./Bacillus thuringiensis
6. Herbicides like Roundup and 2, 4-D etc.

It is important to note that spraying should be in morning or exactly right before dim so that bees can reach home in safety and the pesticide/insecticide should be allowed to dry before bees come and get in touch with them.

**Conclusion**

Honey is very nutritious with excellent property of anti-oxidant, anti-bacterial and anti-inflammatory agent as well as for coughs reduction and in wound healing characteristics. The primary concern in the medicinal submission of honey in modern medicine is distinction in its composition and absence of clinical trials. In principle, we recommend honey is an appreciated dietary supplement. However, the usage of honey in different subjects with metabolic disorders covering diabetes mellitus needs to be further explored.

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