Review Article

A Review on change in chemical, morphological and therapeutic activity of honey

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Abstract

The nature's wonder honey has been used as a sweetener and as a food for at least six thousand years ago and the relationship between bees and man started as early as stone-age. Due to the variation of botanical origin and its types honey differs in appearance, sensory perception and composition. Honey is produced by six to eleven species of honey bees. All honey virtually is derived from nectar which is a derivative of phloem sap from specialized cell groups called *nectaries*. Honey mainly contains water, glucose, sucrose, fructose, vitamins like riboflavin, pantothenic acid, niacin etc and some minerals are also present in honey. Honey can be classified according to its botanical source. Depending on its botanical origin its therapeutic effects also differs considerably. Honey is a natural substance which has many health benefits and medicinal properties such as antibacterial, hepatoprotective, hypoglycemic, reproductive, antihypertensive and antioxidant properties. Honey's antimicrobial properties attracted the researchers much to publish research paper on them. In our day to day life it is being used for treatment of hearing loss, bad breath, fatigue, weight loss, pimples, influenza, hair loss, ingestion, toothache, heart diseases, bladder infection, infertility and so many things. Besides this, honey is also being used in industries commercially as nature's wonderful gift. This review highlights the origin based change in chemical, morphological and therapeutic activity of honey and its positive nutritional benefits if consumed at higher doses.

***Keywords*:** Honey, glucose, sucrose, fructose, antioxidant

Introduction

Honey is a natural product mainly used for its therapeutic uses. The main nutritional and health relevant components are carbohydrates, mainly fructose and glucose but also about 25 different oligosaccharides. Although honey is considered as carbohydrate food, its glycomic index varies from a range between 32 and 85, depending on the botanical source. Actually, honey is nothing more than nectar gathered from the blossoms of many flowers by bees. It was the only available natural sweetener for human beings from his very beginings. To gather the sweet honey, man was ready to risk their lives. The first written reference to honey, was found in a sumerien tablet writing, dating back to 2100-2000BC, mentions honey's use as a drug and an ointment (Heinemann, 1975). If we say about ancient culture then, honey was used as both nutritional and medicinal purposes (Allsop and Miller, 1996). According to Bible, king Solomon has said, "Eat honey my son, because it is good."(Old Testament, proverb 24:13). Indeed, Honey has been a common sweetener for food and a powerful medicinal tool for countries. Moreover, it was reported that it contains about 200 substances. The composition of honey depends on the plant source from which it is obtained i.e. the bee feeds. Thus classification of honey also differs accordingly. But primarily honey is composed of fructose and glucose but also contains fructo-oligosaccharides and mainly amino acids, vitamins, minerals and enzymes (Chow, 2002).The pure honey contains alkaloids, auterquinone glycosides, cardiac glycosides, flavonoids & reducing Compounds. Some compounds like Flavonoids (apigenin, pinocombrin, kaempferol, quercetin etc), phenolic acids (ellagic, caffeine etc), ascorbic acid, tocopherols, catalase (CAT), SOD (Superoxide dismutase), reduced glutathione (GSH) and peptides works together to provide synergistic antioxidant effect (Alvarez et al., 2010; Al-Mamary et al., 2002). Honey has had a valued place in traditional medicine for countries (Zumla et al., 1989; Chowdhury, 1999). Substituting honey with sugars in processed food can inhibit harmful and genotoxic effects of mycotoxins and improves the gut micro

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flora. The medicinal and antimicrobial properties of honey in relation to wound treatment have been recognized for approximately 4500 years, where for instance, Prince Hal was treated with rose honey by John Bradmore, a London surgeon. The ancient Egyptians, Assyrians, Chinese, Greeks and Romans employed honey for wounds and diseases of the gut. Honey was the most popular Egyptian drug being mentioned 500 times in 900 remedies. So, honey may be used as a supplementary medicine. But due to lack of scientific support it has a limited use in the recent time (Ali et al., 1991). Hence, there must be sufficient research on honey to utilize the golden gift of nature on behalf of mankind so that it may be used as supplement for medicines for beneficial action on our health and to forget about unwanted side effects of synthetic medicaments.

Composition of Honey

Composition of honey greatly depends on its botanical origin (Persano and Piro, 2004).The carbohydrates are the main constituents, comprising about 95% of the honey dry weight. Beyond carbohydrates, honey contains numerous compounds such as organic acids, proteins, amino acids, minerals, polyphenols, vitamins and aroma compounds. Honey is composed primarily of the sugar glucose and fructose; its third greatest component is water. Honey also contains numerous other types ofsugars, as well as acids, vitamins, proteins and minerals. The pure honey contains alkaloids, auterquinone glycosides,cardiac glycosides, flavonoids & reducing Compounds. Most of the carbohydrates in honey are monosaccharides (withmore fructose than glucose). At a distant third place issucrose; other disaccharides present in honey, albeit in very small quantities, are maltose, isomaltose, nigerose, turanose, and maltulose. At about 1% or less of the total sugars, a small quantity of higher sugars, oligosaccharides (25 different types present), and dextrins arealso present in honey (Doner, 1977; Siddiqui, 1970). Honey also contains a variety of minerals along with other constituents. Tables 1-3 and the figure 1 (Stefan et al., 2008) showed the chemical composition of honey.

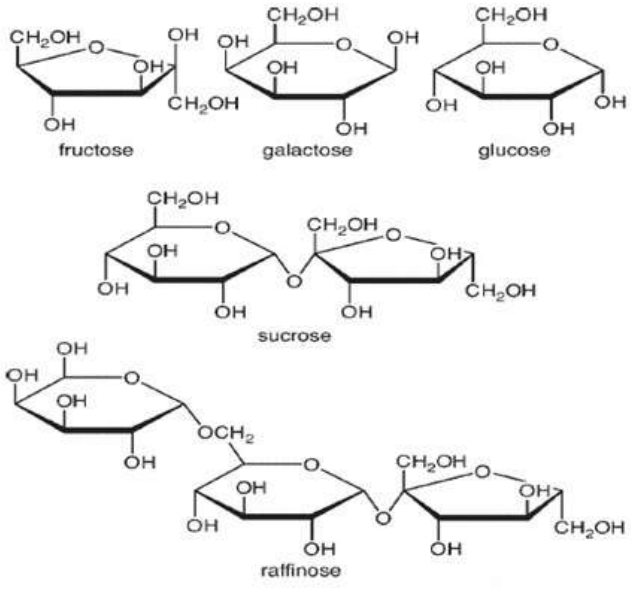

Figure 1. Structures of some common sugars found in nector and honey

Table 1. Occurrence of individual amino acids in 395 floral nectar

Amino acids	Number of Nectars	Percentage of Nectars
Alanine	380	96
Arginine	356	90
Serine	352	89
Proline	344	87
Glysine	332	84
Isolucine	287	73
Threonine	263	67
Valine	260	66
Leucine	255	66
Glutamic acid	245	62
Cysteine	218	55
Phenylalanine	216	55
Tyrosine	204	52
Tryptophan	189	48
Lysine	162	41
Glutamine	162	41
Aspartic acid	128	32
Asparagine	106	27
Methionine	80	20
Histidine	77	19

Table 2. Chemical compositions of U.S. honeys

Components	Average (Percentage)	Range (Percentage)
Water	17.2	12.2-22.9
Fructose	38.4	30.9-44.3
Glucose	30.3	22.9-40.7
Sucrose	1.3	0.2-7.6
Other Disaccharides	7.3	2.7-16.0
Higher Sugar	1.4	0.1-3.8
Gluconic Acid	0.57	0.17-1.17
Other Acids	0.43	0.13-0.92
Lactones	0.14	0.0-0.37
Minerals	0.17	0.02-1.03
Nitrogen	0.04	0.0-0.13

Table 3. Mineral content of light-colored honey

Mineral	Average (ppm)	Range (ppm)
Potassium	205	100-588
Sulfur	58	36-108
Chlorine	52	23-75
Calcium	49	23-68
Phosphorus	35	23-50
Magnesium	19	11-56
Sodium	18	6-35
Iron	2.4	1.2-4.8
Copper	0.3	0.14-0.70
Manganese	0.3	0.17-0.44

Types of honey

Honey can be classified into following types (Singh et al., 2012)

1. Manuka Honey
2. Pasture Honey
3. Jelly Bush Honey
4. Jungle Honey
5. Chestnut Honey
6. Rhododendron Honey
7. Blossom Honey (Hatice et al., 2010)

These varieties of honey are due to the components of its flower sources (Miki Fukuda et al., 2011). The chemical composition and therapeutic uses of honey also depends on its botanical origin (Singh et al., 2012).

Biological Activities of Honey

Honey is a natural product which is safe to consume and does not have any side effects like synthetic medicines. It has various health benefits and its biological activities depend on its chemical constituents and botanical origin.

Antioxidant properties of honey

Honey contains vitamin c, phenol compounds, catalase, peroxides, glucose oxidase enzymes that have antioxidant properties (Bogdanov et al., 2008). Honey also contains flavonoids and carotinoids which represent a high level of antioxidants in honey. Due to this antioxidant activity honey can act as antidepressant during high emotional, physical and intellectual stress (Jaganathan and Mandal, 2009). The antioxidants can prevent different diseases like cancer, cardiovascular diseases, inflammatory disorders, neurological degeneration, wound healing, infectious diseases and aging (Khalil et al., 2010).The term "oxidative stress" describes the lack of equilibrium between the production of free radicals and the antioxidant protective activity in a given organism. Protection against oxidation is thought to prevent some chronic diseases. The oxidative modification of the lipoproteins is considered to be an important factor for the pathogenesis of arteriosclerosis. The antioxidative activity of honey polyphenols can be measured in vitro by comparing the oxygen radical absorbance capacity (ORAC) with the total phenolics concentration.There is a significant correlation between the antioxidant activity, the phenolic content of honey and the inhibition of the in vitro lipoprotein oxidation of human serum (Alzahrani et al., 2012). The antioxidant activity of honey has the ability to protect against MSG (Monosodium glutamate) (Afeefy et al., 2012). Its antioxidant and antibacterial properties help to improve the digestive system (Satarupa and Subha, 2014).It should be considered that the antioxidant activity depends on the botanical origin of honey and varies to a great extent in honeys from different botanical sources.

Hepatoprotective action of honey

A study revealed that Indian honey protects the liver against oxidative damage and it could be used as an effective hepatoprotector against APAP-induced liver damage (Mahesh et al., 2009). It is observed that the administration of natural honey to the rats diminished hepatotoxicity and nephrotoxicity induced by lead acetate in the male rat (Halawa et al., 2009). Honey has the capacity to improve the disrupted liver biochemical markers and alleviated the increase of lipid peroxidation, where the use of honey minimized the toxic effect of AlCl3 in the liver by alleviating its disruptive effect on the biochemical and molecular levels (Shati and Alamri, 2010). An experimental study conducted on mice results suggested the harmful side effects of cadmium on liver and kidney, and it was concluded that honey via its antioxidant activity has the ability to protect against cadmium induced hepatotoxicity and nephrotoxicity (Wafaa et al., 2007). Honey renders most of the disturbed parameters to their normal levels (Garba et al., 2012). Honey can significantly reverse changes in serum levels of AST, ALT, MDA, SOD total protein and also histopathological changes produced by anti-tubercular drugs; honey has significant prophylactic and therapeutic value against anti-tubercular drugs induced hepatotoxicity (Chandane et al., 2013). If someone daily intake natural bees honey at a dose of 2.5g/Kg Body-weight resulted in sufficient amelioration against the hazardous effects of food additives as indicated by the observed improvement in all tested biochemical parameters of kidney functions (Hassan, 2007). So honey is very effective as hepatoprotective if taken at certain doses.

Antibacterial action of honey

The antimicrobial effect of honey is due to different substances and depends on the botanical origin of honey (Persano and Piro, 2004). The low water activity of honey inhibits bacterial growth and thus honey is very much effective as antibacterial agent.Honey glucose oxidase produces the antibacterial agent hydrogen peroxide, but the peroxide production capacity depends also on honey catalase activity. There are also other non-peroxide antibacterial substances with different chemical origin, e.g. aromatic acids, unknown compounds with different chemical properties and phenolics and flavonoids. The low honey pH can also be responsible for the antibacterial activity. Contrary to the non-peroxide activity, the peroxide one can be destroyed by heat, light and storage. These different factors had a bigger effect on the antibacterial activity of blossom honey than on honeydew honey (Hatice et al., 2010). Thus, for optimum antibacterial activity, honey should be stored in a cool, dark place and be consumed when fresh. The antibacterial effect of honey, mostly against gram-positive bacteria, is well documented. Both bacteriostatic and bactericidal effects have been reported for many strains, many of them pathogenic. Further, it was observed that honey has also been shown to inhibit *Rubella* virus in vitro, three species of the *Leishmania* parasite and *Echinococcus*. Honey also inhibits the growth of micro-organisms and fungi. So honey also has some antimicrobial and antiparsitic activity.

Anticancer activity of honey

Honey can also be used as an anticancer agent due to the presence of polyphenols as its constituent. Some polyphenols that are found in honey like Caffeic acid, Caffeic acid phenyl ester, Chrysin, Galangin, Quercetin, Acacetin, Kaempferol, Pinocembrin, Pinobanksin and Apigenin have evolved as promising pharmacological agents in the treatment of cancer (Amiot et al., 1989). It was also observed that administration of honey with alcohol prevent the lesions caused by only chronic alcohol administration (Edrees et al., 2007).The antimutagenic activity of honeys from seven different floral sources (acacia, buckwheat, fireweed, soybean, tupelo and Christmas berry) against Trp-p-1 was tested by the Ames assay and compared to a sugar analogue as well as to individually tested simple sugars. All honeys exhibited a significant inhibition of Trp-p-1 mutagenicity (Wang et al., 2002). Nigerose, another sugar, present in honey (Doner, 1977; Siddiqui, 1970) has an immunoprotective activity (Murosaki et al., 2002). A statistically significant anti-metastatic effect was obtained by oral application of honey. These findings indicate that honey activates the immune system and honey ingestion may be advantageous with respect to cancer and metastasis prevention. In addition, it is postulated that honey given orally before tumour cell inoculation may have a decreased effect on tumour spreading. In another experiment the anti-tumour effect of honey against bladder cancer was examined in vitro and in vivo in mice (Swellam et al., 2003). So it can be said that honey acts very effectively as anti-malignant and anti-tumour substance.

Antibiotic property of honey

Honey has some antibiotic effects also. It was demonstrated that honey retains its antibacterial property even when used in a dilute form. This suggested that apart from high sugar content there are other active components in honey which are responsible for its antibacterial properties. Later it was found that apart from other components, the effect of hydrogen peroxide made honey a potent antibacterial agent (Sackett, 1919). . It is active against antibiotic sensitive and antibiotic-resistant strains of micro-organisms and has the potential not to select for further resistant strains (Manyi-loh et al., 2011).Its antibacterial potentials even against multi-drug resistant bacteria, such as *Staphylococcus aureus, Pseudomonas aeruginosa and Acinetobacter baumanni* have been proved. Clinical observations clearly show that when honey is applied to a wound, less redness, less edema formation and less exudate oozing out occur and that there is less awareness of pain.

Antifungal activity of honey

Honey has significant antifungal activity. In an experiment it was observed that some varieties of South African honey (Wasbessie, bluegum and fynbos) can inhibit the growth of *Candida albicans*. Synergistic action of starch was found on the antifungal activity of honey. But honey showed its antifungal activity with or without starch on *Candida albicans* (Singh et al., 2012).

Anti-inflammatory properties of honey

Anti-inflammatory effects of honey in humans were found after ingestion of 70 g honey. The mean plasma concentration of thromboxane B(2) was reduced that of PGE(2).The ingestion of honey, during an experiment decreased inflammation in an experimental model of inflammatory bowel disease in rats. It was found that honey administration is as effective as prednisolone treatment in an inflammatory model of colitis.The postulated mechanism of action is by preventing the formation of free radicals released from the inflamed tissues. The reduction of inflammation could be due to the antibacterial effect of honey or to a direct anti-inflammatory effect.It was observed that the latter hypothesis was supported in animal studies, where anti-inflammatory effects of honey were observed in wounds with no bacterial infection (Stefan et al., 2008). So these studies prove that honey has anti-inflammatory actions.

Besides these properties, honey also has insulin like activities in diabetes, antihypertensive activities,

hypoglycemic properties, reproductive activities, wound healing properties and so on.

Health benefits of honey

Honey has several beneficial effects on our health. Some health benefits of honey are described below (Singh et al., 2012)

Oral health

There is much debate whether honey is harmful to teeth. Some reports show that honey has much less cariogenic effect than sucrose. Honey has antibacterial activity and due to its antibacterial activity honey ingestion inhibits the growth of bacteria that causes caries and might induce a carioprotective effect. It was shown that Manuka honey, a very potent antimicrobial honey, has a positive effect against dental plaque development and gingivitis and can be used instead of refined sugar in the manufacture of candy. According to electron microscope studies the ingestion of honey causes no erosion of tooth enamel as observed after drinking fruit juice. Ten minutes after consumption of fruit juice tooth erosion was observed, while 30 minutes after honey ingestion the erosion was only very weak. This effect can be explained only partially by the calcium, phosphorous and fluoride levels of honey and other colloidal honey components might also play a role. It can be concluded that honey is much better than sugar and can be used instead of sugar for better oral health.

Gastroenterology

Honey is also very effective in gastric health. Honey is a potent inhibitor of the causing agent of peptic ulcers and gastritis, *Helicobacter pylori*. Honey is not involved in prostaglandin production**,** but it has a stimulatory effect on the sensory nerves in the stomach that respond to capsaicin. Honey intake in rats prevented indomethacin-induced gastric lesions in rats by reducing the ulcer index, microvascular permeability, and myeloperoxidase activity of the stomach. In addition, honey was found to maintain the level of non-protein sulfhydryl compounds (e.g. glutathione) in gastric tissue subjected to factors inducing ulceration. The oligosaccharides present in honey cause an increase of bifidobacteria and lactobacilli and exert the prebiotic effect in a synergistic mode of action.In clinical studies with infants and children it was observed that honey shortens the duration of bacterial diarrhoea and did not prolong the duration of non-bacterial diarrhoea. In certain cases, consumption of relatively large amounts of honey (50 to 100 g) can lead to a mild laxative effect in individuals with insufficient absorption of honey fructose. In ancient books also, the gastroenterology of honey was mentioned. According to the Muslim holy book "The Holy Hadith", dating back to the 8th century AD prophet Mohamed recommended honey against diarrhoea. Also, the Roman physician Celsus (ca. 25 AD) used honey as a cure for diarrhoea. So, it can be said that honey is very much beneficial in gastric disorders.

Infant health

Honey has various health benefits on infant health. The application of honey in infant nutrition used to be a common recommendation during the last centuries. Infants on a diet with honey had better blood formation and a higher weight gain than when a diet without honey was applied. Honey was better tolerated by babies than sucrose and compared to a water based placebo significantly reduced the crying phases of infants. Infants had a higher weight increase when fed by honey than by sucrose, and showed less throw up than the sucrose controls.When infants were fed on honey rather than on sucrose an increase of haemoglobin content, a better skin colour and no digestion problems were encountered. Infants on honey diet had a better weight increase and were less susceptible to diseases than infants fed normally or when given blood building agents. So, it is obvious that using honey instead of sugar is much beneficial for better development and health of infants.

Conclusion

Honey is a natural sweetener and also the valuable gift of nature. It has a very close relationship with human beings since the ancient ages. The stone- age hunter-gatherer people used honey as their main food supplement. But with the progression of age the uses and importance of honey has been improved drastically. Now a days honey is being used in cough, cold, burns, wounds, to increase immunity, in cosmetic purposes and so many things. It is because of its chemical composition. The main nutrition and health relevant components are carbohydrates, which makes it an excellent energy source especially for children and sportsmen. Besides this the other trace elements along with carbohydrates like glucose and fructose produces numerous nutritional and biological effects like- antimicrobial, antioxidant, antiviral, anti parasitic, anti-inflammatory and immunosuppressive activities. Due to variation of botanical origin, honey differs in appearance, sensory perception and composition. Thus their therapeutic effect also varies accordingly. But the health benefits of honey are only applicable if it is consumed at a higher dose of 50 to 80 g per day. So, honey can be used as supplement for medicines if taken at a higher dose. And the composition of honey and its therapeutic and health benefits depend on its botanical origin to a greater extent. This fact was not often considered in the reviewed studies and must be considered at future to fully utilize this golden gift of nature in the favor of mankind.

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