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#### **Review Article**

# Medicinal Uses of Honey

Motuma Adimasu Abeshu<sup>1\*</sup> and Bekesho Geleta<sup>2</sup>

<sup>1</sup>John Snow, Inc (JSI), Ethiopia, Addis Ababa, Ethiopia

<sup>2</sup>Ethiopian Public Health Institute, Addis Ababa, Ethiopia

\*Corresponding author: Motuma Adimasu Abeshu, Vaccine Supply Chain Advisor, John Snow, Inc. (JSI), Ethiopia, P.O Box 27236, Addis Ababa, Ethiopia, Tel: +251 921462246; E-mail: motumad4@gmail.com

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#### Abstract

Honey is one of nature's wonders. For long, honey has been used as important source of carbohydrates and natural sweetener. Honey contains sugars, organic acids, minerals, and proteins, enzymes and vitamins in trace amounts. The simple sugars in honey are responsible for its sweetness, hygroscopicity, energy value and other physical properties.

Honey's use as medicine has been limited due to lack of scientific report. In recent days, however, there is resurgence. Its greatest medicinal potential is its application as topical agent to wounds and skin infections. Honey has anti-inflammatory, immune boosting property, and exhibits broad spectrum antibacterial activity, which are attributed both to physical factors: acidity and osmolarity, and chemical factors: hydrogen peroxide, volatiles, beeswax, nectar, pollen and propolis. Its antioxidant activity is attributed to: glucose oxidase, catalase, ascorbic acid, flavonoids, phenolic acids, carotenoid derivatives, organic acids, Maillard reaction products, amino acids, and proteins. Honey prevents and treats gastrointestinal disorders such as peptic ulcers, gastritis and gastroenteritis. It also poses prebiotic effects and promotes health of gastrointestinal tract.

Honey has proven safety for use. Compared to glucose and sucrose, it has lower glycemic and incremental indices in type I diabetic patients. It's simple sugars are absorbed directly into bloodstream without digestion and can serve as an athletic aid.

Keywords: Honey; Medicinal uses; Nutrition; Traditional medicines

#### Introduction

Honey is the natural sweet, viscous substance produced by honeybees from the nectar of blossoms or from the secretion of living parts of plants or excretions of plant sucking insects on the living parts of plants, which honeybees collect, transform and combine with specific substances of their own, store and leave in the honey comb to ripen and mature. Honey is one of nature's wonders. Honey has been around for a long time and yet we know little about it. Honey has been a common sweetener for foods and a powerful medicinal tool for centuries. It is the simplest and often the best way to soothe a sore throat and it can be taken at any time [1].

Honey is often eaten as an energy food. It has simple sugars that are absorbed directly into bloodstream without digestion. Honey mixes well as a sweetener in hot and cold drinks. It goes with nearly all foods. The moisture absorbing quality of honey helps breads, cakes, cookies and candies stay fresh longer [2].

Natural medicinal products have been used for millennia in the treatment of multiple ailments. Although many have been superseded by conventional pharmaceutical approaches, there is currently, resurgence in interest in the use of honey and honey products by the general public [3].

Honey's greatest medicinal potential is its application as topical agent to wounds and skin infections [4]. Honey has anti-inflammtory, antioxidant and immune boosting property. Much of the therapeutic properties of honey are due to the high sugar concentration and the resulting osmotic effect [5], low PH and acidity [6], and due to hydrogen peroxide generated from the oxidative conversion of glucose to gluconic acid by glucose oxidase upon dilution [1]. Studies indicate that hydrogen peroxide takes the biggest credit for the medicinal value of honey.

Honey applied to wounds, burns and ulcers promotes faster healing by clearing infections and rendering sterility, through promotion of tissue growth and regeneration, and preventing dehydration of the infected site [7-10].

#### **Composition and Physical Characteristics of Honey**

Honey is essentially a highly concentrated water solution of two sugars: dextrose and levulose, with small amounts of at least 22 other more complex sugars. Honey, also, contains minor constituents such as flavoring materials, pigments, organic acids, and minerals [11].

Surveys of floral honey composition have established that the three major components are fructose, glucose, and water, averaging 38.2, 31.3 and 17.2%, respectively. Glucose and fructose are the only monosaccharides in honey. It is these sugars combined in various forms that comprise the di-and trisaccharide fractions of floral honey [12,13]. Honey's sugar accounts for 95 to 99% of honey dry matter, and 85 to 95% of total sugars [1]. These simple sugars give honey its sweetness, hygroscopic properties, energy value, and other physical properties [11].

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Honey contains various organic acids which contribute to its flavor complex. Because of its great sweetness, however, the acidity of honey is largely masked. According to White [11], the most important acid in honey is gluconic acid, which is derived from dextrose. Other acids isolated from honey are acetic acid, butyric acid, citric acid, malic acid, formic acid, succinic acid, lactic acid and pyroglutamic acid, and inorganic acids such as phosphoric and hydrochloric acids.

The mineral composition of honey varies. According to Vanhanen et al. [14], New Zealand honey's mineral content ranges between 0.02 % to 0.4% depending on whether it is light or a dark honey type. Nandaa et al. [15], state a range of 0.12 to 0.28%, and Adebiyi et al. [16] indicate the range of mineral content of Nigerian honey between 0.02% to over 1%, with an average of 0.17%.

Honey consists of nitrogenous compounds such as enzymes and proteins in trace quantities. These groups comprise of enzymes and some other proteins. The enzymes originate from the salivary secretions of the worker bees, which plays an important role in the formation of honey [1].

The most important enzyme in honey is invertase (also known as saccharase or sucrase), which converts the sucrose of nectar into invert sugars: dextrose and levulose found in honey. Another important enzyme in honey is diastase (amylase). Other enzymes reported in honey are catalase and phosphatase [11]. The amount of protein in honey ranges between 0.1 to 0.6% [11,17]. Generally, the relative quantity of proteins in honey compounds is considered a quality index.

Honey contains vitamins [11] and phenolic compounds [18] in trace quantities. Some of the phenolic compounds in honey responsible for antioxidant effect are flavonols, flavones, flavonones, benzoic and cinnamic acids.

The fact that honey is naturally a concentrated sugar solution gives its characteristic physical properties such as high grade viscosity, stickiness, sweetness, relatively high density, tendency to absorb moisture from the air, and immunity from spoilage [1,11].

# Nutritional Benefits of Honey

For a long time in human history, honey was an important source of carbohydrates and the only widely available sweetener [1]. Dr. Fessendensaid that "honey's many benefits are interrelated, much like the cells of a honeycomb, and at the very least, there are no known medical reasons not to enjoy honey as part of a healthy diet and lifestyle for adults and children over the age of twelve months" [19].

# **Energy Source**

As food, honey is mainly composed of the simple sugars fructose and glucose, which form the basis of almost all indications on how, when and why to use it. The main consideration is the fact that honey provides immediately available calories, from which it derives its energy value.

Honey is a natural source of readily available carbohydrates providing 64 calories per tablespoon [20]. Main sugars of honey are the monosaccharides, fructose and glucose. During digestion the principal carbohydrates fructose and glucose are quickly transported into the blood and can be utilized for energy requirements of the human body.

Honey contains about 0.1 to 0.6% proteins, mainly enzymes and amino acids [11,17]. However, its contribution to human protein intake is marginal with respect to quantity.

# Non-energetic Nutrients

Different unifloral honeys contain different amounts of minerals. However, the amount of vitamins and minerals is so small that its contribution to the recommended daily intake (RDI) is marginal (Table 1).

Nutrient	Unit	Average amount in 100 g honey	Recommended daily intake
Energy equivalent	Kcal	304	2800
Vitamins			
B1 (Thiamin)	mg	0.004 - 0.006	1.5
B2 (Riboflavin)	mg	0.002- 0.06	1.7
Nicotinic acid (niacin)	mg	0.11- 0.36	20
B6 (Pyridoxine)	mg	0.008 - 0.32	2
Pantothenic acid	mg	0.02 - 0.11	10
C (Ascorbic acid)	μg	2.2-2.4	60
Minerals			
Calcium	mg	4-30	1000
Chlorine	mg	2-20	
Copper	mg	0.01-0.1	2
Iron	mg	1-3.4	18
Magnesium	mg	0.7-13	400
Phosphorous	mg	2-60	1000
Potassium	mg	10-470	-
Sodium	mg	0.6-40	-
Zinc	mg	0.2-0.5	15

Table 1: Nutrients in honey in relation to human requirements [1].

Honey contains a number of other trace elements [20]. From the nutritional point of view the minerals chrome, manganese and selenium are of nutritional importance [21,22]. The elements sulphur, boron, cobalt, fluorine, iodine, molybdenum and silicon can be important in human nutrition too.

Honey contains choline and acetylcholine [11]. Choline is an essential for cardiovascular and brain function, and for cellular membrane composition and repair, while acetylcholine acts as a neurotransmitter [23].

# **Medicinal Uses of Honey**

Honey has been used as medicine in many cultures for a long time [1]. However, it has limited use in medicine due to lack of scientific report. In recent days, honey is becoming acceptable as a reputable and effective therapeutic agent. Its beneficial role has been endorsed to its

antimicrobial, anti-inflammatory and anti-oxidant activities as well as boosting of the immune system.

#### Antibacterial activity

Honey has proven antimicrobial activity [24]. Honey inhibits a broad spectrum of bacterial species. The alcohol extracts of honey exhibit an inhibitory effect to array of bacterial species including aerobes and anaerobes, Gram positives, and Gram negatives [25]. Honey has powerful antimicrobial effects against pathogenic and nonpathogenic micro-organisms (yeasts and fungi), even against those that developed resistance to many antibiotics. The antimicrobial effects could be bacteriostatic or bactericidal depending on the concentration that is used [3].

According to Mohapatra et al. [25], methanol, ethanol, and ethyl acetate extracts of honey exhibits in vitro antibacterial activity against Gram-positive bacteria (Staphylococcus aureus, Bacillus subtilis, Bacillus cereus, Enterococcus faecalis, and Micrococcus luteus) and Gram-negative bacteria (Escherichia coli, Pseudomonas aeruginosa, and Salmonella typhi).

Honey has bactericidal effect against P. aeruginosa [26]. At Minimum Inhibitory Concentrations (MIC) of 9.5% (w/v), and Minimum Bactericidal Concentration (MBC) of 12% (w/v), honey exhibits bactericidal effect with a 5 log reduction estimated within 257 min. Honey with carbohydrate solutions  $\geq 15\%$  (v/v) effectively inhibits H. pylori [5]. In vitro tests of isolates of Campylobacter spp. are highly susceptible to honey solution [27].

According to Hassanein et al. [7], bacterial isolates from wounds of hospital patients: Aeromonas schubertii, Haemophilius paraphrohaemlyticus, luteus, Cellulosimicrobium Micrococcus cellulans, Listonella anguillarum and Acinetobacter baumannii, exhibit sensitivity to solutions of honey at various concentrations ranging between 25% and 40%.

Many bacterial pathogens have developed resistance to antibiotic introduced into clinical practice. Using a medical-grade honey, wound pathogens, including those with high levels of innate or acquired antibiotic resistance, were killed by 4.0-14.8% honey, which is a concentration that can be maintained in the wound environment. Resistance to honey could not be induced under conditions that rapidly induced resistance to antibiotics [28].

According to Cooper et al. [29], Methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-sensitive enterococci (VSE) isolated from infected wounds and 20 strains of vancomycinresistant enterococci shown sensitivity to honey at various concentrations. Honey exhibits synergistic effect against MRSA [30], where, sub-lethal concentrations of manuka honey (6%w/v) have a marked effect in enhancing the susceptibility of Methicillin-resistant Staphylococcus aureus to Oxacillin, and reverses resistance developed against the drug (Table 2).

Progresses are made in enhancing the antibacterial efficacy of honey by combining with other ingredients. According to Kwakman et al. [31], medical grade honey enriched with antimicrobial peptides such as synthetic Bactericidal Peptide 2 (BP2) has rapid bactericidal activity against Pseudomonas aeruginosa, Staphylococcus epidermidis,

<i>Enterococcus faecium, Burkholderia cepacia</i> , and methicillin-resistant <i>S. aureus</i> (MRSA).				
Bacterial Species	Disease caused			
Bacillus anthracis	Anthrax			
Corynebacterium diphtheriae	Diphtheria			
Escherichia coli	diarrhoea, septicaemia, urinary infections, wound infections			
Haemophilus influenzae	Ear infections, meningitus, respiratory infections, sinusitis			
Klebsiella pneumoniae	Pneumonia			
Mycobacterium tuberculosis	Tuberculosis			

	infections, wound infections	
Haemophilus influenzae	Ear infections, meningitus, respiratory infections, sinusitis	
Klebsiella pneumoniae	Pneumonia	
Mycobacterium tuberculosis	Tuberculosis	
Proteus spp.	Septicaemia, urinary infections	
Pseudomonas aeruginosa	urinary infections, wound infections	
Salmonella spp.	Diarrhea	
Salmonella choleraesuis	Septicaemia	
Salmonella typhi	Typhoid	
Salmonella typhimurium	Wound infections	
Serrata marcescens	septicaemia, wound infections	
Shigella spp.	Dysentery	
Staphylococcus aureus	Abscesses, boils, carbuncles, impetigo, wound infections	
Streptococcus faecalis	Urinary infections	
Streptococcus mutans	Dental carries	
Streptococcus pneumoniae	Ear infections, meningitis, pneumonia, sinusitis	
Streptococcus pyogenes	Ear infections, impetigo, puerperal fever, rheumatic fever, scarlet fever, sore throat, wound infections	
Vibrio cholerae	Cholera	
Actin pyogenes, Klebsiella pneumoniae, Nocardia asteroides, Staphylococcus aureus, Streptococcus dysgalactiae, Streptococcus agalactiae	Mastitis	
Epiderm floccosum, Microsporum canis, Microsporum gypseum, Trichophyton rubrum, Trichophyton tonsurans, Trichophyto mentagrophytes var.	Tinea	
E. coli, Salmonella, Shigella, Vibrio, Helicobacter Pylori	Peptic ulcer	

Table 2: List of bacterial species sensitive to honey/honey products and diseases they cause.

#### Mechanism of antibacterial activity

Honey has been demonstrated in many studies to have antibacterial effects [32]. This antibacterial activity of honey is attributed both to physical factors: acidity and osmolarity, and chemical factors: hydrogen peroxide, volatiles, beeswax, nectar, pollen and propolis [33]. Honey is a concentrated solution of monosaccharide sugars, leading to hygroscopicity [1,11] of honey with low water activity. When honey concentrate is applied to microorganisms, it poses antimicrobial effect through its osmotic property [5,32].

Hydrogen peroxide in honey is activated by dilution with body fluids. When honey is used, hydrogen peroxide of concentration as low as 1 mmol/l will slowly be released and acts as an antiseptic [34]. The pH of Honey is commonly between 3.2 and 4.5. This relatively acidic pH level inhibits the growth of many bacteria [6,32]. Others components responsible for antibacterial activity of honey include phenolics, carbohydrates, Maillard products, proteins, antibiotic-like peptides methylglyoxal, and other non-determined substances [4].

#### The antioxidant property of honey

Honey is being used since long time both in medical and domestic needs, but only recently its antioxidant property has come to limelight. With increasing demand for antioxidant supply in the food, honey is becoming popular as a source of antioxidant [35]. Oxidative stress results from lack of balancing chemical reaction between the production of free radicals and the natural protective effect of our body resulting into cellular damage and disruption of genetic structure [36,37].

The molecular mechanisms explaining how normal cells undergo transformation to cancer cells induced by tumor promoters have been the subject of intense investigation. However, studies have revealed the mitogen-activated protein (MAP) kinase signaling pathways are activated differentially by various tumor promoters. Tumor promoters such as UV, 12-O-tetradecanoylphorbol-13-acetate (TPA), Epidermal Growth Factors (EGF), or Arsenic stimulate membrane receptors that activate various Mitogen-Activated Protein (MAP) kinase cascades. MAP kinase cascades regulate transcription factors with a proven role in carcinogenesis. Cellular responses may be survival, development, proliferation, apoptosis, regulation of cell cycle, inflammation, and differentiation [38].

Antioxidants bind to the Transcription Factors and prevent harmful effects as cancer, cardiovascular diseases, inflammatory disorders, neurological degeneration, wound healing, infectious diseases and aging [36,37,39]. Honey has been found to contain significant antioxidant activity attributed to glucose oxidase, catalase, ascorbic acid, flavonoids, phenolic acids, carotenoid derivatives, organic acids, Maillard reaction products, amino acids, proteins [18,40-42].

The main antioxidants in honey are the phenols, such as quercetin, hesperetin and chyrsin, and the Maillard products called melanoidins [1,18,35]. The phenol quercetin directly binds to and strongly inhibits cellular transcription factors' activities. The inhibition of the transcription factors surpasses the phosphorylation and activation process which avoids cellular effect of the free radicals. It, also, induces apoptosis (programmed cell death) of human osteosarcoma cells and reduces protein expression levels in human fibrosarcoma cells [39].

#### Wound healing property of honey

Wound is an injury to the body (from violence, accident, or surgery) that typically involves laceration or breaking of a membrane (as the skin) and usually damage to underlying tissues. It causes destruction of tissue, disruption of blood vessels, and extravasations of blood constituents and hypoxia [43].

The development of wound infection has deleterious effects on patients by causing increased pain, discomfort and inconvenience and can lead to life-threatening illness or even death. Also, it interrupts the healing process, contributing to extended hospital stays, as well as increased treatment costs in terms of antibiotics, dressings and staff time [29]. Wound healing can be affected by endogenous (pathophysiology) and exogenous (micro-organisms) factors. The risk of wound infection increases as local conditions favor bacterial invasion and growth [43].

Honey is one of naturally existing remedies that has been applied in the treatment of wounds. It promotes faster wound healing through its regenerative tissue growth and epitheliazation effects, with little or no formation of scars [44-47]. Ali-Wali et al. [44] state that honey's physical effect, such as acidity and osmotic effect, and its chemical effect, such as antimicrobial activity of hydrogen peroxide at the wound site, added to the nutritional, antioxidant and immunoactivating property, when taken orally, are the prime sources of wound healing property. Furthermore, prostaglandins and nitric oxides play a major role in the healing process.

Honey has proven safety for use. External application of honey dressings as well as application to mucous layers of the body cavities didn't show signs of allergic reaction and side effects. With the use of honey, no allergic reaction is elicited and no significant side effects were reported, and there is rapid elimination of wound odor, improvement of granulation and epithelialization, reduction of amount of exudates, and sterilization of wounds from microbes [29,44,46-48].

Wound healing process can also be obstructed by exogenous (microbiological) factors. According to Efem et al. [48], unprocessed honey inhibited most of the fungi (*Aspergillus fumigates, Aspergillus flavus, Penicillium citrinum, Trichopyton rubrum, Trichophyton tonsurans, Candida albicans*) and bacteria (*Streptococcus pyogenes, Enterococcus faecalis, Staphylococcus aureus, Escherichia coli, Kliebsella pneumonia, Proteus mirabilis, Proteus spp, Bacteroides fragilis, Clostridium welchii, Clostridium tetani*) except *Pseudomonas aeruginosa* and *Clostridium oedematiens*) causing wound infection and surgical infection.

According to clinical trial conducted by Lund-Nielsen et al. [46] on seventy-five patients with advanced stage cancer and malignant wounds, the application of honey-coated bandages reduced wound size for 62% of patients and improvement in wound cleanliness for 58% of patients.

Split-Thickness Skin grafting is a widely used technique for coverage of skin defects. During the healing of skin graft donor sites, infection, delay in healing, fluid and electrolyte imbalances, scar formation, and pain are the problems that can be observed. The use of honeyimpregnated gauzes is effective, safe, and practical, where they provide faster epithelization time and a low sense of pain [47].

Owing to the curing effect of honey on various kinds of wounds, medicated honey dressings are gaining widespread acceptance and clinical applications. Derma Sciences Medihoney<sup>®</sup> Dressing with Active Manuka honey received FDA approval for providing a moist environment conducive to wound healing. These are tulle dressings comprised of 95% Active Manuka Honey and 5% calcium alginate, and are offered in several sizes including 0.5, 1, and 1.5 ounces. According to the FDA, Medihoney<sup>®</sup> dressings are indicated for the management of light to moderately exuding wounds as: diabetic foot ulcers, venous or arterial leg ulcers, partial or full thickness pressure ulcers/sores, first and second partial thickness burns, and traumatic and surgical wounds [49].

A study conducted in United Kingdom shows that healing times of wounds after treatment with Medihoney<sup>®</sup> are reduced compared with conventional treatment and, although not reaching statistical significance, the results are of clinical significance. Honey is suitable for wounds at all stages of healing [8]. According to Simon et al. [9], malignant wounds of various etiologies are effectively managed with antibacterial honey.

Honey resists resistance, Blair et al. [28] pointed out that it is unlikely resistance to honey will develop, even with increased use. The gene expression signature of *E. coli* cells exposed to active Leptospermum honey<sup>®</sup> indicates that it has a mode of action that is distinct from conventional antibiotics. This, added to ideal properties of wound dressing, including maintenance of a moist wound environment (which is essential for timely healing), nontoxicity, antiinflammatory actions, debriding activity, reduction in scarring and the stimulation of re-epithelialization, vitalizes the use of honey in wound care. Topical application of honey for the treatment of burns is the most practiced clinical application [1,44,45].

Subrahmanyam [10] studied a total of 104 cases of superficial burn injury to assess the efficiency of honey as a dressing in comparison with silver sulfadiazine gauze dressing. In the 52 patients treated with honey, 91 per cent of wounds were rendered sterile within 7 days, and 87% healed within 15 days. The study has shown that the healing properties of honey helped burn wounds to heal earlier and with fewer complications than conventional treatment.

The accelerative effect of honey in the wound, ulcer and skin burn healing process is related to its physical properties of hygroscopicity, hypertonicity, lower pH, and complex chemical composition. However, the stimulatory effects obtained when honey was administered orally or parenterally suggest that a tissue growth factor may be involved, rather than stimulation of growth being a consequence of wound acidification or improved nutrition of the tissue [44].

# Other Uses of Honey

#### Gastroenterology

Honey is reported to have effects of preventing and treating gastrointestinal disorders such as peptic ulcers, gastritis, and gastroenteritis. Honey is a potent inhibitor of the causing agent of peptic ulcers and gastritis, *Helicobacter pylori* [5]. Honey is natural and will not raise blood-sugar levels; a mix of honey and water is a good cure for colic [50].

Honey has prebiotic effects: increasing the population of bacterial microflora important for the health of gastrointestinal tract. According to Ustunol [51], the consumption of honey increases the population of normal flora called bifidobacteria, where its constitutents were found to pose prebiotic effect that resembles the effect of fructo-oligosaccharides (FOS).

#### Honey and diabetics

Honey contains a good proportion sugars with: dextrose (31%), levulose (38%), and about 1.3% sucrose. Cane sugar yields, in effect (after hydrolysis in the intestine), 52.5 percent of each sugar. On a weight basis, honey is approximately as sweet as granulated sugar; hence more sweetening power might be considered available to the diabetic at a lower dextrose "price" from honey than from granulated sugar [42].

Studies have shown that honey consistently produces a lower glycemic effect when compared to glucose and sucrose in normal volunteers and type I diabetics, and that honey or sucrose at breakfast do not have additional acute hyperglycemic effects over an isoglucidic amount of bread in type II diabetics [52]. Compared to glucose and sucrose, honey has lower glycemic and incremental indices in type I diabetic patients [53].

#### **Sports nutrition**

Carbohydrate consumption prior to, during and after exercise enhances performance and speeds recovery. Honey is a natural source of readily available carbohydrates and is as effective as glucose for carbohydrate replacement during endurance exercise [20]. It helps maintain muscle glycogen, also known as stored carbohydrates, which are the most important fuel source for athletes to help them keep going.

Honey serves as an athletic aid. Pre-exercise, as with many carbohydrates, pure honey may be an effective form to ingest just prior to exercise. When honey is eaten before a workout or athletic activity, it is released into the system at a steady rate throughout the event. During exercise, consuming carbohydrates, such as honey, during a workout helps muscles stay nourished longer and delays fatigue, when compared to not using any aid or supplement. Post-exercise, ingesting a combination of carbohydrates and protein immediately following exercise (within 30 minutes) is ideal to refuel and decrease delayedonset muscle soreness. Therefore, honey is a great source of carbohydrate to combine with post-workout protein supplements. In addition to promoting muscle recuperation and glycogen restoration, carb-protein combinations sustain favorable blood sugar concentrations after training National Honey Board [20].

#### Conclusion

Honey is a natural sweet, viscous substance produced by honeybees. It is eaten as food, used as common sweetener and has been used for centuries for medicinal purposes. Honey has simple sugars that are absorbed directly into bloodstream without digestion. The moisture absorbing quality of honey helps breads, cakes, cookies and candies stay fresh longer. Honey has anti-inflammatory, antioxidant and immune boosting property attributed to the high sugar concentration and the resulting osmotic effect, low  $P^H$  and acidity, and hydrogen peroxide. Despite impressive records of honey as medicinal agent, various studies indicated high variability among honeys of different floral origin in their composition as well as their medicinal uses. Therefore, if honey has to be used as medicinal agent, standardization and quality control is highly recommended.

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