Honey–Health and Therapeutic Qualities

Provided by the National Honey Board

Introduction

Honey is a popular sweetener throughout the world. According to an Associated Marketing survey conducted for the National Honey Board in 1997, almost 77 percent of U.S. households use honey along with other sweeteners and syrups and 45 percent of them consider honey a good value because it is "natural/good for you/better for you than sugar." Overall, honey has a positive profile with nearly 62 percent of users "especially liking" it for its taste and flavor, 24 percent because it is natural and 16 percent because it is good for you.[1]

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From ancient times, honey was not only used as a natural sweetener but also as a healing agent. Many health-promoting and curative properties attributed to it are the basis for some traditional folk medicine treatments throughout the world today. Of the consumers who use honey, 93 percent consider honey a healthful product, recognizing it as a pure, natural product. Fifteen percent think of it as a good home remedy.[1]

History of honey as medicine

Stone age paintings in several locations dating to 6000 BC or earlier depict honey hunting, documenting human use of honey for at least 8000 years. References to honey as a medicine are found in ancient scrolls, tablets and books—Sumarian clay tablets estimated to be 6200 BC, Egyptian papyri dated from 1900-1250 BC, Veda (Hindu scripture) about 5000 years old,[2] the Holy Koran,[3,4] the Talmud, both the old and new testaments of the Bible, sacred books of India, China, Persia and Egypt[3,4] and Hippocrates 460-357 BC.[2] Clearly, honey was ubiquitous and our ancestors' use of it for medicinal purposes was universal.

Honey was prescribed for a variety of uses including baldness, contraception and as a wound treatment. Frequently, honey was mixed with herbs, grains and other botanicals from the geographic area. Table 1 summarizes some of the ways honey has been used through the ages. Uses that have continued into modern folk medicine include treatment for coughs and sore throats, lotus honey for eye diseases in India, infected leg ulcers in Ghana, earaches in Nigeria, topical treatment of measles in the eyes to prevent corneal scarring, gastric ulcers and constipation.[5]

20th Century practices and research

Much of the literature in the early part of the 20th Century contains reports of antimicrobial and wound healing properties of honey. In 1919, Sackett reported that antibacterial activity increased in diluted honey.[11] Russian soldiers during World War I used honey to prevent infections in wounds and to accelerate healing.[12] Germans used honey and cod liver oil for ulcerations, burns, fistulas and boils in addition to a honey salve (mixed with egg yolk and flour) for boils and sores.[9]

In a 1992 review by Molan, it was noted that in 1937, Dold, et al. began intensive study on the antimicrobial activity of honey and called it "inhibine".[11] In 1963, White, et al, identified "inhibine" as hydrogen peroxide, which is formed by the glucose oxidase system.[13] Throughout the 1930s, there were numerous medical journal reports on the effectiveness of honey in clearing bacterial infection in wounds. Intensive laboratory studies for the treatment of infections became available in the mid-1940s with the medical profession taking note of the value of honey. However, the introduction of antibiotics shifted the focus to synthetic and mass-produced treatments.

During the 1930s, 1940s and 1950s, researchers were documenting the wound healing properties of honey, leading to a treatment still in practice today.[14,15,16,17,18] The past two decades have brought a resurgence of interest in learning more about antimicrobial and wound healing properties of honey. Reports from different parts of the world generally affirmed the effectiveness of honey in treating various wounds, burns and serious infections.[6,12,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41] Research objectives have included comparisons of honey wound dressings to other treatments as well as identification of more effective honeys. Other research focused on the pathogens against which honey acted and the mechanisms by which it acts. In studies that compared it to a solution of sugar with similar osmotic pressures, honey was shown to be particularly active against gram negative bacteria and higher fungi while sugar solutions did not have the antimicrobial activity.[32,42] In addition, research on *Salmonella*, *Escherichia coli*, *Aspergillus flavus*, *Aspergillus niger* and *Penicillium chrysogenum* showed honey to have more pronounced inhibitory effect than individual sugars.[42,43]

Table 1 - Selected Historical Uses of Honey [2,3,4,5,6,7,8,9,10]

Source	Use
Hippocrates (460-357 BC)	Wound healing
Celsius (circa 25 AD)	Laxative; cure for diarrhea and upset stomach; for coughs and sore throats; to agglutinate wounds; eye diseases
Ancient Greeks, Romans and Chinese	Topical antiseptic for sores, wounds and skin ulcers
Aristotle (384-322 BC)	Refers to pale honey as a "good salve for sore eyes and wounds"
Dioscorides (circa 50 AD)	States that pale yellow honey from Attica was the best honey, being "good for all rotten and hollow ulcers" as well as for sunburn, inflammation of throat and tonsils and as a cure for coughs
Chinese	Prevent scars; remove discoloration and freckles and improve the general appearance of the skin; abscesses and hard swelling or callosity of skin; for cancer applied to inflamed wounds to reduce the pain and lessen the drawing; diluted honey used for inflammation of the eye; treat small-pox; remove worms and for diseases of the mouth and throat
Culpepper's *Complete Herbal* (17th Century)	Many remedies, e.g., uses of garden rue for "worms of the belly"
Sir John Hill (1759)	Book on "The Virtues Of Honey In Preventing Many Of The Worst Disorders, And In The Cure Of Several Others"
van Keetal (1892)	Antibacterial activity reported
American Pharmaceutical Association (1916-1935)	For general coughs – mixture of barley water, honey and the juice of one lemon; honey of rose with borax for treating sore throats and skin ulcers
U.S. Medical Archives	Many applications and prescriptions; prevention of infection in wounds

Other aspects of honey and its use in various clinical conditions have also been investigated. For example, the carbohydrate absorption from a commercial brand of honey (blossom honeydew honey) in Greece was studied in 20 normal, white subjects. The results of a breath hydrogen test, reports of loose stools within 10 hours of consumption of the test doses of honey vs. glucose and fructose mixture demonstrated carbohydrate malabsorption. The researchers suggested that fructose was the malabsorbed carbohydrate leading to the laxative effect of honey. This study provides scientific support for the common Greek practice of treating constipation with honey.[44,45]

In recent years, with the advent of functional foods, research expanded to include the health promoting aspects of honey. A number of studies on the phytochemical and antioxidant content of honey and its impact on gastrointestinal health and energy metabolism have identified potential new roles for honey in diets.

Composition of Honey

Nutrients

Honey is a supersaturated sugar solution with approximately 17.1 percent water. Fructose is the predominant sugar at 38.5 percent, followed by glucose at 31 percent. Disaccharides, trisaccharides and oligosaccharides are present in much smaller quantities. Besides carbohydrates, honey contains small amounts of protein, (including enzymes), vitamins and minerals. Honey yields 64 calories per tablespoon, making it a more concentrated source of energy than other common sweeteners. (See Table 2.)

Table 2 - Nutrient Values of Honey[51]

Nutrient	Average amount per 1 Tbsp serving (21g)	Average amount per 100g
Water	3.62g	17.10g
Calories	64	304
Total Carbohydrate	17.46g	82.40g
Fructose	8.16g	38.50g
Glucose	6.57g	31.00g
Maltose	1.53g	7.20g
Sucrose	0.32g	1.50g
Other carbohydrates	0.85g	4.00g
Dietary Fiber	0.04g	0.20g
Total Fat	0	0
Cholesterol	0	0
Total Protein	0.06g	0.30g
Ash	0.04g	0.20g
Vitamins *(data not available for Biotin and Vitamin B-12)*		
Thiamin	0	0
Riboflavin	0.01mg	0.04mg
Niacin	0.03mg	0.12mg
Pantothenic acid	0.01mg	0.07mg
Vitamin B-6	0.01mg	0.02mg
Vitamin B-12	0	0
Folate	0.42mcg	2.00mcg
Vitamin C	0.11mg	0.50mg
Vitamin A	0	0
Vitamin D	0	0
Vitamin E	0	0
Vitamin K	0	0
Minerals		
Calcium	1.27mg	6.00mg
Phosphorus	0.85mg	4.00mg
Sodium	0.85mg	4.00mg
Potassium	11.02mg	52.00mg
Iron	0.09mg	0.42mg
Zinc	0.05mg	0.22mg
Magnesium	0.42mg	2.00mg
Selenium	0.17mg	0.80mg
Copper	0.01mg	0.04mg
Manganese	0.02mg	0.08mg

While the amino acid content is minor, the broad spectrum of approximately 18 essential and non-essential amino acids present in honey is unique and varies by floral source. Proline is the primary amino acid with lysine being the second most prevalent. Other amino acids found in honey include phenylalanine, tyrosine, glutamic and aspartic acids. The glutamic acid is a product of the glucose oxidase reaction.[13] Proline and other amino acids are contributed by pollens, nectar or by the bees themselves.[46,47,48,49,50]

Bees use a variety of plants to create honey and consequently, the nutritional profile of honey varies accordingly. Some studies have been done on honeys from different botanical origins to evaluate the differences in sugar content,[52] amino acid content[53] and other components. These compositional differences can influence the value of a specific honey for medicinal or health-promoting purposes.

Phytochemicals

In recent years, research has identified a number of phytochemicals in various foods, including honey. Phytochemicals are substances in plants. It is now recognized that many phytochemicals can have health-promoting activities. Antioxidants, a major group of phytochemicals, reduce the risk of tissue oxidative damage.

Honey is known to be rich in both enzymatic and non-enzymatic antioxidants, including catalase, ascorbic acid, flavonoids and alkaloids.[46,54,55] A unique flavonoid, pinocembrin, is present in high quantities in propolis and honey. Other flavonoids found in honey are pinobanksin, chrysin, galangin, quercetin, luteolin and kaempferol. Different honeys have different flavonoid profiles, depending on the floral source for the nectar. Similarly, the ascorbic acid content of honey ranges from 0.5-6.5mg/100g with an average of 2.4mg/100g or 5mg/ml.[56] However, some specific varieties of honey have been reported to contain as much as 75-150mg ascorbic acid per 100g, while most honey contain less than 5mg/100g.[57]

In vitro experiments on the inhibition of oxidation in a model system using various honeys demonstrated a wide variation in the antioxidant capacity among floral sources. Honey made by bees fed herbal extracts exhibited greater antioxidant activity than normal honey.[58] In general, higher antioxidant content was found in darker honeys and in honeys with higher water content.[59] Some honeys, such as buckwheat honey, are comparable to fruits and vegetables, such as orange pulp, broccoli and sweet peppers, in their antioxidant content on a weight basis.

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Enzymes

Honey contains a number of enzymes including glucose oxidase, invertase, diastase (amylase), catalase and acid phosphatase.[46] The glucose oxidase reaction produces glutamic acid and hydrogen peroxide from glucose. It also produces glucolactone that equilibrates with gluconic acid. The hydrogen peroxide contributes to the antimicrobial properties of honey.

Invertase converts sucrose to fructose and glucose. It is added to the nectar by the bees as either gluco-invertase or fructo-invertase.[60] Some invertase is found in honey and may continue its activity in extracted honey. However, high temperatures will inactivate it.

Diastase (amylase) splits starch chains to randomly produce dextrins and maltose. Originating from bees and pollen,[46] it is added during the ripening of nectar. The diastase content varies according to floral source. Long storage periods and exposure to high temperatures for a prolonged period of time inactivate diastase. Researchers recommend 85 °C for 5 minutes to denature diastase in honey; also a pH outside the optimum range of 5.3-5.6 will decrease diastase activity.[61]

Catalase, found in small amounts in honey, produces oxygen and water from hydrogen peroxide. The inverse relationship between catalase activity and hydrogen peroxide content has been used to determine the hydrogen peroxide level of honey, formerly called the "inhibine number".[62]

Organic acids

Organic acids contribute a slight tartness to the flavor of honey and add to its antimicrobial properties. Gluconic acid, the major organic acid, is the product of the enzymatic glucose oxidase reaction. It has been shown to increase calcium absorption.[63] Honey contains many other organic acids—butyric, acetic, formic, lactic, succinic, malic, citric, maleic, oxalic and pyroglutamic. As with many other components in honey, the organic acid content varies according to the floral source.[46,64,65]

Other relevant properties (pH, osmotic pressure, water activity)

Honey possesses a number of properties that contribute to its various roles in human health. Actual values vary by floral source.

Acidic environment (average values)[51]

- Low pH 3.9 Range 3.4-6.1
- Acids 0.57% Range: 0.017-1.17% (primarily gluconic acid)

High osmotic pressure and low water activity Aw[51]

- 0.5 (16% water) to 0.6 (18.3% water) in the 40-100 °F (4-37 °C) temperature range, depending on its water content, temperature, floral source and other factors.

Viscosity, which decreases rapidly as temperature rises; 1% moisture is equivalent to about 3.5 °C in its effect on viscosity.[51]

Antimicrobial Activity

Mechanisms

A number of characteristics of honey contribute to its antimicrobial activity. The enzymatic glucose oxidation reaction and some of its physical properties are considered to be the major factors. Other factors include high osmotic pressure/low water activity (Aw), low pH/acidic environment, low protein content, high carbon to nitrogen ratio, low redox potential due to the high content of reducing sugars, a viscosity that limits dissolved oxygen and other chemical agents/ phytochemicals.[66]

Honey researcher, Peter Molan, PhD, has written an extensive review of the research on the antimicrobial factors in honey[67,68] and has summarized the key aspects of his research on a Web site at the University of Waikato, Hamilton, New Zealand:[69]

- Honey is a supersaturated sugar solution with a low water activity (Aw), which means that there is little water available to support the growth of bacteria and yeast. Many species of bacteria will grow if the Aw is between 0.94-0.99 and the Aw of ripened honey (0.56-0.62) does not support the growth of yeast. Diluted honey with a higher Aw will not be effective against those species of bacteria that grow most rapidly at an Aw of 0.99.
- The natural acidity of honey will inhibit many pathogens. The minimum pH value for some species that commonly infect wounds ranges from 4.0-4.5. Dilution of honey, especially with body fluids, will raise the pH and lessen the antibacterial effectiveness that results from its acidity.
- Glucose oxidase is an enzyme secreted by the bees to form honey from nectar. It converts glucose in the presence of water and oxygen to gluconic acid and hydrogen peroxide. The resulting acidity and hydrogen peroxide preserve and sterilize the honey during the ripening process. Full-strength honey has negligible amounts of hydrogen peroxide and active glucose oxidase. Transition ions and ascorbic acids rapidly decompose hydrogen peroxide to oxygen and water while the low pH inactivates the enzyme. However, dilution of honey results in a 2,500-50,000 increase in enzyme activity and a "slow-release" antiseptic that does not damage tissue.
- The peroxide-generating system does not account for all of the observed antibacterial activity. Several substances with antibacterial activity are found in honey in small quantities that are too low to contribute significantly to antibacterial activity: pinocembrin, terpenes, benzyl alcohol, 3,5-dimethoxy-4-hydroxybenzoic acid (syringic acid), methyl-3,5-dimethoxy-4-hydroxybenzoate (methyl syringate), 3,4,5-trimethoxybenzoic acid, 2-hydroxy-3-phenylpropionic acid, 2-hydroxybenzoic acid and 1,4-dihydroxybenzene. Support for the existence of non-peroxide antimicrobial factors comes from reports of continued activity after honey has been treated with heat, thereby inactivating the glucose oxidase, and after honey has been treated with catalase to remove the peroxide activity.

Not all honeys are created equal in antimicrobial activity due to differences in levels of peroxide production and non-peroxide factors, which vary by floral source and processing. The presence of metal ions, ascorbic acid and catalase from the nectar can destroy the hydrogen peroxide. Heat and light can destroy the glucose oxidase enzyme. The original method for measuring antibacterial activity was to determine the "inhibine number" defined as the degree of dilution (done in a stepwise fashion) to which a honey will retain its antibacterial activity. Most studies now report antimicrobial activity as minimum inhibitory concentration (MIC), the minimum concentration necessary for complete inhibition of growth.[69] Studies on large numbers of honey samples show a wide range of activity and many with only a low level of activity.[70,71]

While there are insufficient data to clearly identify the antibacterial activity of all honeys, there is some evidence of high levels in honeydew honey (a sweet liquid excreted by sucking insects[72] which tap into leaves) from the conifer forests of the mountainous regions of central Europe[69] and manuka honey (honey from the *Leptospermum* species) from New Zealand.[67,70,73] In a study by Willex, et al, manuka honey had the highest levels of non-peroxide activity among 26 different types of honey from various floral sources. It strongly inhibited two strains of bacteria (*Escherichia coli* and *Staphylococcus aureus*).[74]

An *in vitro* study compared the antibacterial action of a pasture honey (a polyfloral honey in which the nectar comes from various clovers and pasture weeds such as thistle and dandelion) and manuka honey on coagulasepositive *S. aureus* strains from infected wounds. The isolates showed little difference in their sensitivity to both honeys. The pasture honey with a higher peroxide generation and the manuka honey with non-peroxidal antibacterial activity were both effective at low concentrations (3-4 percent v/v and 2-3 percent v/v, respectively).[75]

Researchers evaluated crude honey from different regions in Egypt for antimicrobial effects. While all samples had similar effects on gram negative and gram positive bacteria in concentrations as low as 6.25 percent, they were ineffective against *Candida albicans* and *Aspergillus niger*. Fractions extracted from the honey were also evaluated for their antimicrobial activity. Of the four fractions, only ethylacetate honey extract was effective against bacteria, *Candida* and molds. Further study of this extract in an ointment base revealed that the ingredients in the base influenced its release and its stability was dependent on both temperature and the base.[76]

Numerous other studies document the variability in antimicrobial activity among honeys.[77,78,79,80,81,82,83,84] To assure the effectiveness of a specific honey for use as an antimicrobial agent, its activity should be assayed and storage conditions monitored to limit exposure to heat and light.[69] Testing for the antibacterial component in manuka honey, called the "Unique Manuka Factor" (UMF), uses a standard laboratory procedure to assess antibacterial activity and compare it with the potency of a standard antiseptic (phenol or carbolic) solution. The number rating for the honey is the percent solution that matches its potency. Thus, an active manuka honey with a rating of 10 is equivalent to a 10 percent solution of phenol in its antibacterial potency.[85]

Table 3 - Infections Caused by Bacterial Pathogens That Are Sensitive to the Antibacterial Activity of Honey[67]

Infection	Pathogen
Anthrax	*Bacillus anthracis*
Diphtheria	*Corynebacterium diphtheriae*
Diarrhea, septicemia, urinary infections, wound infections	*Escherichia coli*
Ear infections, meningitis, respiratory infections, sinusitis	*Haemophilus influenzae*
Pneumonia	*Klebsiella pneumoniae*
Meningitis	*Listeria monocytogenes*
Tuberculosis	*Mycobacterium tuberculosis*
Infected animal bites	*Pasteurella multocida*
Septicemia, urinary infections, wound infections	*Proteus* species
Urinary infections, wound infections	*Pseudomonas aeruginosa*
Diarrhea	*Salmonella* species
Septicemia	*Salmonella cholerae-suis*
Typhoid	*Salmonella typhi*
Wound infections	*Salmonella typhimurium*
Septicemia, wound infections	*Serratia marcescens*
Dysentery	*Shigella* species
Abscesses, boils, carbuncles, impetigo, wound infections	*Staphylococcus aureus*
Urinary infections	*Streptococcus faecalis*
Dental caries	*Streptococcus mutans*
Ear infections, meningitis, pneumonia, sinusitis	*Streptococcus pneumoniae*
Ear infections, impetigo, puerperal fever, rheumatic fever, scarlet fever, sore throat, wound infections	*Streptococcus pyogenes*
Cholera	*Vibrio cholerae*

Pathogens sensitive to honey

Research has demonstrated that many bacterial pathogens and fungi are sensitive to the antimicrobial activity of honey. Table 3 lists infections that are caused by pathogens that are sensitive to honey and Table 4a summarizes honey-sensitive pathogens and the lowest effective concentration (percent v/v) of honey reported to exhibit antibacterial activity. Table 4b summarizes the antimicrobial effect of honey on fungi.

A recent study documented the sensitivity of multiresistant strains of *Burkholderia cepacia* to manuka honey at concentrations below 6 percent (v/v). *B. cepacia* causes pulmonary infections in cystic fibrosis and chronic granulomatous disease patients as well as bacteremia, urinary tract infections and wound infections in hospitalized patients. It is a natural inhabitant of soil, water and vegetation and has been associated with foot lesions in soldiers after training in swampy waters. Suggested clinical applications for treating *B. cepacia* with honey include honey aerosols as an adjunct to antibiotic therapy and topically for superficial infections and wounds.[86]

Table 4a - Summary of Honey Concentrations Reported to Inhibit the Growth of Selected Bacterial Species[67]

Bacteria	Concentration of Honey for Complete Microbicidal Action (% by vol.)	Concentration of Honey for Complete Inhibition of Growth (% by vol.)	Concentration of Honey for Partial Inhibition of Growth (% by vol.)
Alcaligenes species		10-100*	
Alcaligenes faecalis	7.4		
Bacillus species	50		
Bacillus anthracis	2.5	1.3-100*	
Bacillus cereus		17-100	
Bacillus cereus var. mycoides		17-100*	8
Bacillus pumilus	1.3	1.3-25*	8-25
Bacillus stearothermophilus		42*	
Bacillus subtilis	[50]	10*-100*	5-25
Citrobacter freundii		3.6-10*	
Corynebacterium diphtheriae	5-17	2.5-25	
Edwardsiella tarda	99		
Escherichia coli	7.4-99	0.25*-100*	0.7-17
Haemophilus influenza		10	
Klebsiella species		10*	
Klebsiella pneumoniae	15-20	10-100*	40
Listeria monocytogenes		£25-30	
Micrococcus species		10*	
Micrococcus luteus		10*-42*	
Mycobacterium tuberculosis	100	4.5	1.2
Neisseria species		10*	
Proteus species		10*-20	5
Proteus mirabilis	30	3.6-100*	1.4-5
Streptococcus pyogenes	0.6	0.6-100*	0.7-10
Streptococcus salivarius		25*	
Streptomyces species			25
Vibrio cholerae		17-20	
Vibrio cholerae (proteus)		17	

**Signifies active concentration is lower because honey is diluted by diffusion in agar. Brackets signify completion of inhibition listed as "sensitive to honey."*

Clinical conditions that respond to treatment with honey

Historically, honey has been used to treat a number of clinical conditions. Recent research on gastrointestinal disorders, candidosis, tinea and ophthalmological disorders has been conducted to confirm the efficacy of honey treatments.

Ulcer/Gastritis/Diarrhea

Support for using honey as a treatment for peptic ulcers and gastritis comes from traditional folklore and from numerous reports in modern times.[5] The discovery of the role of *Helicobacter pylori* as a causative factor in peptic ulcers led to research on the antibacterial activity of honey as the explanation for its therapeutic action. Research confirmed that *H. pylori* was sensitive to honey with a median level of antibacterial activity due to hydrogen peroxide at concentrations of 20 percent and to manuka honey with non-peroxide antibacterial activity at a concentration of 5 percent. However, a clinical trial with a small number of subjects did not demonstrate the effectiveness of manuka honey on *H. pylori.* Other research has focused on mechanisms by which honey can protect and heal gastric mucosa through the stimulation of blood supply, an anti-inflammatory action related to the antioxidant properties present in honey, and the stimulation of growth of new epithelial cells.[87,88]

Infantile gastroenteritis and diarrhea are usually treated with a rehydrating glucose and electrolyte solution. The glucose aids in the absorption of electrolytes and the uptake of water. When honey at 5 percent (v/v) concentration replaced the glucose in rehydration fluid, the duration of the diarrhea was shortened in patients with bacterial gastroenteritis compared to a control group on standard therapy. In patients with viral diarrhea, the duration was neither shortened nor lengthened, confirming that the response was due to the antibacterial activity of honey. Honey was shown to be as effective as glucose in rehydration. Like glucose, honey aids in the uptake of sodium and water. In addition, fructose, the predominant sugar in honey, promotes potassium and additional water uptake without increasing sodium uptake. Besides the antibacterial activity, honey may promote the repair of damaged intestinal mucosa, stimulate the growth of new tissues and work as an anti-inflammatory agent.[5,87]

Further research investigated the sensitivity of gastroenteritis-causing bacteria to pasture honey with hydrogen peroxide activity and to manuka honey with non-peroxide activity as well as to an artificial honey (i.e., a sugar solution that mimics the composition of honey). Both the pasture honey and the manuka honey exhibited bacteriostatic (prevention of growth) and bactericidal (killing of bacteria) activity. At 4-8 percent (v/v), the pasture honey was bacteriostatic and at 5-10 percent (v/v) bactericidal. The manuka honey required slightly higher concentrations of honey—5-11 percent (v/v) for bacteriostatis and 8-15 percent (v/v) for bactericide. The artificial honey was only bacteriostatic at 20-30 percent (v/v), illustrating that the antibacterial activity of honey was not just related to acidity and osmotic effect.[7]

Table 4b - Summary of the Concentration of Various Honeys That Have Been Reported to Inhibit the Growth of Selected Fungi Species[67]

Fungi	Concentration of Honey for Complete Microbicidal Action (% by vol.)	Concentration of Honey for Complete Inhibition of Growth (% by vol.)	Concentration of Honey for Partial Inhibition of Growth (% by vol.)
Aspergillus flavus		60-75	25
Aspergillus fumigatus		3.1	
Aspergillus niger		75	25
Aspergillus parasiticus		60	
Candida albicans	100	1.6-100*	
Candida psuedotropicalis	10		
Candida reukaufii	50		
Candida stellatoidea	50		
Candida tropicalis	50		
Penicillium spp		3.1	
Penicillium chrysogenum		75	25
Saccharomyces spp	[50]		

**Signifies active concentration is lower because honey is diluted by diffusion in agar. Brackets signify completion of inhibition listed as "sensitive to honey."*

Candidosis

Candidosis, the vaginal yeast infection caused by *Candida albicans*, may be treatable with honey. Research using honey distillates and clinical isolates demonstrated that the honey distillates were comparable to commercial antimycotic preparations in their ability to inhibit *Candida*.[89] Other research found 0.1 and 0.2 mL of volatile oil from Hungarian honey was inhibitory as well.[82]

Tinea

Cutaneous or superficial mycoses, or tineas such as ringworm and athletes foot, caused through infection by fungi called dermaphytes (*Deuteromycontina*) are common but very difficult to treat. Frequently, a concomitant bacterial infection exists due to poor host immunity. The antimicrobial properties of honey offer the potential to treat both the fungal and bacterial infections. Research on two types of honey—a pasture honey with average antibacterial activity due to hydrogen peroxide activity and a manuka honey with an average level of non-peroxide antibacterial activity—were investigated for their anti-fungal properties against clinical isolates of seven species of dermaphytes. Results demonstrated that growth was inhibited by the hydrogen peroxide in the pasture honey and by the non-peroxide activity in the manuka honey. More honey was needed to inhibit some of the dermaphytes than is needed to inhibit bacteria. However, less dilution by body fluids is likely with a tinea.[7]

Ophthalmologic Disorders

Honey has been used since ancient times to treat eye disorders. Numerous reports from around the world detail the use of honey to treat blepharitis (inflammation of the eyelids), catarrhal conjunctivitis, keratitis (inflammation of the cornea) and various ailments/injuries to the cornea as well as chemical and thermal burns to the eye. In general, treatment is successful in achieving remission or stopping the progression of the disease. Honey is usually applied as an ointment. In a study with 102 patients who had various eye disorders that did not respond to conventional treatment, 85 percent experienced improvement and the other 15 percent had no further deterioration when treated with honey. The only adverse reaction reported was a transient stinging sensation and redness in the eye shortly after the honey was applied.[5]

Veterinary applications

Laboratory studies show that various bacteria that cause mastitis in dairy cattle are sensitive to honey. If the same level of effectiveness is demonstrated when animals with mastitis are treated with honey, then it could be used as a more consumer-friendly alternative to antibiotics.[7]

Food Safety

Antimicrobial activity against food-borne pathogens and spoilage microorganisms

Honey may contain organisms from bees, soil, air and dust that are introduced during its collection and production by the bee and during post-harvest handling.[66,90] However, while *Clostridium botulinum* is found in a small percentage of honey,[91,92,93,94] no other vegetative cells of disease-causing organisms have ever been isolated.[66] A number of inoculation studies have been conducted to assess the ability of honey to inhibit bacteria found naturally in it and other food contaminants. Table 5 summarizes the results of many of these studies.

Table 5 - Honey Inoculation Studies[66]

Species	Temperature (∞C)	Survival Time	Reference
Non-spore forming intestinal bacteria	Room temperature	A few days	Sackett (1919)
Escherichia coli	20	< 10 days	Tysset & Durand (1973)
Erwina amylovara	4	8 weeks	De Wael et al. (1990)
Edwardsiella tarda	20	< 10 days	Tysset & Durand (1973)
Mycobacterium chelonie	20	26 days	Tysset & Durand (1973)
Mycobacterium phlei	20	17 days	Tysset & Durand (1973)
Mycobacterium tuberculosis	20	67 days	Tysset et al. (1979)
M. tuberculosis bovis	20	77 days	Tysset et al. (1979)
M. tuberculosis avium	20	71 days	Tysset et al. (1979)
Proteus vulagaris	20	< 10 days	Tysset & Durand (1973)
Pseudomonas aeruginosa	20	8 hours	Tysset & Durand (1973)
Salmonella derby	10	6 months, 13 days	Tysset & Durand (1976)
Salmonella dublin	10	2 years, 4 months, 12 days	Tysset & Durand (1976)
Salmonella enteritidis	20	34 days	Tysset & Durand (1973)
Salmonella enteritidis	10	1 year, 11 months, 5 days	Tysset & Durand (1976)
Salmonella typhi	10	4 months, 21 days	Tysset & Durand (1976)
Salmonella typhimurium	10	30 days	Tysset & Durand (1973)
Salmonella typhimurium	10	2 years, 4 months, 12 days	Tysset & Durand (1976)
Serratia marcescens	20	18 days	Tysset & Durand (1973)
Shigella	10	2 months, 22 days	Tysset & Durand (1976)

The inhibitory activity of honey from six floral sources on six foodborne pathogens, *Escherichia coli* O157:H7, *Salmonella typhimurium*, *Shigella sonnei*, *Listeria monocytogenes*, *Staphylococcus aureus* and *Bacillus cereus* was evaluated. Results demonstrated that hydrogen peroxide as well as non-peroxide components such as antioxidants contributed to the inhibition of growth of *S. sonnei*, *L. monocytogenes* and *S. aureus*. In general, the darker honeys, which contain more antioxidants, were more inhibitory. Based on this study, it appears that antibacterial activity of honey may be partly due to its antioxidants but more research is needed to determine the effects of processing and activity in different food systems.[95] Thus, antioxidants in honey may play a positive role in food safety beyond food preservation.

Researchers from Cornell University investigated the antimicrobial activity of different types of American honeys against six food pathogens and six food spoilage microorganisms *in vitro*. The honeys exhibited both peroxide and non-peroxide antimicrobial activity, which varied according to the floral source. In this particular study, two types (tarwood and Montana buckwheat) were effective at impeding the growth of *Listeria monocytogenes* at one-quarter and one-eighth dilution, respectively. At stronger dilutions, they impeded the growth of *Lactobacillus*, *Bacillus*, *Escherichia coli* and *Salmonella*.

At full-strength, Chinese buckwheat was effective against *E. coli* and *Salmonella*. The antimicrobial effect appeared to vary by the type of bacteria—the high sugar content of honey seemed to inhibit the gram negative bacteria but a threshold inhibitory level was needed to prevent growth of the gram positive bacteria.[96]

Honey appears to present another option for enhancing the safety and shelf life of foods. A number of recent studies have shown that honey will lower bacteria counts in poultry and fish products. Researchers at Clemson University used 15 percent dried honey in a processed turkey luncheon-meat type product and found no bacterial growth after 11 weeks of refrigerated storage.[97] At the University of Georgia at Athens, when honey was added to a coating for shrimp and to a marinade and coating for catfish, microorganisms were either lower than the control or not detected. The researchers also demonstrated that honey added to a hydrated batter system suppressed the growth of *Staphylococcus aureus* during processing.[98,99]

Table 6 - Types of Wounds Treated Successfully with Honey[5]

Abrasions
Abscesses
Amputations
Bed sores (pressure sores, decubitus ulcers)
Burns
Burst abdominal wounds following caesarian delivery
Cancrum
Cervical ulcers
Chilblains
Cracked nipples
Cuts
Diabetic foot ulcers and other ulcers
Fistula
Foot ulcers in lepers
Infected wounds arising from trauma
Large septic wounds
Leg ulcers
Malignant ulcers
Sickle cell ulcers
Skin ulcers
Surgical wounds
Tropical ulcers
Varicose ulcers
Wounds to the abdominal wall and perineum

Wound Healing

Properties and mechanisms

Empirical evidence established honey as a treatment for wounds and sores in ancient times. Today an extensive body of scientific literature on the wound healing capabilities of honey confirms its value as both an antimicrobial agent and a promoter of healing.[100]

A multitude of wound types have successfully been treated with honey dressings. Table 6 lists the variety found in an extensive review of the medical literature. There have only been a few cases reported where improvement did not occur—a Buruli ulcer, a small group in which only a small amount of honey was applied, two cases with immunodepression, one who stopped treatment because of a painful reaction to honey, one burn that had only a good initial response and an ulcer complicated by the presence of varicose veins.[5]

Clearly, the antimicrobial activity in honey that prevents and treats infections is fundamental to its wound healing properties. However, scientific evidence points to a more diverse role for honey in the process.[10,26,32,34,74, 101,102,103,104] Observed therapeutic effects attributed to using honey as a wound dressing include rapid healing, stimulation of the healing process, clearance of infection, cleansing action on wounds, stimulation of tissue regeneration, reduction of inflammation, and the comfort of the dressings due to lack of adhesion to the tissues.[5]

Healing is a complex, dynamic process that involves many systems and cell types. Molecular and cellular components are responsible for the degradation and repair of tissues that occur during healing.[105] While the exact mechanisms for all the observed effects of honey when applied to wounds, burns and skin ulcers are yet to be defined, recent research clarifies and elucidates some possible explanations. Table 7 summarizes properties of honey, clinical outcomes and possible mechanisms based on *in vitro* studies, animal models and clinical data.

As a medical treatment, honey is rather innocuous. Other than occasional stinging when applied to wounds and redness in the eye, no adverse affects have been reported. In addition, allergy to honey is rare. In theory, wound botulism from naturally occurring *Clostridium botulinum* spores is possible but in practice, this has never been reported. Since high heat is known to inactivate the antimicrobial factors in honey, pasteurization or other heat treatments are not sterilization options. However, treatment with gamma-irradiation

Table 7 - Reported Wound Healing Capabilities of Honey[87,105,106]

Property	Anticipated Clinical Outcomes	Suspected Mode of Action
Antimicrobial activity	• Sterilization of wound • Inhibition of potential wound pathogens and protein-digesting enzymes that destroy tissues • Deodorization of foul-smelling wounds • Protective barrier to prevent cross-contamination	• Production of hydrogen peroxide • Action of non-peroxide components (phytochemicals) • Acidity • Stimulation of immune system—multiplication of β-lymphocytes and T-lymphocytes; activation of neutrophils; release of cytokines by monocytes; supply of glucose for "respiratory burst" and for energy production in macrophages; acidity to assist in bacteria-destroying action of macrophages • Glucose metabolism by the infecting bacteria to lactic acid instead of metabolism of amino acids from serum and dead cells to malodorous ammonia, amines and sulfur compounds • High viscosity creates physical barrier that limits exposure to environmental pathogens
Anti-inflammatory activity	• Resolution of edema and exudates • Reduction of pain • Reduction in keloids and scarring	• High osmolarity leading to fluid outflow to create layer of dilute solution of honey in plasma or lymph, resulting in moist conditions necessary for healing and no adhesion to the surface of the wound • Decrease in leukocytes associated with inflammation • Inhibition of reactive oxygen intermediates (ROI) production as a result of antioxidant activity • Suppression of the inflammatory process through the scavenging of free radicals by antioxidants
Stimulation of rapid healing	• Increased phagocytosis • Increased autolytic debridement • Increased angiogenesis • Promotion of granulation tissue • Cell proliferation • Collagen synthesis • Re-epithelialization with less need for skin grafts	• Stimulatory effects of glycosylated honey proteins or other components on macrophages • Clearing of debris with moist dressing • Increased nutrification of tissues secondary to the outflow of lymph and the nutrients in honey (i.e., glucose, amino acids, vitamins and minerals) • Increased oxygen supply secondary to the outflow of lymph and the acidity of honey • Controlled low hydrogen peroxide production with antioxidant protection that modifies proteins important to cell growth and debridement

will kill the spores while leaving the components responsible for antimicrobial activity intact.[87,107]

Much of the literature on the use of honey in wound healing (and in other areas of research) does not give the type of honey used. All honey is not equal in its effectiveness and care must be taken to ensure that the type used has adequate antimicrobial activity. Extensive research at the University of Waikato, Hamilton, New Zealand, has demonstrated the value of manuka honey (not found in the United States) from the *Leptospermum* species as a wound dressing. Commercial standardized and sterilized versions of manuka or other *Leptospermum* honey in squeeze-out tubes, syringes and impregnated dressings are available from several manufacturers by mail order. In New Zealand, active manuka honey with a rating of UMF 10 or higher is commonly used in these products.[85,87,108,109,110]

In recent years, honey has been rediscovered as a treatment for wound healing.[111] Laboratory research has verified its efficacy against many of the common pathogens that infect wounds, including some of the antibiotic resistant bacteria such as MRSA (Methicillan-resistant *Staphylococcus aureus*) and VRE (Vancomycin-resistant enterococci).[112,113] In these studies, an artificial honey, a supersaturated sugar solution that mimics the composition and osmolarity of honey, is used as the control to demonstrate the antimicrobial components in honey that are not related to its osmotic pressure. As can be seen in Table 8, honey at less than 10 percent (v/v) concentration inhibited the pathogens including the MRSA with manuka honey exhibiting inhibition at the lowest concentrations (2.3-6.6 percent v/v).[105]

Table 8 - Honey Minimum Inhibition Concentration (% v/v) for Bacteria Isolated from Infected Wounds[105]

Organism	Artificial Honey	Manuka Honey	Pasture Honey
Enterococcus faecalis	28.6	6.6	8.4
Esherichia coli	23.4	4.0	7.8
Klebsiella oxytoca	27.8	3.7	7.5
MRSA (Methicillan-resistant *Staphylococcus aureus*)	>30	2.3	2.9
Proteus mirabailis	28.6	5.2	6.3
Proteus morganii	22.8	3.6	5.1
Serratia marcescens	>30	5.5	7.0

Promotion of healing

Clinically, there are numerous reports of healing severe wounds with honey wound dressings. Most striking was the remarkable recovery of an adolescent boy in the United Kingdom who had chronic infected lesions caused by meningococcal septicemia that resulted in extensive tissue necrosis, necessitating amputations of his legs below the knees and distal and middle phalanges on both hands. After several months, numerous skin grafts on his legs and a pressure ulcer were heavily infected by *Pseudomonas* and *Staphylococcus aureus* and failed to heal with conventional treatment. Treatment with dressing pads impregnated with sterilized active manuka honey from New Zealand led to complete healing within 10 weeks.[114]

Table 9 - Recommendations by Molan for Dressing Wounds with Honey[108]

1. Start using honey on a wound from the onset.
2. Use only honey that has been selected for use in wound care.
3. Use dressings that will hold sufficient honey in place on a wound to get a good therapeutic effect.
4. Ensure that honey is in full contact with the wound bed.
5. If a non-adhering dressing is used between the honey dressing and the wound bed, it must be sufficiently porous to allow the active components of the honey to diffuse through it.
6. Ensure that honey dressings extend to cover any area of inflammation surrounding wounds.
7. Use a suitable secondary dressing to prevent leakage of honey.
8. Change the dressings frequently enough to prevent the honey from being washed away or excessively diluted by wound exudate.
9. When using honey to debride hard eschar (slough), scoring and softening the eschar by soaking with saline will allow better penetration of the honey.

In order to capitalize on all the advantages honey offers as a wound dressing, its application needs to be tailored to the type of wound and its degree of severity. The exudate from the wound will dilute the honey, so the fluid outflow will determine the frequency of dressing changes. Honey needs to be in contact with the wound; inflamed and deep wounds require more honey so it can diffuse into the tissues. Cavities and depressions in a wound bed need to be filled with honey before the dressing is applied. It is best to apply the honey to the dressing instead of the wound itself. Dressings should extend beyond the edges and surround affected tissues. Occlusive or other secondary bandages help to prevent honey from oozing out from the dressing.[7,108,115] The recommendations in Table 9 summarize Dr. Molan's guidelines for dressing wounds with honey. Patients are encouraged to discuss honey as a potential therapeutic agent with their physicians.

Burns

Burns have more adverse effects on the body than just damage to the skin and tissues. Hemodynamic (heart), hematological, gastrointestinal, endocrinologic, and neurologic systems are all affected as well. Management of burn victims requires re-establishment of a barrier that will protect the internal environment from external contaminants but also help hold in and regulate fluids and tissues under repair.

Honey may be able to heal burns as well or better than conventional dressings.[116] A series of studies by Subrahmanyam in India has shown that dressings with pure, unprocessed, undiluted honey obtained from hives (floral origin and antimicrobial activity of the honey not specified in the reports) had advantages over standard medical treatments such as OpSite®,[26] silver sulfadiazine[29] and traditional, low-cost treatments such as boiled potato peels[30] but not over early tangential excision and skin grafting of moderate burns.[117] Results from the studies comparing different dressings demonstrated that honey is an effective dressing which speeds healing, sterilizes wounds, reduces pain with enhanced formation of granulation tissue and lessens inflammation and scarring. Its viscous quality protects the surface from infection and scraping. Other benefits are the ease of dressing changes and its lower cost. Additionally, skin grafts were successfully held at room temperature in honey prior to grafting instead of being rehydrated in saline solution.[27]

Minimal scarring has been observed when wounds and burns are treated with honey.[118] Subrahmanyam[25] noted less scarring in burn patients, including deep wound patients and patients with second and third degree burns.

In regulatory terms, honey is considered to be a medical device as are wound dressings such as OpSite®. In 1999, the Therapeutic Goods Administration of Australia approved the use of Medihoney®, which is 100 percent honey, as a primary wound dressing. Two new products were introduced in The Netherlands during 2001. One is Medisoft®, a plaster containing a neutral woven carrier of ethylvinylacetate (EVC) and pure honey. The other is a sterile mix of honey and other substances such as lanolin, sunflower oil and zinc oxide.[119]

Infected wounds and burns

Of course, infected wounds and burns are more difficult to manage clinically. Honey has been evaluated recently for its usefulness in dealing with these conditions. Research in the 1990s found honey to be effective in healing infected non-healing skin wounds.[22,24] Studies on Fournier's gangene treated with topical unprocessed honey showed rapid improvement with decreased edema and discharge, rapid regeneration with little or no scarring, wound debridement and reduced mortality.[120,121] Animal studies with buffalo calves compared honey to ampicillin and nitrofuazone in treating infection and found that honey decreased infection and healing time and was generally more effective.[122,123]

Surgical wounds

In 1955, Bulman used honey as surgical dressing for vulvectomies because of its bactericidal capabilities. He also noted success in treating ulcerations following radical surgery for carcinoma of the breast and varicose veins with honey.[18] In 1970, other researchers reported using undiluted honey following radical operations for carcinoma of the vulva, resulting in no infections, minimal debridement and reduced hospital stays.[124] In the 1980s, a number of studies used mice to investigate honey in surgical wound healing and found that there was more granulation, smaller wounds and more rapid healing.[12,125] Other research evaluated the use of honey and microtape for wound closure in women with wound disruption following Cesarean sections and showed healing within 2 weeks.[34] Based on these examples, topical application of honey to surgical wounds holds much promise as a low cost, effective treatment.

Pressure sores and skin ulcers

Healing properties of honey on skin ulcers is well documented. Numerous studies have demonstrated that the use of unprocessed/undiluted honey resulted in rapid debridement and epithelization, quick recovery, wound cleanliness, improved taking of grafts and ease of dressing changes. Table 10 summarizes some of the key studies.

Table 10 - Studies on Healing Pressure Sore and Skin Ulcers

Researcher	Description/Finding(s)
Efem (1988)[21] Zumla and Lulat (1989)[6] McInerney (1990)[22] Bourne (1991)[31] Somerfield (1991)[24] Ankra-Badu (1992)[126]	Documented healing properties on skin ulcers
Efem (1988)[21]	Clinical observations on wound healing in 59 patients with single ulcers that had failed to heal; used 15-30mL fresh unprocessed/undiluted honey from bee hives as dressing; rapid debridement, rapid epithelization; quick recovery
Farouk, et al. (1988)[127]	Unprocessed bee honey in Sudan; septic wounds, chronic ulcer and pyrogenic abscesses; increased granulation, wound cleanliness and prompt taking of grafts; ease of dressing changes reduced duration of treatments; lack of allergies; low cost
Weheida, et al. (1991)[128]	Treatment of pressure ulcer in orthopedic patients; accelerated healing time
Isenberg, et al. (1995)[129]	Pressure sore retrospective study of traditional topical agents; 75 percent no improvement or worsened; 40 percent died in hospital
Blomfield (1993)[19]	Successful treatment of wounds with honey under dry dressing in accident and emergency room departments
Wood, et al. (1997)[130]	Manuka honey helped heal leg ulcers also treated with antibiotics
Zumla and Lulat (1989)[6]	Proposed treatment of leprosy—clean smelling wounds would reduce patient isolation and help with physiological and psychological state

Energy/Carbohydrate Metabolism

Basic principles

Energy production and utilization is a complex system in which chemical reactions convert nutrients in food to energy. While carbohydrates, protein and fat can all be used as substrates, glucose is the preferred fuel source. Thus, carbohydrate metabolism is closely tied to energy metabolism. Digestible disaccharides and polysaccharides are broken down into monosaccharides before absorption. The monosaccharides, fructose and galactose, are converted to glucose for use in energy production or to glycogen for storage until glucose is needed by the body. Hormones, such as insulin, play a major role in regulating carbohydrate, protein and fat metabolism and availability as substrates for energy.

Total energy needs of an individual are determined by many factors—body size and composition, gender, activity/exercise and special metabolic needs. To maintain a constant source of energy for normal body functions and activity, excess fuels are stored as glycogen in muscles and the liver and as fat in adipose tissue. Energy intake from food that is greater than needs results in excess energy being stored for later use. Conversely, energy intake that is less than needs results in energy stores of glycogen and fat being used.

Honey and athletic performance

The ability to produce energy greatly influences athletic performance. In the past few decades, the relationship between nutrition and exercise capabilities as a means for improving performance has been investigated. Carbohydrate ingestion prior to, during and after exercise affects an athlete's performance and recovery.

Research on the effects of fructose and glucose feeding demonstrated that neither was ideal. Fructose alone is poorly absorbed, can cause intestinal distress, has a low insulin response and spares muscle glycogen.

Glucose is well absorbed, quickly metabolized for energy but has a high insulin response that stimulates glycogen storage instead of mobilization, which is important for athletes who need a more constant supply of glucose. Studies have shown that a mixture of carbohydrates is better tolerated and better suited for fatigue prevention and enhanced performance.[131]

Products designed to provide a combination of carbohydrates are commercially available. Honey is a natural fructose-glucose carbohydrate mixture with some oligosaccharides, protein, vitamins and minerals. As such, it potentially offers many of the performance advantages of the beverages and gels that are commonly used by athletes.

A series of studies conducted at the University of Memphis investigated the effectiveness of honey as a carbohydrate source for athletes before and after resistance training and during endurance exercise. Overall, these studies demonstrated that honey performs as well as commercially available carbohydrate gels and can be considered a natural, economical alternative source of carbohydrate for athletes. A brief summary of each study follows.

- The first study compared the effects of a placebo, dextrose, sucrose, fructose maltodextrin, honey or PowerGel™ on glucose and insulin levels and on subjective ratings of hypoglycemia. Glycemic and insulinemic responses indicated that honey is the optimal carbohydrate for pre-exercise ingestion, producing only modest increases in glucose and insulin without a threat of hypoglycemia.[132,133]

- The second study investigated the effects of ingesting sucrose, maltodextrin or powdered honey with protein following resistance exercise on substrate levels and markers of catabolism. Results varied for the various carbohydrates and suggested that the type of carbohydrate ingested with protein after exercise may affect the anabolic hormonal profile during recovery. Honey and maltodextrin appeared to elicit a more favorable response.[134]

- The third study examined the effects of a pre-exercise feeding of a placebo, dextrose, honey or PowerGel™ on glucose, insulin and markers of catabolism following resistance exercise. Substrate availability, hormone levels and markers of catabolism were not significantly affected by any of the carbohydrate gels in this study, although some anticatabolic trends were observed. Further research is needed in this area.[135]

- The fourth study explored the usefulness of honey as a source of carbohydrate for endurance athletes. Subjects ingested 15 grams of a non-caloric flavored gel, a dextrose gel or honey prior to and during cycling time trials. Compared to the placebo, honey reduced the time to complete the trial and increased the cycling power and was equal to the dextrose gel, suggesting that honey may be a useful alternative carbohydrate source for endurance athletes.[136]

Honey is a natural fructose-glucose carbohydrate mixture with some oligosaccharides, protein, vitamins and minerals. As such, it potentially offers many of the performance advantages of the beverages and gels that are commonly used by athletes.

Use by diabetics

Diabetes is a multi-faceted disease with different manifestations, causes and complications. However, a consistent finding is an elevated blood glucose concentration along with abnormalities of glucose, lipid and protein metabolism. In the past, avoidance of sugars and sweets was advised in order to maintain blood glucose levels close to normal. But advances in research on the effects of different carbohydrates on glucose levels, called the glycemic index (GI), have shown that sucrose is not more glycemic than many starches. The 2002 recommendations from the American Diabetes Association state that the total amount of carbohydrate in meals and snacks is more important than the type of carbohydrate in producing the glycemic response. Thus, common sugars, such as sucrose and fructose, and other nutritive sweeteners, such as honey, are allowed as part of the total carbohydrate content of an individual's diet.[137]

Research on the GI of honey is limited and has yielded inconclusive results. In normal subjects, the values showed a lower rise in blood glucose when compared to glucose.[138,139] In one study of individuals with Type I (insulin dependent) and Type II (insulin resistant) diabetes, normal individuals and those with Type I diabetes had a significantly lower GI with honey than with glucose or sucrose and those with Type II had similar values for all three samples.[140] Two other studies in individuals with Type II diabetes showed no significant difference when compared to bread[141] and to bread and sucrose.[142] These results support the stance of the American Diabetes Association that honey has neither an advantage nor disadvantage over sucrose or foods sweetened with sucrose when included as part of the total carbohydrate in an individual's diet.[137]

Poor wound healing is a complication of diabetes for which the pathogenesis is still unclear. Other clinical conditions common in diabetics contribute to an environment that is not conducive to healing—peripheral vascular disease, decreased immuno-competency and peripheral neuropathy. Frequently, wounds become infected and chronic in character.[105] As discussed earlier, honey wound dressings are effective at healing chronic and infected wounds. Theoretically, blood glucose levels could be affected by absorbed glucose from the wound. However, this has not be observed in clinical practice.[87]

Antioxidant Activity

Antioxidants in food preservation and human health

Antioxidants play a role in combating damage caused by oxidizing agents, such as oxygen, in foods and in the human body. Natural and synthetic antioxidants have a long history as preservatives in the food supply. Their role in the human body has yet to be fully elucidated but much evidence indicates a role in countering the effects of naturally occurring free radicals that are associated with a number of diseases and the aging process.[143,144]

Antioxidants are used as preservatives in foods to specifically retard deterioration, rancidity or discoloration due to oxidation caused by light, heat and some metals. Rancid food generally lacks eating quality and can contain potentially toxic substances that can be harmful if consumed. Antioxidants buffer the oxidizing agent to prevent reactions with unsaturated fatty acids.

In the body, highly reactive compounds derived from oxygen, called free radicals and reactive oxygen species (ROS), are formed during metabolism. These compounds are then free to interact with a number of lipid and protein components in cell membranes and enzymes as well as DNA. These damaging reactions may result in cancer, heart disease, stroke, cataracts, Alzheimer's, arthritis and some of the symptoms of old age.[143,144,145] Antioxidants intercept free radicals before they can do damage. The protective antioxidant mechanisms employ both enzymatic (such as catalase) and non-enzymatic substances (such as tocopherols, phenolics, flavonols, catechins, ascorbic acid and carotenoids).

Antioxidant content of various honeys

Research from the Departments of Plant Biology and Entomology at the University of Illinois at Urbana-Champaign has shown that antioxidant capacity of different honeys varies by floral source and is positively correlated with color and water content. When the water-soluble content of 14 unifloral honeys was measured, a 20-fold variation existed between the highest, 1995 Illinois buckwheat honey, and the lowest, 1994 California button sage honey. Darker honeys were higher in antioxidants as were those with higher water content.[59]

Another study from the Department of Food Science and Human Nutrition at the University of Illinois at Urbana-Champaign set out to isolate and characterize the antioxidants present in seven different honeys. Components that were identified and/or quantified included phenolic compounds, ascorbic acid and the enzymes glucose oxidase, catalase and peroxidase. The oxygen radical absorbance capacity (ORAC) assay was used to measure antioxidant properties of the honeys. ORAC values ranged from 3.1-16.3 mmol Trolox equivalents (TE)/g honey, with the darkest honey having the highest value. The phenolic content correlated with ORAC values of honey while the enzyme activity and ascorbic acid were low, indicating that phenols were responsible for the antioxidant activity of the honeys. However, additional research on single phenolic and other compounds in honey indicate that the antioxidant capacity is due to the combination of a wide range of active compounds beyond phenolics.[146,147,148] ORAC values for many fruits and vegetable range from 0.5-19 mmol TE/g fresh weight.[149,150] Thus, honey has potential to serve as a dietary antioxidant. Research on the effects of processing and storage on antioxidant capacity of honey is now underway.

Bioactivity and bioavailability of honey antioxidants

Additional research on bioactivity was conducted on the honeys for which ORAC values were determined in the above study. Two different measures were made on the honeys and a sugar analogue. The *in vitro* lipoprotein oxidation test measured oxidative reactions when serum is exposed to copper and the Ames mutagenicity assay measured inhibition of Trp-p-1 mutagenicity. Results showed that the honeys were more effective at inhibiting lipoprotein oxidation than the sugar analogue, indicating that honey has potential as a biological antioxidant. There were differences in the antioxidant activity as measured by the ORAC assay of specific honeys, which may be due to the difference in phenolic profile. The honeys and the sugar analogue exhibited significant antimutagenicity activity to Trp-p-1. It seems that the sugar components may partly be responsible for the antimutagenicity of honey as opposed to the antioxidant phenolics.[151]

Further research on the health promoting components in honey has begun. In a study designed to assess the potential of honey as a dietary antioxidant, *in vitro* antioxidant capacity of honey from various floral sources was measured in a biologically relevant system and the acute effect of black tea with the honeys was measured *ex vivo* in a controlled human intervention study. All honeys exhibited a dose-dependant inhibition of lipoprotein oxidation *in vitro*. A slight increase of water-soluble plasma antioxidants followed the consumption of black tea with honey but did not affect lipoprotein oxidation dramatically when measured *ex vivo*.[152]

Researchers from the Department of Nutrition and Internal Medicine at the University of California at Davis studied the bioavailability and efficacy of honey antioxidants. The effects on plasma phenolic content and plasma antioxidant capacity in healthy human subjects were measured after consumption of corn syrup and buckwheat honey at 1.5g/kg body weight. Results demonstrated the bioavailability and bioactivity of phenolic antioxidants in honey on an acute basis and suggest a high efficiency of anitoxidant transfer from honey. Future research needs include determining the efficacy of different floral sources, assessing the long-term antioxidant protection afforded by honey and the antioxidant potential of honey when used as a food additive.[153]

Prebiotic Properties

Definition and role in human health

A prebiotic is a non-digestible dietary supplement that modifies the balance of the intestinal microflora stimulating the growth and/or activity of the beneficial organisms and suppressing potentially deleterious bacteria.[154] The most common prebiotics today are nondigestible oligosaccharides, such as fructooligosaccharides (FOS), galacto-oligosaccharides (GOS) and inulin. A probiotic is a live microbial food supplement that improves the intestinal microbial balance in the host organism.[154]

Bifidobacteria are one of the bacteria considered important to the health of the gastro-intestinal tract (GI). Clinical studies have associated beneficial effects such as immune enhancement and anti-carcinogenicity with the presence of bifidobacteria in the GI tract. Thus, recent research has focused on how to ensure its presence in adequate quantities through the addition of probiotics or prebiotics in a suitable carrier such as fermented milk. However, the challenge when adding bifidobacteria to milk as a probiotic is to maintain a viable, large population during processing and refrigerated storage.

Honey as a prebiotic in fermented milk

Health-conscious consumers seek out fermented dairy products such as yogurt for their perceived prophylactic and therapeutic properties. Lactic acid bacteria, *Streptococcus thermophilus* and *Lactobacillus delbruekii spp* *bulgaricus (Lactobacillus bulgaricus)*, are commonly used for starter cultures in these products. A study conducted in the Department of Food Science and Human Nutrition at Michigan State University compared the use of honey, sucrose and fructose in fermented skim milk inoculated with *Streptococcus thermophilus*, *Lactobacillus acidophilus*, *Lactobacillus delbruekii* spp *bulgaricus* and *Bifidobacterium bifidum*. Despite its antimicrobial properties, honey did not inhibit the growth of these organisms, and therefore, appears suitable as a sweetener in fermented milk products. While all sweeteners supported the growth of all four organisms, honey enhanced the growth of the bifidobacteria.[155]

Scientists continue to explore the connection between honey and health found in traditional folklore medicine.

Growth and viability of bifidobacteria in fermented milk can be enhanced significantly by the incorporation of FOS and GOS in milk prior to fermentation.[156] Honey contains a variety of oligosaccharides varying in their degree of polymerization. The unique composition of honey suggests that it could enhance the growth, activity and viability of bifidobacteria in milk and thus, fermented dairy products. To fully evaluate this hypothesis, a comprehensive study on growth-promoting and prebiotic activity of U.S. clover honey on bifidobacteria was conducted at Michigan State University.

The series of experiments aimed to determine the effect of honey on commercially available bifidobacteria strains in milk, to identify the components in honey responsible for growth-promoting activity, to determine the prebiotic activity of these components in honey and to compare the growth-promoting and prebiotic effects of honey and commercially available oligosaccharides. A number of key findings emerged from this research:[157,158,159]

- Honey enhanced the growth, activity and viability of commercial strains of bifidobacteria typically added to manufactured fermented dairy products. However, this effect was strain-specific.
- There was a synergistic effect among the carbohydrate components of honey in promoting growth and activity of bifidobacteria.
- The *in vitro* effect of honey on the growth and activity of intestinal *Bifidobacterium* spp was similar to that of commercial oligosaccharides (FOS, GOS and inulin).

The oligosaccharide and carbohydrate content of honey varies according to its floral source and therefore, the effectiveness of honey as a prebiotic can be expected to vary as well. As discussed above, honey possesses inhibitory properties against a number of pathogens. This antimicrobial activity also varies according to floral source. Research is now underway to evaluate the ability of honey from different floral sources to support the growth of intestinal bifidobacteria and/or other gut flora and to suppress deleterious bacteria in the gut.[160]

Areas Currently Under Investigation

Scientists continue to explore the connection between honey and health found in traditional folklore medicine. They seek to clarify the scientific reality and basis for its multifaceted functionality in health and disease. For example, honey has been demonstrated to suppress immune responses against different allergens in mice. This immunosuppressive activity may be helpful in some clinical conditions.[161]

Dental health

Little is known about the effect of honey on oral health. Honey contains only small amounts of sucrose, the primary dietary sugar that causes plaque to adhere to teeth. Honey also contains phytochemicals, which may have antimicrobial activity against oral pathogens. Therefore, honey may have a more positive role in oral health than one would think likely, considering its high concentration of fermentable sugars.

The wound healing and antimicrobial properties of honey may be of value in the treatment of tooth extraction, oral surgery and infections as well as periodontitis. One small clinical trial in patients after surgical removal of impacted third molars showed that using honey in the socket resulted in less pain, postoperative complications and swelling. Anecdotal reports and single case reports of honey successfully being used as a treatment for mouth ulcers, infection and erosion of the gingiva and maxilla after bone grafting, and stomatis during radiotherapy indicate that honey may have a role as a therapeutic agent in oral disease.[162]

To date, studies on the cariogenicity of honey have yielded contradictory results. However, many of these studies were done without regard for choosing a honey with known antimicrobial activity. A recent study using honey with standardized antimicrobial activity measured the minimum inhibitory concentration needed for species of bacteria involved in the development of dental caries. Results showed the inhibition of growth and acid production of *Streptococcus mitis*, *Streptococcus sobrinus* and *Lactobacillus caseii* with concentrations of honey at 7 percent, 7.5-8.5 percent and 8-12 percent, respectively, and no dextran production with 10 percent honey solutions. The addition of 10 percent honey to 10 percent sucrose also resulted in a 75-89 percent reduction in dextran production.[162]

A study from Israel examined the antibacterial activity of wildflower honey in twelve normal volunteers and twelve neck and head irradiated cancer patients. Results showed that the total bacteria count in saliva was not different before and after honey consumption in either group but *Streptococcus mutans* was significantly lower in the cancer group after honey consumption. For individuals susceptible to caries due to radiation-induced xerostomia, honey may be another anticariogenic agent.[163]

The acidity of honey has the potential to erode dental enamel if held in the mouth for prolonged periods of time. However, a component in honey, believed to be an organic phosphate ester, protects against demineralization during short time exposures, such as would occur with honey candy. With prolonged exposures, the protective agent is degraded by saliva and some decalcification was observed in a study where subjects held a teaspoon of honey in their mouths for 5 minutes. In cases where honey might be used as a therapeutic agent in direct contact with teeth, degradation of the protective agent by saliva is unlikely to occur.[162]

Based on the hypothesis "that honey is no more cariogenic than sugar and that honey contains healthy antioxidants and other phytochemicals that benefit oral health by the suppression of oral pathogens,"

Table 11 - Health and Therapeutic Attributes of Honey

Attribute	Key Properties	Value in Health & Disease
Antimicrobial activity	Low water activity High osmostic pressure Hydrogen peroxide production High acidity Non-peroxidal components	• Management of infections, such as gastritis, candidosis, tinea, wounds and ophthalmologic disorders • Management of food pathogens and spoilage microorganisms • Potential anti-cariogenicity via suppression of oral pathogens
Promotion of wound healing	Antimicrobial activity Stimulation of immune system High viscosity and osmolarity Altered metabolism of glucose and amino acids by infecting bacteria and new tissue Antioxidant activity	• Wound dressing for infected ulcers, surgical wounds, pressure sores and burns
Antioxidant activity	Presence of phenolic compounds, ascorbic acid, enzymes (glucose oxidase, catalase and peroxidase)	• Food preservation • Potential protection against cellular damage from free radicals and ROS
Energy source	Concentrated source of fructose, glucose and other di-, tri- and oligosaccharides	• Athletic performance • Can be used as part of a diabetic meal plan
Prebiotic	Presence of a variety of oligosaccharides that can promote the growth and activity of bifidobacteria	• Incorporation in fermented milk products with bifidobacteria to improve gastrointestinal health

researchers in the College of Dentistry at The University of Illinois at Chicago are conducting a series of studies to assess the potential of honey as a functional food for oral health. The program is focusing on four areas of study—the effects of honey on the growth and cariogenic properties of plaque bacteria, upon the formation and acidity of human dental plaque, on caries formation and the use of honey for the treatment of aphthous ulcers (canker sores).[164]

Summary

The value of honey is recognized by medical authorities the world over. In Australia, it has been approved as a "Therapeutic Good" to be used as:

- Antiseptic dressing to promote healing of wounds, burns and skin ulcers
- Topical antibacterial agent for the treatment of acne and other skin infections
- Topical antibacterial agent for the treatment and prevention of diaper-rash
- Topical antibacterial and moisturizing agent for the treatment of atopic eczema
- Topical antifungal agent for the treatment of tineas
- Antiseptic salve for conjunctivitis and blepharitis
- Antibacterial agent and rehydrating agent for the treatment of gastroenteritis
- Antibacterial agent and healing-promoting agent for the treatment of dyspepsia and peptic ulcers[165]

Natural healing resources for consumers cite the therapeutic qualities of honey for wound healing and treating gastrointestinal disorders, such as ulcers and diarrhea, as well as being a good source of energy,[166,167] spiking consumer interest in using honey for more than a sweetener. The history and science of honey confirm that it has a role in health promotion and disease treatment. Table 11 summarizes the health and therapeutic attributes of honey. Medical professionals and consumers need to be aware of the variation in the composition and properties of honey from different floral sources and choose accordingly.

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References

1 Report on consumer uses and attitudes towards honey. 1997. Prepared for the National Honey Board. Associated Marketing, Chicago, IL.

2 Jones, R. 2001. Honey and healing through the ages. In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.

3 Beck, D.F., and Smedley, D. 1997. "Honey and Your Health: A Nutrimental, Medicinal and Historical Commentary." (Originally published in 1938) Health Resources, Inc., Silver Springs, MD.

4 Mcintosh, E.N. 1995. "American Food Habits in Historical Perspective." Praeger Publishers, Westport, CT.

5 Molan, P.C. 2001. Why honey is effective as a medicine. 1. Its use in modern medicine. In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.

6 Zumla, A. and Lulat A. 1989. Honey—a remedy rediscovered. J. R. Soc. Med. 83: 384-385.

7 Molan, P.C. 2002. Selection of honey as a wound dressing. Waikato Honey Research Unit, University of Waikato, http://honey.bio.waikato.ac.nz/selection.shtml

8 American Pharmaceutical Association. 1916; 1926; 1935. The National Formulary IV.

9 Newman, T.G. 1983. Honey Almanac. Newman, Chicago, IL.

10 Kelly, E.C. 1940-1941. Medical Classics. Williams and Wilkins Company, Baltimore, MD, V 1-5: 10.

11 Molan, P.C. 1992. The antibacterial activity of honey. 1. The nature of antibacterial activity. Bee World 73: 5-28.

12 Bergman, A., Yanai, J., Weiss, J., Bell, D. and Menachem, P.D. 1983. Acceleration of wound healing by topical application of honey, an animal model. Am. J. Surg. 145: 374-376.

13 White, J.W., Subers, M.H. and Schepartz, A.I. 1963. The identification of inhibine the antibacterial factor in honey, as hydrogen peroxide and its origin in a honey glucose-oxidase system. Biochem. Biopysi. Acta 73: 57-79.

14 Gundell, M. and Blattner, V. 1934. Über die wirkung des honigs auf bakerien und infizierte wunden. Arcj. Hyg/ 112: 319-332.

15 Zaiss. 1934. Der honig in ausslicher anwendung. Munch. Med. Wschr. 11: 1891.

16 Temnov, V.A. 1944. Bactericidal properties of honey and utilization of honey and other beekeeping products for healing of wounds. Bee World 25(11): 86-87.

17 Gubin, A.F. 1945. The beekeeping institute during the war: honey in medicine. Pchelovodstvo (1): 25-29.

18 Bulman, M.W. 1955. Honey as a surgical dressing. Midd. Hosp. J. 55(6): 188-189.

19 Blomfield, R. 1993. Honey for decubitus ulcers. JAMA 224(5): 905.

20 Armon, P.J. 1980. Honey: a cheap antibiotic. Trop. Doct. 10: 91.

21 Efem, S.E.E. 1988. Clinical observation on the wound healing properties of honey. Br. J. Surg. 75: 679-681.

22 McInerney, R.J.F. 1990. Honey—a remedy rediscovered. J. R. Soc. Med. 83(2): 127.

23 Grange, J.M. 1990. Reply: honey and propolis as possible promoters of the healing of ulcers in leprosy. Lepr. Rev. 61(2): 195.

24 Somerfield, S.D. 1991. Honey and healing. J. R. Soc. Med. 84(3): 179.

25 Subrahmanyam, M. 1991. Topical application of honey in treatment of burns. Br. J. Surg. 78: 497-498.

26 Subrahmanyam, M. 1993. Honey impregnated gauze versus polyurethane film (OpSite®) in the treatment of burns—a prospective randomised study. Br. J. Plast. Surg. 46: 322-323.

27 Subrahmanyam, M. 1993. Storage of skin grafts in honey. Lancet 341: 63-64.
28 Subrahmanyam, M. 1994. Honey impregnated gauze versus amniotic membrane in treatment of burns. Burns 24(4): 331-333.
29 Subrahmanyam, M. 1997. A prospective randomised clinical and histologicial study of superficial burn wound healing with honey and silver sulfadiazine. Burns 24: 157-161.
30 Subrahmanyam, M. 1996. Honey dressing versus boiled potato peel in the treatment of burns: a prospective randomized study. Burns 22(6): 491-493.
31 Bourne, I.H.J. 1991. Honey and the healing of leg ulcers. J. R. Soc. Med. 84: 11.
32 Efem, S.E.E., Udoh, K.T. and Iwara, C.I. 1992. The antimicrobial spectrum of honey and its clinical significance. Infection 20(4): 228-229.
33 Jones, C. 1992. Bad language. The Veterinary Record 130(9): 192.
34 Phuapradit, W. and Saropala, N. 1992. Topical application of honey in treatment of abdominal wound disruption. J.Obstet.Gynaecol. 32(4): 381-384.
35 Greenwood, D. 1993. Honey for superficial wounds and ulcers. Lancet 341(8837): 90-91.
36 Adesunkanmi, K. and Oyelami, O.A. 1994. The pattern and outcome of burn injuries at Wesley Guild Hospital, Ilesha, Nigeria: a review of 156 cases. J. Trop. Med. Hyg. 97: 108-112.
37 Hejase, M.J., Simonin J.E., Bihrle, R. and Coogan, C.L. 1996. Genital Fournier's Gangrene: Experience with 38 Patients. Adult Urology. 47(5): 734-739.
38 Molan, P.C. 1996. Honey for treatment of infections. Bee Informed 3(2): 6-9.
39 Munstedt, K. and Lang, U. 1997. Honey's wound healing properties. Am. Bee J. 137(4): 296-297.
40 Ndayisaba, G., Bazira, L. and Habonimana, E. 1992. Treatment of wounds with honey. 40 cases. Presse-Med. 21(32): 1516-1518. (Abstract only - French.)
41 Ndayisaba, G., Bazira, L., Habonimana, E. and Muteqanya, D. 1993. Clinical and bacteriological outcome of wounds treated with honey. Review of Chiropractic Orthopedic Reparatrice Appar Mot. 79(2): 111-113.
42 Radwan, S.S., El-Essaway, A.A. and Sarhan, M.M. 1984. Experimental evidence for the occurrence in honey of specific substances active against microorganisms. Zid. Mikrobiol. 139: 249-255.
43 Chirife, J., Scarmato, G. and Herszage, L. 1982. Scientific basis for the use of granulated sugar in treatment of infected wounds. The Lancet March 6, 1(8271): 560-561.
44 Ladas, S.D., Haritos, D.N. and Raptis, S.A. 1995. Honey may have a laxative effect on normal subjects because of incomplete fructose absorption. Am. J. Clin. Nutr. 62: 1212-1215.
45 Ladas, S.D. and Rapitis, S.A. 1999. Honey, fructose absorption and the laxative effect. Nutrition 15(7-8): 591-592.
46 Crane, E. 1976. "Honey: A Comprehensive Survey," Corrected edition. International Bee Research Association/Heinemann, London.
47 White J.W., Reithof, M.L. and Kushnir, I. 1961. Composition of honey. VI. The effect of storage on carbohydrates, acidity and diatase content. J. Food Sci. 26: 63-71.
48 Baumgarten, F. and Mockesel, I. 1956. Ube die papierchromatographische Auffindung freier Aminosauren im Bienenhonig. Z. Bienenforsch 3: 181-184.
49 Maslowski, P. and Mostowske, I. 1963. Electrochromatograficzne badania skladu wolnych aminokwasow w niektorcych odmianach miodow. (Electrochromatographic estimation of free amino acids in different honeys.) Pszczel Zesz Nauk 71(1): 1-6.
50 Bergner, K.G. and Koromi, J. 1968. Zum Aminosaurengehalt von Honigen. Z. Bienenforsch 9(5): 182-184.
51 USDA data obtained from Genesis® R&D Nutrition Analysis program Version 7.01 from ESHA Research, Salem, Oregon.
52 Flodhazi, G. 1994. Analysis and quantification of sugars in honey of different botanical origin using high performance liquid chromatography. Acta Alimentaria 23(3): 299-311.
53 Pawlowska, M. and Armstrong, D.W. 1994. Evaluation of enantiomeric purity of selected amino acids in honey. Chirality 6: 270-276.
54 Bogdanov, S. 1989. Determination of pinocembrin in honey using HPLC. J. Apicultural Res. 28(1): 55-57.

55 Berenbaum, M., Robinson, G. and Unnevehr, L. 1995-1996. Antioxidant properties of Illinois honeys. Grant Proposal for National Honey Board. University of Illinois at Urbana-Champaign.

56 Haydek, M.H., Palmer, L.S., Tanquary, M.C. and Vivano, A.E. 1942. Vitamin content of honey. J. Nutrition 23: 581-588.

57 White, J.W. 1978. Honey. Adv. Food Res. 24: 288-374.

58 Rosenblat G., Angonnet, S., Goroshit, A. Tabak, M. and Neeman, I. 1997. Antioxidant properties of honey produced by bees fed with medical plant extracts. In "Proceedings of the International Conference on Bee Products: Properties, Applications and Apitherapy" held in Tel Aviv, Israel, May 26-30, 1996, p. 49-55. Plenum Press, New York.

59 Frankel, S. Robinson, G.E., and Berenbaum, M.R. 1998. Antioxidant capacity and correlated characteristics of 14 unifloral honeys. J. Apicultural Res. 37(1): 27-31.

60 Ensminger, A.H., Ensminger, M.E., Konlande, J.E. and Robson, J.R.K. 1983. "Food and Nutrition Encyclopedia." Pegus Press, Clovis, CA.

61 Babacan, S., Pivarnik, L.F. and Rand, A.G. 2002. Honey amylase activity and food starch degradation. J. Food Sci. 67(5): 1625-1630.

62 White, J.W., Subers, M.H. and Schepartz, A.I. 1963. The identification of inhibine. Am. Bee J. 102(11): 430-431.

63 Fournier, P. and Dupuis, Y. 1975. Modulation of intestinal absorption of calcium. J. Physiol. Paris 70: 479-491.

64 Stinson, E.E., Subers, M.N., Petty, J. and White, J.W. 1963. The composition of honey. V. Separation and identification of the organic acids. Arch. Biochem. Biophys 6-12.

65 Goldscmidt, S. and Burket, H. 1955. Die Hydrolyse des cholingischen Honigwirkstoffes und anderer Cholinester mittels Cholinesterasen und deren Hemmung im Honig. Hoppe-Seyler's Z. Physiol. Chem 301: 78-89.

66 Snowden J.A. and Cliver, D.O. 1996. Mircoorganisms in honey. Int. J. Food Microbiol. 31: 1-26.

67 Molan, P.C. 1992. The antibacterial activity of honey. 1. The nature of antibacterial activity. Bee World 73: 5-28.

68 Molan, P.C. 1992. The antibacterial activity of honey. 2. Variation in the potency of the antibacterial activity. Bee World 73: 59-76.

69 Molan, P.C. 2002. Honey as an antimicrobial agent. Waikato Honey Research Unit, University of Waikato, http://honey.bio.waikato.ac.nz/honey_intro.shmtl, http://honey.bio.waikato.ac.nz/honey_1.shmtl, http://honey.bio.waikato.ac.nz/honey_2.shmtl, http://honey.bio.waikato.ac.nz/honey_ref.shmtl.

70 Allen, K.L., Molan, P.C. and Reid, G.M. 1991. A survey of the antibacterial activity of some New Zealand honeys. J. Pharm. Parmacol. 43: 817-822.

71 Allen, K.L., Molan, P.C. and Reid, G.M. 1991. The variability of the antibacterial activity of honey. Apiacta 26: 114-21.

72 Morse, R.A. and Flottum, K. 1990. "The ABC & XYZ of Bee Culture," 40th ed. The A.I. Root Co., Medina, OH.

73 Molan, P.C. and Russell, K.M. 1988. Non-peroxide antibacterial activity of some New Zealand honeys. J. Apicultural Res. 27(4): 252-256.

74 Willix, D.J., Molan, P.C. and Harfoot, C.G. 1992. A comparison of the sensitivity of wound-infecting species to the antibacterial activity of manuka honey and other honey. J. Appl. Bacteriol. 73: 388-394.

75 Cooper, R.A., Molan, P.C. and Harding, K.G. 1999. Antibacterial activity of honey against strains of *Staphylococcus aureus* from infected wounds. J. R. Soc. Med. 92: 283-285.

76 Zaghloul, A.A., El-Shattawy, H.H., Kassem, A.A., Ibrahim, E.A., Reddy, I.K. and Khan, M.A. 2001. Honey, a prospective antibiotic: extraction, formulation, and stability. Pharmazie 56(8): 643-647.

77 James, O.B. O'L., Segree, W. and Ventura, A.K. 1972. Some antibacterial properties of Jamaican honey. W. I. Med. J. XXI(7): 7-17.

78 Tomlinson, J.T. and Williams, S.C. 1985. Antibiotic properties of honey produced by the domestic honey bee *Apis mellifera* (Hymenoptera: Aphidae) Pan Pacific Entomologist 6(14): 346-347.

79 Molan, P.C., Smith I.M. and Reid, G.M. 1988. A comparison of the antibacterial activities of some New Zealand honeys. J. Agric. Res. 27(4): 252-256.

80 Farouk, A., Hassen, T., Kashif, H., Khalid, S.A., Mutawali, I. and Wadi, M. 1988. Studies on Sudanese bee honey: laboratory and clinical evaluation. Int. J. Crude Drug Res. 26(3): 161-168.

81 Basson, N.L. and Grobbler, S.R. 1997. The effect of honey on human tooth enamel and oral bacteria. In "Proceedings of the International Conference on Bee Products: Properties, Applications and Apitherapy" held in Tel Aviv, Israel, May 26-30, 1996, p. 65-71. Plenum Press, New York.
82 Toth, G., Lemberkovics, E. and Kutasi-Szabo, J. 1987. The volatile components of some Hungarian honeys and their antimicrobial effects. Am. Bee J. 127(7): 496-497.
83 Wootton, M., Edwards, R.A. and Rowse, A. 1978. Antibacterial properties of some Australian honeys. Food Technology in Australia, May 175-176.
84 Obaseiki-Ebor, E.E., Afonya, T.C.A. and Onyekweli, A.O. 1983. Preliminary report on the antimicrobial activity of honey distillate. J.Pharm. Pharmacol. 35: 748-749.
85 Molan, P.C. 2002. What's special about active manuka honey. Waikato Honey Research Unit, University of Waikato, http://honey.bio.waikato.ac.nz/special.shtml
86 Cooper, R.A., Wigley, P. and Burton, N.F. 2000. Susceptibility of multiresistant strains of *Burkholderia cepacia* to honey. Lett. Appl. Microbiolog. 31(1): 20-4.
87 Molan, P.C. 2001. Why honey is effective as a medicine. 2. The scientific explanation of its effects. In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.
88 Sato, T. and Miyata, G. 2000. The nutraceutical benefit, part III: honey. Nutrition 16: 468-469.
89 Obaseiki-Ebor, E.E. and Afonya, T.C.A. 1984. *In vitro* evaluation of the anticandidiasis activity of honey distillate (HY-1) compared to that of some antimycotic agents. J.Pharm. Pharmacol. 36: 283-284.
90 Jay, J.M. 1992. "Modern Food Microbiology." Chapman & Hall, New York.
91 Nakano, H., Yoshikuni, Y., Hashimoto, H. and Sakaguchi, G. 1992. Detection of *Clostridium botulinum* in natural sweetening. Int. J. Food Microbiol. 43: 183-195.
92 Nakano, H. and Sakaguchi, G. 1991. An unusually heavy contamination of honey product with *Clostridum botulinum* Type F and *Bacillus alvei*. FEMS Mircrobiology Letters 79: 271-178.
93 Midura, T.F., Snowden, S. Wood, R.M. and Arnon, S.S. 1979. Isolation of *Clostridium botulinum* from honey. J. Clin.Microbiol. 9(2): 282-283.
94 Sugiyama, H., Mills, D.C. and Kuo, L.J.C. 1978. Number of *Clostridium botulinum* spores in honey. J. Food Prot. 41(11): 848-850.
95 Taormina, L.R., Niemara, B.A. and Beuchat, L.R. 2001. Inhibitory activity of honey against foodborne pathogens as influenced by the presence of hydrogen peroxide and level of antioxidant power. Int. J. Food Microbiol. 69: 217-225.
96 Mundo, M.A., Padilla-Zakour, O.I. and Worobo, R.W. 2002. Antimicrobial activity of honey against food pathogens and food spoilage microorganisms. Presented at Ann. Mtg., Inst. of Food Technologists, Anaheim, CA, June 15-19.
97 Antony, S., Han, I.Y., Rieck, J.R. and Dawson, P.L. 2000. Effect of dry honey on the oxidation in turkey breast meat. Poultry Sci. 79:1846-1850.
98 Huang, Y-W., Chu, H-Y., Li, Y. and Gates, K.W. 1999. Development of battered and marinated catfish products using honey as an ingredient. Presented at Ann. Mtg., Inst. of Food Technologists, Chicago, IL, July 24-28.
99 Miraglio, A.M. 1999. Wholesome and practical. The National Provisioner December: 38,40,41,42.
100 Molan, P.C. 2002. The evidence for honey promoting wound healing. University Of Waikato—Honey Research Unit, http://honey.bio.waikato.ac.nz/evidence.shtml.
101 McCarthy, J. 1995. The antibacterial effects of honey: medical fact or fiction. Am. Bee J. 5: 341-342.
102 Olin, B.R. 1995. Honey. The Lawrence Review of Natural Products 1995: 1-2.
103 Armstrong, S. and Otis, G.W. 1995. The antibacterial properties of honey. Bee Culture 9: 500-02.
104 Subrahmanyam, M. 1991. Topical application of honey in treatment of burns. Br. J. Surg. 78: 497-498.
105 Cooper, R. 2001. How does honey heal wounds? In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.
106 Jones, K.P. 2001. The role of honey in wound healing and repair. In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.
107 Molan, P.C. and Allen, K.L. 1996. The effect of gamma-irradiation on the antibacterial activity of honey. J. Pharm. Pharmacol. 48: 1206-1209.

108 Molan, P.C. 2002. Re-introducing honey in the management of wound and ulcers—theory and practice. Ostomy Wound Manage. 48(11). In press.

109 Tissue Viability Society. 2002. Product News. J. Tissue Viability 12(1): 30.

110 Molan, P.C. 2002. Where to get honey for medical use. Waikato Honey Research Unit, University of Waikato, http://honey.bio.waikato.ac.nz/where.shtml.

111 Molan, P.C. 2001. Potential of honey in the treatment of wounds and burns. Am. J. Clin. Dermatol. 2(1): 13-19.

112 Allen, K.L., Hutchinson, G. and Molan, P.C. 2000. The potential for using honey to treat wounds infected with MRSA and VRE. Presented at the First World Healing Congress, Melbourne, Australia, Sept. 10-13.

113 Cooper, R.A., Halas, E., Davies, R. Molan, P.C. and Harding, K.C. 2000. The inhibition of Gram-positive cocci of clinical importance by honey. Presented at the First World Healing Congress, Melbourne, Australia, Sept. 10-13.

114 Dunford, C., Cooper, R.A. and Molan, P.C. 2000. Case Report: Using honey as a dressing for infected skin lesions. Nursing Times 96(14): 7-9.

115 Molan, P.C. 1999. The role of honey in the management of wounds. J. Wound Care 8: 415-418.

116 Postmes, T.J., Bosch, M.M.C., Dutrieuex, R., van Baare, J. and Hoekstra, M.J. 1997. Speeding up the healing of burns with honey: An experimental study with histological assessment of wound biopsies. In "Proceedings of the International Conference on Bee Products: Properties, Applications and Apitherapy" held in Tel Aviv, Israel, May 26-30,1996, p. 57-63. Plenum Press, New York.

117 Subrahmanyam, M. 1999. Early tangential excision and skin grafting of moderate burns is superior to honey dressing: a prospective randomised trial. Burns 25: 729-731.

118 Cowley, G. and Elliott, D. 1990. A simpler way to save lives. Newsweek May 7: 68.

119 Postmes, T. 2001. The treatment of burns and other wounds with honey. In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.

120 Efem, S.E.E. 1991. Recent advances in the management of Fournier's gangrene: preliminary observations. Surgery 113(2): 200-204.

121 Hajase, M.J., Simonin, J.E., Bihrle, R. and Coogan, C.L. 1996. Genital Fournier's gangrene: experience with 38 patients. Adult Urology 47(5): 734-739.

122 Gupta, S.K., Singh, H., Varshney, A.C. and Prakash, P. 1992. Therapeutic efficacy of honey in infected wounds in buffaloes. Indian J. of Animal Sci. 62(2): 521-523.

123 Kumar, A., Sharma,V., Gupta, K., Singh, H., Prakash, P. and Singh, S.P. 1992. Efficacy of some indigenous drugs in tissue repair in buffaloes. Indian Veterinary J. 70(1): 42-44.

124 Cavanagh, D., Beazley, J. and Ostapowicz, R. 1970. Radical operation for carcinoma of the vulva, a new approach to wound healing. J. Obstet. Gynaecol. British Commonwealth 77: 1037-1040.

125 Kandil, A., Elbanby, M., Abd-Elwahed, K., Sehly, G.A. and Ezzet, N. 1987. Healing effect of true floral and false nonfloral honey on medical wounds. J. Drug Res. Egypt 17(1-2): 71-76.

126 Ankra-Badu, G.A. 1992. Sickle cell leg ulcers in Ghana. East Afr. Med. J. 69(7): 366-369.

127 Farouk, A., Hassan, T., Kashif, H., Khalid, S.A., Mutawali, I. and Wadi, M. 1988. Studies on Sudanese Bee Honey: Laboratory and Clinical Evaluation. Int. J. Crude Drug Research 26(3): 161-168

128 Weheida, S.M., Nagubib, H.H., El-Banna, H.M. and Marzouk, S. 1991. Comparing the effects of two dressing techniques on healing of low grade pressure ulcers. J. Medical Research Institute 12(2): 259-278.

129 Isenberg, J.S., Ozuner, G. and Restifo, R.J. 1995. The natural history of pressure sores in a community hospital environment. Ann. Plast. Surg. 35(4): 361-365.

130 Wood, B., Rademacher, M. and Molan, P. 1997. Manuka honey: A low cost leg ulcer dressing. N. Z. Med. J. 110(1040): 107

131 Brouns, F., Saris, W.H.M., Beckers, E., Adlecreutz, van der Wusse, G.J., Keizer, H.A., Kuipers, H., Menheere, P., Wagenmakers, A.J.M. and ten Hoor, F. 1989. Metabolic changes induced by sustained exhaustive cycling and diet manipulation. Int. J. Sports Med. 10: S49-S62.

132 Kreider, R.B., Rasmussen, C., Lundberg, J., Cowan, P., Greenwood, M., Earnest, C.P. and Almada, A.L. 2000. Effects of ingesting carbohydrate gels on glucose, insulin and perception of hypoglycemia. FASEB J. 14: A490.
133 Rasmussen, C., Kreider, R.B., Lundberg, J., Cowan, P., Greenwood, M., Earnest, C.P. and Almada, A.L. 2000. Analysis of glycemic index and insulin response index of various carbohydrate gels. FASEB J. 14: A489.
134 Kreider, R.B., Lundberg, J., Rasmussen, C., Cowan, P., Greenwood, M., Earnest, C.P. and Almada, A.L. 2000. Effects of ingesting protein with various forms of carbohydrate following resistance-exercise on substrate availabiity and markers of catabolism. J. Strength. Cond. Res. 14: 366.
135 Earnest, C.P., Kreider, R.B., Lundberg, J., Rasmussen, C., Cowan, P., Greenwood, M. and Almada, A.L. 2000. Effects of pre-exercise carbohydrate feedings on glucose and insulin responses during and following resistance exercise. J. Strength Cond. Res. 14: 361.
136 Lancaster, S., Kreider, R.B., Rasmussen, C., Kerkick, C., Greenwood, M., Almada, A. and Earnest, C.P. 2001. Effects of honey supplementation on glucose, insulin and endurance cycling performance. FASEB J. 15: LB315.
137 American Diabetes Association. 2001. Position statement: nutrition recommendations and principles for people with diabetes mellitus. Diabetes Care 24 (Supplement 1) Clinical Practice Recommendations.
138 Foster-Powell, K. and Brand Miller, J. 1995. International tables of glycemic index. Am. J. Clin. Nutr. 62: 871S-893S.
139 Shambaugh, P., Worthington, V. and Herbert, J.H. 1990. Differential effects of honey, sucrose, and fructose on blood sugar levels. J. Manipulative and Physiol. Ther. 13(6): 322-325.
140 Samanta, A., Burden, A.C., and Jones, G.R. 1985. Plasma glucose responses to glucose, sucrose, and honey in patients with diabetes mellitus: an analysis of glycaemic and peak incremental indices. Diabet. Med. 2: 371-373.
141 Katsilambros, N.L., Philippides, P., Touliatou, A., Georgeakopoulos, K., Kofotzouli, L., Frangaki, D., Siskoudis, P., Marangos, M. and Sfikakis, P. 1988. Metabolic effects of honey (alone or combined with other foods) in Type II diabetes. Acta. Diabetol. 25: 197-203.
142 Bornet, F., Haardt, M.J., Costagliola, D., Blayo, A. and Slama, G. 1985. Sucrose or honey at breakfast had no additional acute hyperlycemic effect over an isoglucidic amount of bread in type 2 diabetic patients. Diabetologia 28(4): 213-217.
143 Cross, C.E., Halliwell B., Forish, E.T., Pryor, W.A., Ames, B.N. and Saul, R.L.D. 1987. Oxygen radical and human disease. Ann. of Intern. Med. 107: 526-545.
144 Hensley, K. and Floyd, R.A. 2002. Reactive oxygen species and protein oxidation in aging: a look back, a look ahead. Arch Biochem Biophys 397(2): 377-383.
145 Kinsella, J. E., Frankel, E., German, B. and Kanner, J. 1993. Possible mechanisms for the protective role of antioxidants in wine and plant foods. Food Technol. 47(4): 85-89.
146 Gheldof, N., Wang, X. and Engeseth, N.J. 2001. Characterization of the antioxidants in honeys from different floral sources. Presented at Ann. Mtg., Inst. of Food Technologists, New Orleans, LA, June 23-27.
147 Gheldof, N. and Engeseth, N.J. 2002. Antioxidant capacity of honeys from various floral sources based on the determination of oxygen radical absorbance capacity and inhibition of *in vitro* lipoprotein oxidation in human serum samples. J. Agric. Food Chem. 50(10): 3050-3055.
148 Gheldof, N., Wang, X. and Engeseth, N.J. 2002. Identification and quantification of antioxidant components of honeys from various floral sources. In press.
149 Cao, G., Sofic, E. and Prior, R.L. 1996. Antioxidant capacity of tea and common vegetables. J. Agric. Food Chem. 44: 3426-3431.
150 Wang, H., Cao, G. and Prior, R.L. 1996. Total antioxidant capacity of fruits. J. Agric. Food Chem. 44: 701-705.
151 Wang, X.H. and Engeseth, N.J. 2002. Antimutagenic effect of honeys against Trp-p-1. Presented at Ann. Mtg., Inst. of Food Technologists, Anaheim, CA, June 15-19.
152 Geldolf, N. and Engeseth, N. 2002. *In vitro* and *ex vivo* antioxidant effect of honey. Presented at Ann. Mtg., Inst. of Food Technologists, Anaheim, CA, June 15-19.
153 Schramm, D.D. and Keen, C.L. 2002. Buckwheat honey, a natural sweetener, conveys antioxidant protection to healthy human subjects. Presented at Ann. Mtg., Inst. of Food Technologists, Anaheim, CA, June 15-19.
154 Tannock, G.W. (editor). 1999. “Probiotics: A Critical Review.” Horizon Scientific Press, Wymondham, UK.

155 Chick, H., Shin, H.S. and Ustunol, Z. 2001. Growth and acid production by lactic acid bacteria and bifidobacteria in skim milk containing honey. J. Food Sci. 66: 478-481.

156 Shin, H.S., Lee, J.H., Pestka, J.J. and Ustunol, Z. 2000. Growth, activity and viability of commercial *Bifidobacterium* spp in skim milk containing oligosaccharides and inulin. J. Food Sci. 65: 884-887.

157 The National Honey Board. The effect of honey on the growth of bifidobacteria. Longmont, CO.

158 Kajiwara, S., Hasand, G. and Ustunol, Z. 2002. Effect of honey on growth and acid production by intestinal *Bifidobacterium* spp: An *in vitro* comparison to commercial oligosaccharides and inulin. J. Food Prot. 65:214-218.

159 Ustunol, Z. and Gandhi, H. 2002. Growth and viability of commercial *Bifidobacterium* spp in honey-sweetened skim milk. J. Food Prot. 64(11): 1775-1779.

160 Ustunol, Z. 2001. Oligosaccharide composition and content of honey from different floral sources and their influence on growth of intestinal microflora. Grant proposal for the National Honey Board. Michigan State University.

161 Duddukuri, G.R., Kumar, P.S., Kumar, V.B. and Athota, R.R. 1997. Immunosuppressive effect of honey on the induction of allergen-specific humoral antibody response in mice. Int. Arch. Allergy Immunol. 114: 385-388.

162 Molan, P.C. 2001. The potential of honey to promote oral wellness. General Dentistry 49(6): 584-589.

163 Sela, M., Maroz, D. and Gedalia, I. 2000. *Streptococcus mutans* in saliva of normal subjects and neck and head irradiated cancer subjects after consumption of honey. J. Oral Rehabil. 27(3): 269-270.

164 Wu, C.D., Ashrafi, S.S., Lingstrom, P.K. and Wefel, J.S. 2001. Honey and oral/dental health. Grant proposal for the National Honey Board. University of Illinois at Chicago.

165 Australia Ministry for Health and Aged Care. 1999. Therapeutic Goods (listing) Notice 1999 (No.1) Therapeutic Goods Act 1989.

166 Anonymous. 1999. Nature's Remedies: Honey. "The Complete Guide to Natural Healing." International Masters Publishers AB Inc. Pittsburgh, PA.

167 Yeager, S. 1998. Honey: the best from the bees. In "The Doctor's Book of Food Remedies." Rodale Press. Emmaus, PA.

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