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Medical uses of honey.

Amy E. Jeffrey, Carlos M. Echazarreta.

Facultad de Medicina Veterinaria y Zootecnia, Universidad Autónoma de Yucatán, Mérida, Yucatán, México.

SUMMARY.

This article reviews reports on the use of honey in the treatment of human disorders which are supported by clinical tests and published in medical journals.

Firstly, the composition of honey is described, followed by a revision of its effect on the growth of several strains of pathogenic bacteria in laboratory tests. Finally, the influence of honey on gastroenteritis, gastric ulcers, wounds and other disorders is reviewed.

Key words: honey; natural products, gastroenteritis, gastric ulcer, wound healing, antibacterial activity.

RESUMEN.

USOS MEDICOS DE LA MIEL.

Este artículo revisa los reportes sobre el uso de la miel en el tratamiento de padecimientos en humanos, incluyendo sólo aquellos que están apoyados por pruebas clínicas y publicados en revistas médicas.

Se describe en primer lugar la composición de la miel, seguida por una revisión de sus efectos sobre el crecimiento de varias cepas de bacterias patógenas en pruebas de laboratorio. Por último, se revisa la influencia de la miel en la gastroenteritis, ulceras gastricas, heridas y otros problemas de salud.

Palabras clave: Miel, productos naturales, gastroenteritis, úlcera gástrica, úlcera cutánea, antibacteriano.

Introduction.

Since ancient times honey has been used for its medicinal properties in many cultures. Currently, information on the use of honey for the treatment of many human diseases can be found in general magazines, beekeeping journals and natural products leaflets, an suggesting a wide variety of unfounded properties. In contrast, medical reports supported by tests are few and far between.

In this review, we describe the constituents of honey and examine the information available that is supported by laboratory or clinical studies in which honey has shown positive results for the control of pathogens or the improvement of human health.

Correspondence: Carlos M. Echazarreta, Ap. Post 4-116, Mérida 97100, Yucatán, México. Tel (99) 234009, Fax (99) 234009.

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Composition of honey.

The precise composition of honey varies according to the plant species on which the bee forages, but the main constituents are the same in all honeys. The average composition of honey is given in table 1.

Table 1
Average composition of honey

Component	Average (%)
Moisture	17.2
Fructose	38.19
Glucose	31.28
Sucrose	1.31
Disaccharides, calculated as maltose	7.31
Higher sugars	1.5
Free acid as gluconic	0.43
Lactone as Gluconolactone	0.14
Total acid as gluconic	0.57
Ash	0.169
Nitrogen	0.041

Data was collected from 490 samples of US honey (1).

More than 95% of the solids in honey are carbohydrate, and sensitive analytical and separation techniques have revealed honey to be a highly complex mixture of sugars, most of which are in the immediately digestible form in the small intestine. In addition to those named in Table 1, the following have been identified as constituents of honey: isomaltose, nigerose, turanose, maltulose (2); kojibiose (3); alpha beta-trehalose, gentiobiose, laminaribiose (4); maltotriose, 1-kestose, panose, isomaltosyl glucose, erlose, isomaltosyltriose, theanderose, centose, isopanose, isomaltosyltetraose and isomaltosylpentaose (5). Many of these sugars are not found in nectar but are formed during the ripening and storage effects of bee enzymes and the acids of honey.

The predominant acid found in honey is gluconic acid. Its presence in all honey originates largely from the activity of glucose oxidase which the bees add at ripening (6) and to a lesser extent from the bacterial action which occurs (7). The pH of honey ranges from 3.2 to 4.5.

The mineral and vitamin content of honey is very low, 0.02 % of its weight and given the low consumption of honey they have no significant nutritional benefit to man.

Honey also contains a number of amino acids, proline, phenyalanine and aspartic acid being those with a concentration of greater than 200 ppm (8).

The main enzymes found in honey which are derived from the hypopharyngeal glands of worker honeybees, are invertase (which inverts sucrose to glucose and fructose); glucose oxidase (which oxidises glucose to gluconic acid and hydrogen peroxide in the presence of water); and amylase (diastase), which breakdown starch.

The enzymes in honey which originate from plants are catalase (a regulator of glucose oxidase activity); acid phosphatase; and a small proportion of amylase (9-10).

The enzyme glucose oxidase is of considerable interest because its activity causes the production of hydrogen peroxide which not only stablizes the ripening nectar against spoilage but has microbicidal action.

Antibacterial activity of honey.

The reasons for the antibacterial activity of honey are controversial. A laboratory demonstration of its antibacterial activity was first carry out by Dold *et al.* (11) who gave the name 'inhibine' to the substance which inhibited bacteria. Adock (12) first suggested the possibility that hydrogen peroxide was responsible for the antibacterial activity of honey since both the antibacterial activity of honey and hydrogen peroxide were destroyed by light. White and Subers (13) reported that hydrogen peroxidase which is produced by the glucose oxidase of honey could be the inhibitory substance against bacteria. However, it is known that honey itself, as well as bacteria produce a catalase that eliminates hydrogen peroxide. But although catalase is active with high concentrations of hydrogen peroxide, it is of low activity with physiological levels. The amount of catalase necessary to destroy the antibacterial activity was found to be unexpectedly high (6,12). A solution of hydrogen peroxide used as an antiseptic is likely to be far less effective than a "slow release preparation" in the form of honey (14). Hydrogen peroxide rapidly breakdown into water and oxygen and its production and decomposition are continuous. The hydrogen peroxide concentration remains stable under a given

set of conditions of temperature, sugar concentration etc., and is sufficiently high to give good protection against some harmful microorganisms by a biochemical mechanism which disrupts their metabolism. The same system is thought to operate when honey is diluted with water and for this reason, honey has been successfully used as a microbicidal wound dressing. Lavie (15) found an additional group of light-sensitive, heat-stable antibacterial factors in honey which inhibited the growth of *Bacillus subtilis, B. alvei, Escherichia coli, Pseudomona pyocyanes, Salmonella* and *Staphylococcus aureus*. Conversely, microorganisms that survive well in honey are the sugar-tolerant (osmophilic) yeasts, mostly belonging to the genera *Saccharomyces* and *Zygosaccharomyces* (16).

Non-dissociated organic acids also play a role in the antimicrobial activity of honey (17-18) since they are very soluble in cell membranes (19) and induce alterations in the cellular permeability and in oxidative phosphorylation (20). Bogdanov (21) extracted a substance belonging to the group of flavonoids, noted for their antibacterial capacity, from honey. Molan and Russel (22) have reported that the floral source of honey may also be responsible for some of the antibacterial activities of honey.

Most commercial honey is produced by the species, *Apis mellifera*. However some work has been done with other species of bees. An interesting study was carried out by Cortopassi-Laurino and Gelli (23). In their work, a comparison was made between the physico-chemical properties and antibacterial activity of honey produced by Africanized honey bees (*A. mellifera*) and *Melliponinae* (stingless bees) in Brasil. For both types of honey at a concentration of 5-25%, *Bacillus stearothermophilus* was found to be the most susceptible and *E. coli* the least susceptible of the seven bacterial isolates tested (the other five being, *B. subtilis, B. subtilis Caron, Staphylococcus, Klebsiella pneumoniae* and *Ps. aeruginosa*).

Classifying the honey according to the predominant floral source, honey produced by africanized honey bees from predominantly *Mimosa* and *Eucalyptus* had the greatest antibacterial activity. *Melipona subnitida* honey produced from *Mimosa bimucronata* and *Plebia* species honey produced from *Borreria/Mimosa* exhibited the greatest antibacterial activities (23).

Gastroenteritis.

Infections of the intestinal tract are common throughout the world, affecting people of all ages. The infectious diarrhoea exacerbates nutritional deficiencies in various ways, but as in any infection, the calorific demand is increased. Pure honey has bactericidal activity against many enteropathogenic organisms, including those of the *Salmonella* and *Shigella* species, and enteropathogenic *E. coli* (24).

In vitro studies of *Helicobacter pylori* isolates which cause gastritis have been shown to be inhibited by a 20% solution of honey. Even isolates that exhibited a resistance to other antimicrobial agents were susceptible (25).

In a clinical study, the administration of a bland diet and 30 mL of honey three times a day was found to be an effective remedy in 66% of patients and offered relief to a further 17%, while anaemia was corrected in more than 50% of the patients (26).

A clinical study of honey treatment in infantile gastroenteritis was reported by Haffejee and Moosa (27). They found that by replacing the glucose (111 mmol/l) in the standard electrolyte-containing oral rehydration solution recommended by the World Health Organisation/UNICEF (28), as well as the solution of electrolyte composition 48 mmol/l sodium, 28 mmol/l potassium, 76 mmol/l chloride ions, with 50 ml/l honey (29), the mean recovery times of patients (aged 8 days to 11 years) were significantly reduced. Honey was found to shorten the duration of diarrhoea in patients with bacterial gastroenteritis caused by organisms such as *Salmonella, Shigella* and *E. coli*. They recommended that honey was a safe substitute for glucose as long as it provided 111 mmol/l each of glucose and fructose. The high sugar content of honey means that it could be used to promote sodium and water absorption from the bowel.

Gastric ulcers.

Clinical and animal studies have shown that honey reduces the secretion of gastric acid. Additionally, gastric ulcers have been successfully treated by the use of honey as a dietary supplement (30). An 80% recovery rate of 600 gastric ulcer patients treated with oral adminstration of honey has been reported (30). Radiological examination showed that ulcers disappeared in 59% of patients receiving honey.

Animal experiments have shown that theadministration of a honey solution via a tube in

the stomach of rabbits prior to them being administered with 0.5 g ethanol per kg body weight, accelerated alcoholic oxidation. A more recent animal study (31) showed that honey administered subcutaneously or orally before oral administration of ethanol affords protection against gastric damage and reverses changes in pH induced by ethanol.

A controlled clinical trial demonstrated the use of fructose in the treatment of acute alcoholic intoxication. A small but significant increase ocurred in the rate of fall of blood-ethanol levels and it was concluded that fructose may be beneficial in shortening the duration of alcoholic intoxication (32).

Wound healing properties.

Wet dressings or any form of irrigation moisten the tissues and therefore delay healing. Dry dressings adhere to the surface, causing pain and injure the granulating surface every time they are changed. Oily dressings prevent the surface secretions from escaping freely and may cause them to spread onto the neighbouring skin surfaces and cause undesirable reactions or toxic effects. Conversely, honey is an effective treatment of wounds because it is non-irritating, non-toxic, self-sterile, bactericidal, nutritive, easily applied and more comfortable than other dressings (33).

The treatment of wounds with honey has rendered them bacteriologically sterile within 7-10 days of the start of the treatment and promoted healthy granulation of tissue (34). Patients suffering from wound breakdown after operation for carcinoma of the vulva were treated by pouring honey into the wounds twice daily. The wounds became bacteriologically sterile within 3-6 days and *in vitro* studies of bacteria cultured from the wounds showed that undiluted honey not only failed to sustain growth of the bacteria (*Proteus mirabilis, Ps. aeruginosa, E.coli, Streptococcus faecalis, Clostridium perfingens* and *S. aureus*), but actually killed them. The *in vitro* anti-fungal activity of honey has been also tested on *Candida albicans, C. pseudotropicalis, C. stellatoidea* and *C. tropicalis*. They were all found to be susceptible (35).

Generous soaking of wounds and abcess cavities with honey, sometimes using castor oil to facilitate dressing, was found to include the following advantages: first, cross-infection of wounds often encountered with conventional therapy, was prevented because honey forms a mechanical and/or chemical barrier to infectious agents; second, the acceptance of grafts was prompt, in contrast to the inconsistent acceptance of grafts following antibiotic application; and third, a shorter duration of treatment and therefore hospitilization. Honey was also found to be more effective as an antibacterial agent against several *Pseudomonas* and *Staphylococcus* strains than the antibiotic, gentamicin (36).

In a clinical study involving 59 patients with wounds and ulcers (37), most of which had failed to respond to conventional treatments, 15-30 ml fresh honey was applied daliy. The bacteria isolated from 58 of these wounds (*E. coli, S. aureus, P. mirabilis*, mixed coliforms, *Klebsiella* species, and *S. faecalis*) were all susceptible to honey *in vitro*. One other bacteria, *Ps. pyocyanea* did not undergo complete lysis *in vitro* tests but it was completely sterilised *in vivo.* In one case in which the patient had a Buruli ulcer infected with *Mycobacterium ulcerans*, honey treatment was ineffective an *in vitro* tests showed the mycobacteria to be resistant to honey. This may be due to the higher lipid content of its cell wall, preventing dehydration of the bacteria as well as the penetration by inhibine, the thermolabile and photolabile bactericidal substance in honey (38).

Chemical debridement action of honey has been reported to be of greatest advantange in Fourier's gangrene, Cancum oris and decubitus ulcers, as the sloughs of these separated more quickly in these than in other types (39).

Another clinical study (40) comprising of 50 patients with wounds, compared the use of honey as a treatment with the antiseptic Salvon (15% cetrimide, 1.5% chlorohexidine gluconate). Honey cleared 60% of the treated wounds in 6 days whereas Salvon cleared only 36% of wounds within the same period. Bacteria isolated form the wounds were *P. mirabilis, Staphylococcus, coliform bacteria, enterococci, E. coli, Haemophilus, Pseudomonas* and *Klebsiella.*

In a more recent report on honey treatment of wounds, ulcers and skin graft preservation, the importance of sterile, residue-free honey for medical use was pointed out by Postmes *et al.* (41). They advise to use honey derived from specified-pathogen-free hives, which have not been treated with drugs, and are gathered in areas where no pesticides are used. In this work, it was found that the antibacterial activity of their honey samples remained constant over more than a year.

In an extensive review on the antibacterial activity of honey (42), it was suggested than honeys intended for therapeutic use, should be assayed for their antibacterial activity as a form of quality assurance. It is also recommended that honey is protected from light to prevent possible reduction of its antibacterial activity.

Diabetes.

There is a need for sweetners in the diabetic diet to improve overall dietary compliance. Since fructose is absorbed more slowly from the gastrointestinal tract than glucose and is rapidly taken up by the liver, blood sugar levels rise only minimally after fructose ingestion (43-44). Bornet *et al*. (45) demonstrated the sucrose or honey at breakfast have no additional acute hyperglycaemic effect over and isoglucocidic amount of bread in type II diabetic patients. In addition, a clinical study by Katsilambros *et al*. (46), indicated that honey could be a suitable sweetner for the type II diabetic diet since fat-rich foods added to honey result in higher triglyceride and insulin serum concentrations.

Conclusion.

The above information shows that in microbiological and clinical tests, honey offers advantages in controling bacterial growth and in the treatment of certain health problems. The ease of administration for the treatment of wounds, the absence of antibiotic resistance as found with conventional antibiotics, the lack of side effects in alieviating gastric pain and shortening the duration of diarrhoea are all desirable features. Even in modern day society, the medical use of honey still has a place.

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