Apitherapy - A sweet approach to dental diseases - Part I : Honey

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Abstract:

Natural products have been used for several years in folk medicine. One such natural medicine is Apitherapy; which is the medical use of honey, propolis, pollen, royal jelly, bee venom etc. Honey has an effective antibacterial potential to combat oral pathogens and holds promise for the treatment of periodontal diseases, mouth ulcers, and other diseases of the oral cavity. As people are realizing that modern medicine is not the soul remedy for infections today. So, many of us are looking back to the past for the alternative approaches with least possible side effects like apitherapy. This review article throws a light on the evolution of apitherapy and its clinical importance in dentistry.

Keywords: Apitherapy, Honey, Phytotherapy, Plant Origin

Introduction:

APITHERAPY, or “bee therapy” (from the Latin word ‘apis’ which means bee) is the medicinal use of products made by honeybees. This can include the use of honey, propolis, pollen, royal jelly, and bee venom. According to Dr. Stefan Stangaciu, Apitherapy is defined as, ‘the art and science of treatment and holistic healing through the honey bee and her products for the benefit of mankind and all the animal kingdom.[1]’

Therapies involving the honeybee have existed for thousands of years and some may be as old as human medicine itself. In ancient times, honey was considered the food of the gods and the symbol of wealth and happiness. It is a sweet syrupy substance produced by honeybees from the nectar of flowers and used by humans as a sweetener and a spread. The Bible refers to heaven as the "Land of Milk and Honey”.[2]

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Honey was used to treat infected wounds as long ago as 2000 years before bacteria were discovered to be the cause of infection. In 50 AD, Dioscorides described honey as being "good for all rotten and hollow ulcers."[3] More recently, honey has been reported to have an inhibitory effect to around 60 species of bacteria including aerobes and anaerobes, gram-positives and gram-negative microorganisms.[4]

Propolis is resinous material/sap that is collected after it oozes out from tree bark and bud. After bees have collected propolis they mix it with wax flakes and their saliva in the hive. This mixture is what they use to cover the interior of the hive. Though bees use propolis to reinforce their hive walls and protect the hives from infection, humans use these products to boost their immune system. Propolis is similar to aspirin in its functions without its side effects. It also helps to reduce swollen sore throats.[5,6]

Pollen (reproductive spores of seed-bearing plants) is collected by bees from flowers. Benefits of bee pollen extracts include detection and immunization against allergies. Pollen is considered as part of the apitherapy foods since they provide relief for bodily weakness, premature aging, constipation and weight loss.[6]

Royal jelly is a thick, milky mix of nutrients, which is produced from a combination of honey and pollen. All of the bees in a hive consume this substance, but larvae that consume it exclusively and in high doses grow larger than the other bees, thus enabling them to become queens of the hive.[6]

Bee venom therapy can be administered two ways: directly from a bee sting or by a prepared injection. Bee venom causes inflammation where it is introduced on the body. The inflammation triggers the body to increase circulation to that point and to create anti-inflammatory hormones to relieve pain. By injecting bee venom directly to the joint that is painful, the body’s anti-inflammatory response will treat the arthritic joint.[7]

Historical perspective: [1,8-10] The history of apitherapy can be traced back to the ancient Egyptians when they used it as a treatment for arthritis. The honeybee has played an important role for thousands of years. The use of honey has been documented in several religious texts including the Veda (a book of Hindu scriptures) and the Bible. 4000-year-old tablets even record the use of honey in ancient

Sumeria. Honey was important to the ancient Egyptians as well. They depicted bees making propolis, a gummy material from trees, on vases and ornaments, and even used honey to embalm their dead. Hippocrates, who lived between 460-367 BC, said that "honey cleans sores and ulcers of the lips, heals carbuncles and running sores". Ancient Greeks athletes even drank honey for an energy boost. Pliny, a Roman scholar, wrote about propolis in the book Natural History claiming it reduces swelling, soothes pain, and heals sores. He swore that a glass of honey and cider vinegar would clean the system and bring good health. Bee products remained important and in 1597 John Gerard wrote about the healing power of propolis in 'The History of Plants' (Stangaciu, 1999). In the 19th century bacteria was found to be the cause of infection. In 1919 a study confirmed that honey had antibiotic powers[4]. By the 1940's antibiotics had grown popular in the medical world and made honey obsolete. However, honey continued to be used in folk medicine and as a last resort for patients not responding to modern treatment. In the 1989 issue of the Journal of Royal Society Medicine an editorial expressed that "the time has come for conventional medicine to lift the blinds off this "traditional remedy" (honey) and to give it due recognition" (Molan, 1999). With the recent rise in popularity of alternative medicines, apitherapy is beginning to be re-acknowledged.

Honey:

1) **Overview**
2) **Chemical composition**
3) **Types**
4) **Antibacterial Potential**
5) **Clinical significance in dentistry**

Overview:

Honey is defined as a sweet liquid substance produced by bees from the nectar gathered from flowers and stores by them for food. The color and flavor are determined by the flowers used. It was the early man's source of sugar. About 80% of honey is levulose and dextrose, the remainder mostly water. Levulose and dextrose are simple sugars or monosaccharides and are the building blocks of all other sugars.[11] They are already broken down into their smallest form, therefore they do not need to be digested down but can be absorbed immediately when they reach the intestines. It is dextrose and levulose that give honey its high-energy content because they can be put to use immediately. Athletes can use honey diluted with orange juice to give them a boost of energy. When taken after an athletic event it even enables them to recuperate faster. Honey can be used as a health food because of its high content of energy giving sugars.[12]

Chemical composition: [13]

The carbohydrates comprise the major portion of honey. It contains a number of enzymes and free amino acids, of which the most abundant is proline. It also contains trace amounts of vitamin B, minerals and antioxidants like flavonoids and Vit C.

Composition	**%**
Water	22.0
Carbohydrates	79.7
Fiber	0.0
Protein	0.2
Ether extract	0.0
Ash	0.1

Table 1: Composition

Sugars (total)	73%
Fructose	48
Glucose	45
Sucrose	1
Others	6

Table 2: Carbohydrates

Invertase	Convert sucrose to glucose and fructose
Amylase	Convert starch to smaller units
Glucose oxidase	Convert glucose to gluconolactone to gluconic acid and hydrogen peroxide
Catalase	Convert hydrogen peroxide to water and oxygen
Acid phosphorylase	Removes inorganic phosphate from organic phosphates

Table 3: Enzymes

Free amino acids (% of total N)	41.7%
Lysine	6
Histdine	2.1
Arginine	1
Aspartic acid	4.2
Threonine	1
Serine	2.9
Glutamic acid	4.7
Proline	71.8
Gycine	0.4
Alanine	1.1
Cysteine	-
Valine	1.4
Metheonine	-
Isoleucine	0.7
Leucine	0.6
Tyrosine	0.8
Phenylalanine	1.4

Table 4: Proteins and Amino acids

Minerals [13]	ppm
K	339
Na	120
Ca	9
Mg	13
Fe	25

Table 5: Minerals

Riboflavin
Niacin
Folic acid
Pantothenic acid
Vitamin B6
Vitamin C

Table 6: Vitamins

Flavonoids (pinocembrin)
Vitamin c
Catalase
Selenium

Table 7: Antioxidants

TYPES[14]:

Honey is available in four forms: comb, extracted, chunk and creamed.

Comb Honey (*honeycomb*)

Is section of the waxen comb filled with honey just as the bees stored it naturally.

Extracted Honey (*Liquid)*

It is the honey which is separated from the comb. It is prepared by cutting off the wax cappings and whirling the comb in a honey extractor, where centrifugal force moves the honey out of the cells. This type is most readily available and used.

Chunk Honey

Consist of a chunk of honey filled in a jar with liquid honey poured around it.

Creamed Honey (*granulated*)

Is extracted honey whipped into a semisolid state similar to the consistency of butter. It is very easy to spread on toast or rolls.

Antibacterial potential: [4, 15]

The antibacterial property of honey was first recognized in 1892 by van Ketel[16]. The MIC (minimum inhibitory concentration) of the honey was found to range from 1.8% to 10.8% (v/v), indicating that the honeys had sufficient antibacterial potency to stop bacterial growth if diluted at least nine times[17]. Important factors which influence the antibacterial effectiveness of honey are as follows [4, 15]:

1. **Its hygroscopic properties:** This effect is based on high osmotic properties so it can extract water from bacterial cells and cause them to die. Honey, like other saturated sugar syrups and sugar pastes, has an osmolarity sufficient to inhibit microbial growth[18]. However, it has been shown that wounds infected with *Staphylococcus aureus* are quickly rendered sterile by honey.
2. **Its acidic pH:** Honey is characteristically quite acidic, its pH being between 3.2 and 4.5, which is low enough to be inhibitory to many animal pathogens[19]. The optimum pH for growth of these species normally falls between 7.2 and 7.4.
3. **Hydrogen peroxide:** The major antibacterial activity in honey has been found to be due to hydrogen peroxide produced enzymatically in the honey[19]. The glucose oxidase enzyme is secreted from the hypopharyngeal gland of the bee into the nectar to assist in the formation of honey from the nectar. The hydrogen peroxide and acidity produced by the reaction,

Glucose + H_2O+ O_2 --> Gluconic acid + H_2O_2 serve to preserve the honey. The hydrogen peroxide produced would be of effect as a sterilizing agent only during the ripening of honey. Full-strength honey has a negligible level of hydrogen peroxide because this substance is short-lived in the presence of the transition metal ions and ascorbic acid in honey which catalyze its decomposition to oxygen and water. The enzyme has been found to be practically inactive in full-strength honey, it giving rise to hydrogen peroxide only when the honey is diluted. This is because the acidity produced in the action of the enzyme drops the pH to a point which is too low for the enzyme to work any more. On dilution of honey the activity increases by a factor of 2,500 - 50,000, thus giving a "slow-release" antiseptic at a level which is antibacterial but not tissue-damaging.

4. **Phytochemical Factors**: It has enzymes and tissue nutrition minerals and vitamins that help repair tissue directly [16,20,21]. Several chemicals with antibacterial activity have been identified in honey by various researchers: 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.

5. **Increased lymphocyte and phagocytic activity:** Recent research[22] shows that the proliferation of peripheral blood B-lymphocytes and T-lymphocytes in cell culture is stimulated by honey at concentrations as low as 0.1%; and phagocytes are activated by honey at concentrations as low as 0.1%. Honey (at a concentration of 1%) also stimulates monocytes in cell culture to release cytokines, tumour necrosis factor (TNF)-alpha, interleukin (IL)-1 and IL-6, which activate the immune response to infection.

Clinical significance in dentistry:

1. Oral infections: There has been one report published of honey being used in oral surgery, describing a small clinical trial of the placing of honey in the socket before closure of the wound after surgical removal of impacted third molars. This study showed less pain, less incidence of postoperative complications and less swelling in the honey-treated group than in the untreated control group[23]. It has been reported in a another study[24] that natural honey showed antibacterial action against anaerobic bacteroides present in dental abscess and osteomyelitis.

2. **Mouth ulcers:** A similar rapid alleviation of pain was observed when the gelled honey was used in a case of erosion of the gum and jaw bone due to infection following surgery with bone grafting to repair damage to the jaw from traumatic injury, that had been non-responsive to any conventional treatment for more than six months. In this case the gelled honey was moulded into the infected area and held in place by wearing a mouth guard over it. The infection cleared and the wound healed up within a month after starting the application of the gelled honey. Topical application in the form of spray (from bee products), can be also be used for mouth and upper respiratory tract disease treatment and prevention. The optimal technology of spray is prepared, and concentration of ethanol as extragent 70% and 15% of honey is determined; and the preparation is called propomel[25].

3. Periodontal diseases: Honey having an anti-inflammatory activity raises the possibility of it being useful as a therapeutic agent for periodontitis; the anti-inflammatory activity would block the direct cause of the erosion of the connective tissues and bone. Furthermore, its activating effects on leukocytes could be beneficial, as some periodontitis is due to immune cell hypofunction allowing pathogens to grow unchecked and cause direct tissue damage [26]. Yet immune cell hyperfunction can cause collateral damage to tissues through the release of reactive oxygen species (free radicals), byproducts of inflammation. The initial inflammatory response is elicited by bacterial cell wall components, but reactive oxygen species released from the activated phagocytes feedback as signals to elicit further inflammatory response. The erosive damage caused by the persisting state of inflammation in periodontal disease can be stopped by removing the bacteria causing the continuous stimulation of an inflammatory response or by blocking excessive inflammatory response. It has also been proposed that antioxidants be used to protect the periodontal tissues from the damaging free radicals formed in the inflammatory response. Honey contains a substantial level of antioxidants (Frankel, Robinson, and Berenbaum 1998)[27], and has an anti-inflammatory action that has been clearly demonstrated to be direct and not secondary to the clearance of infection (Molan 2001a)[28]. Another beneficial feature of using honey to treat periodontal disease would be its well established stimulation of the growth of granulation tissue and epithelial cells, which would aid in repair of the damage done by infecting bacteria and by the free radicals from the inflammatory response to them[28]. In a study, eight honeys and three types of propolis were tested and the result proved them effective as an anticalculus agent in toothpastes and mouthwashes[29]. Recent studies by Gribel and Pashinskii indicated that honey possessed moderate antitumor and pronounced anti-metastatic effects in five different strains of rat and mouse tumors. Furthermore, honey potentiated the antitumor activity of chemotherapeutic drug**s** such as 5-fluorouracil and cyclophosphamide[30]. One study suggested that chewing "honey leather" can reduce inflammation of the gingiva[31]. In a study BY OZAN.F et al, Mouthrinse containing propolis was prepared at four different concentrations as 10%, 5%, 2.5% and 1%. Besides, CHX was used as control group. The antibacterial effects of five solutions on oral microorganisms were tested and their cytotoxic effects on human gingival fibroblasts were evaluated by agar diffusion test. At these concentrations, effectiveness of mouthrinse containing propolis samples on oral microorganisms were not found as effective as chlorhexidine. On the contrary, samples found less cytotoxic effects on human gingival fibroblasts than chlorhexidine; the administration of propolis at appropriate concentrations might be effective on oral microorganisms and non-cytotoxic to gingival fibroblasts[32].

4. Stomatitis following radiotherapy The anti-inflammatory action and stimulating effect on tissue repair of honey could possibly be of benefit for the relief of oral conditions resulting from radiotherapy and chemotherapy of cancer. Publications on the use of honey on thermal burns to the skin report that honey reduces inflammation[33].

5. Anti-halitosis: Candy made with honey may also be useful for prevention of halitosis, as honey has been observed to give rapid removal of malodour from infected wounds. It would not be just the antibacterial action of honey involved, as bacteria would use the glucose in honey in preference to amino acids, and thus would produce lactic acid instead of bad-smelling amines and sulphur compounds[28].

6. **Anticariogenic:** It was found that the minimum inhibitory concentrations of honey for *Strep. mitis*, *Strep. sobrinus* and *Lactobacillus caseii* were 7%, 7.5–8.5% and 8–12% respectively. The production of acid by these bacteria was also inhibited[34]. Compared with that produced from sucrose, honey at a concentration of 10% gave 75–80% less acid production from the streptococci and 30% less from *L.caseii*. There was no dextran produced from

10% solutions of the honeys. When the honeys were added at a concentration of 10% to a medium containing 10% sucrose the production of dextran from sucrose was inhibited by 75–89%.

Challeneges ahead of honey therapy[19]:

Although many researches have reported the benefits of honey, some disadvantages have also been found. Honey is frequently (typically) contaminated by yeasts (*Saccharomyces, Schizosaccharomyces* and *Torula* strains), by fungi (*Penicillium* and *Mucor* strains) and by bacterial spores (*Bacillus* and *Clostridium* genus). 4-6 upon dilution of the honey to a less hyperosmotic condition typically > 19% water (v/v,) such as occurs either after oral ingestion or topical application, these microbial contaminants can serve as opportunistic pathogens in susceptible people. Furthermore, altered mental status could be caused by grayanotoxin contaminated in honey.
The physicochemical characteristics of honey, such as its composition, sweetness, color, odor and pH, are somewhat variable and diverse between bee species and between locations or seasons due to foraging from different plant sources. This is directly related to the fact that the properties of honey depend on various factors, including the plant sources, climate, environment and bee species. In Thailand, bee diversity is relatively high. Other than *Apis mellifera*, an imported species, there are four native *Apis* spp. and over seven species of stingless bees. However it has been investigated that honey from the stingless bee, *Trigona laeviceps* Smith (Meliponini: Trigona), is the most common stingless bee species in Thailand. Although the taste and odor of honey from *T. laeviceps* is not favorable amongst many human consumers, it has long been used in traditional medicine in Thailand for both topical and oral applications.

Conclusion:

The curative properties of honey bees and their products have been seen with an eye of speculation since ancient times. The ancient Greeks, Romans, Chinese and Egyptians used honey to heal wounds and to cure gut disease. In its ancient usage there was no recognition of its antibacterial properties - it was just known to be an effective remedy. Now it can be seen that the effectiveness of honey in many of its medical uses is probably due to its antibacterial activity. It is well established that honey inhibits a broad spectrum of bacterial species. But literature is sparse as far as the field of dentistry is concerned. Studies are on to measure the antimicrobial efficacy of honey in oral cavity, but trials need to be carried out to determine to what extent this is true. However it looks like 'apitherapy' as dental spa holds a promising future.

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