



Honey in oral health and care: A mini review

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ABSTRACT

Background: Honey is a natural product made from the nectar of flowers by honey bees and has over 200 compounds in it, including sugars, water, organic acids, minerals and polyphenols - the exact structure and composition of honey often determined by which plant source(s) the honey bee took the nectar from. Honey has been used in diets and medicines for thousands of years; however, this review, for the first time, aims to look at its place in modern medicine concerning oral health.

Highlight: The present review for the first time attempted to address the protective effect of honey in the oral care.

Conclusion: For the first time this review addresses the usefulness of honey against *Streptococcus mutans* infections, dental plaque and caries, gingivitis and halitosis. Honey was also useful in preventing side effects associated with treatment of cancers of the head and neck, namely, radiation induced mucositis, xerostomia and poor wound healing. This is well supported by evidence in literature and was examined in this review.

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1. Introduction

Honey is a natural product made from the nectar of flowers by honey bees. Honey bees visit hundreds of flowers and ingest their nectar into their 'honey stomachs' where digestive enzymes act on the sucrose of the nectar to break it down into glucose and fructose. A single bee will regurgitate this nectar and spit it into the mouth of another bee and the process repeated severally (for about 20 min) until the nectar is fully digested into raw honey. The bees spit the raw honey onto the cells of the honey comb, flap their wings to dry it and then seal their produce in with wax [1,2]. Chemically, 17–20% of honey is made of water but this along with the rest of its make-up, flavor and color (which can be anywhere between colorless, straw-like, amber and black [3] is dependent on the flower the nectar came from. Bees can forage the nectar from one type of plant or many types to make honey and so it can be categorized as monofloral or multifloral (also known as polyfloral) [3].

2. Chemistry of honey

The chemical composition of honey has been studied in great detail and it is believed that there are more than 200 compounds in the natural substance [4,5]. About 90–95% of the dry matter of honey is sugar, followed by water, organic acids, and mineral compounds [3]. The sugars found include monosaccharides - fructose and glucose; disaccharides -maltose, sucrose, maltulose, turanose, isomaltose, laminaribiose, nigerose, kojibiose, gentio-biose, and B-trehalose; and trisaccharides - maltotriose, erlose, melezitose, centose 3-a5, isomaltosylglucose, l-kestose, iso-maltotriose, panose, isopanose, and theanderose, and they are present regardless of the type of honey [5–7]. In addition, honey also contains 4 to 5% fructo-oligosaccharides. Fructo-oligo-saccharides are indigestible molecules that can help digestive health as they are a good source of prebiotics, which aid the probiotics in our intestines [8]. Other compounds found in honey that are good for systemic health include enzymes (such as glucose oxidase and catalase), amino acids [5], vitamins (including vitamins B1, B2, B3, B6, and C), calcium, iron, zinc, and potassium, to name a few. Acetic, butyric, and citric acids are among the organic acids that have been found in honey, along with many polyphenols. Many of the pharmacological effects of honey come

from the polyphenols, and as with all other components of honey, their quantity depends on the source of the nectar [5,8].

3. Traditional and pharmacological uses of honey

The use of honey has been documented for thousands of years in both diets and medicines, proof of which is shown in Stone Age paintings [4]. Ancient civilizations of Egypt, Assyria, China, Greece, Rome and India commonly consumed honey presumably due to its sweet taste and high nutritional content while ancient medical texts by the fathers of medicine, like Aristotle, Hippocrates, and the Arab and Ayurvedic physicians, recorded the medicinal benefits of honey against various ailments [4,9]. In response to these historic uses and the growing resistance to antibiotics, in the last twenty years scientists have looked at the part that honey can play in today's medicine. Their studies have shown that honey has many pharmacological actions, making it beneficial against various injuries and illnesses. These actions include antioxidant, anti-inflammatory, antibacterial, antimutagenic, wound healing, anti-diabetic, antiviral, antifungal and anti-tumoral effects [4,9]. Hence, work has been done to investigate what benefits honey can have in oro-dental care, and this will be the focus of this review.

4. The oral cavity and oral health

The mouth and the body have historically been treated as two separate entities, with dentistry dealing with the problems of one and medicine dealing with the problems of the other. Modern teaching practices aim to resolve this with the view that holistic treatment is what matters in patient care because the two are not discrete; they are hugely influential on each other [10]. More than 100 systemic diseases and more than 500 medications have oral manifestations, with 145 commonly prescribed drugs causing dry mouth, and evidence showing that oral health can affect systemic conditions like diabetes and atherosclerosis [11]. As the beginning of the alimentary system, the oral cavity also has a relationship with the external environment and the responsibility of functions like chewing and speech, while also playing a big role in a person's mental well-being [12]. Some of the most common oral dental ailments/diseases include dental plaque, gingivitis, halitosis,

Table 1
Pharmacological properties of honey those are useful in oro-dental care.

Pharmacological action studied	Observations and reference
Antibacterial effects on oral pathogens	Honey is shown to exert antibacterial effects on nearly 60 species. Reported to be effective on <i>Streptococcus mutans</i> and to prevent development of resistance [9,18,19].
In dental plaque	Manuka honey has been shown to be effective in preventing growth of the biofilm organisms and to reduce the production of acids [24].
In gingivitis	Manuka honey has been shown to be effective in reducing gingivitis [24]. RCT studies indicate honey to be an alternative to traditional remedies for the prevention of dental caries and gingivitis following orthodontic treatment [25]. Double-blind, randomized controlled field trial has shown that manuka honey and raw honey as effective as chlorhexidine as a mouthwash. However chlorhexidine showed the maximum reduction in mean plaque and gingival score [26].
In mitigating malodour	Honey, shown to reduce malodour in people with oral squamous cell carcinomas [27]. Honey shown to be as effective as silver-coated bandages in mitigating odour [28,29].
Anticancer effects	Tualang honey (1–20%) shown to possess cytotoxic effects on cultured oral squamous cell carcinomas [38].
Prevent/reduce radiation-induced mucositis	Multiple reports indicate honey was effective in delaying/preventing/mitigating radiation induced mucositis in people undergoing curative radiotherapy for their head and neck cancer [46–56].
Prevent/reduce radiation-induced xerostomia	Study indicates honey was effective in delaying/preventing/mitigating radiation induced xerostomia in people undergoing curative radiotherapy for their head and neck cancer [59].
Honey enhances healing of refractory wound	Topical application of honey was effective in enhancing wound healing and to mitigate the pain without causing any adverse effects [64]. Honey is shown to be effective in enhancing wound healing in head and neck cancer patients previously exposed to radiotherapy [65]. Tualang honey is also shown to be effective in enhancing post tonsillectomy healing process in children [66].

malodor, microbial infections, and cancers. In the following sections, and in Table 1 and, the usefulness of honey in preventing/mitigating these conditions are addressed.

4.1. Honey in mitigating infections of *Streptococcus mutans*

Conservative estimates are that there are between 500 and 700 different microbial species on different surfaces of the oral cavity [13–17], with a person's oral health and hygiene dictating the ratio of these species. Healthy mouths tend to have more gram-positive bacteria and simpler colonies; unhealthy mouths tend to have more anaerobic, gram-negative bacteria and complex, diverse colonies [14]. Scientific studies have shown that Honey was effective against nearly 60 species of gram-positive, gram-negative, anaerobic, and aerobic bacteria. One of these is *Streptococcus mutans* [9,18,19], a pathogen involved heavily in dental caries. Unlike antibiotics, evidence has found that so far, bacteria do not become resistant to honey [20]. Thus, it is useful to know which infections honey can be used against. This continued sensitivity may be because honey has a different antimicrobial activity from that of antibiotics. Instead of acting on intracellular metabolism or the cell wall of a microorganism, honey acts to stop the growth of microbes with its high sugar content and low pH (bacteriostatic action) and kill bacteria via its antibacterial factors, especially hydrogen peroxide [21–23].

4.2. Honey in mitigating dental plaque

Dental plaque is the thin biofilm, which accumulates on tooth surfaces. Bacteria in the plaque (particularly *S. mutans*, which will be discussed further in the review) metabolize fermentable carbohydrates (especially sucrose) from the diet and produce acids. These acids are responsible for demineralizing and disintegrating tooth structure, and are held in close contact with the tooth by the matrix secreted by the plaque biofilm. This prevents the clearing and remineralising actions of saliva and topical fluoride, resulting in the initiation and progression of dental caries if the biofilm is not mechanically disrupted by tooth brushing. There is a report showing that manuka honey was effective against plaque formation, preventing growth of the biofilm and reducing the amount of acid produced [24].

4.3. Honey in gingivitis

Gingivitis is the inflammation of the gingival tissues in response to the presence of bacteria in the plaque biofilm. It is characterized by erythematous and bleeding gingivae, which are typically swollen at the gingival margins, due to the loss of 'knife-edge papillae' - a characteristic feature of gingival health. Gingivitis is reversible with good oral hygiene practices, but if not corrected, can progress to the irreversible loss of clinical attachment and the alveolar bone - the features of periodontal disease - as plaque migrates towards the apex of the tooth, initiating an inflammatory reaction from the host. This inflammation is similar to that found in inflamed wounds, which manuka honey has, for hundreds of years, shown to rapidly clear bacteria from [24]. Atwa and coworkers [25] conducted a randomized control trial of 20 female orthodontic patients to examine the effect of chewed honey on pH, bacterial counts and bacterial growth compared to sucrose. The trial found that the pH did not go below the threshold pH of 5.5, reduced bacterial counts, and inhibited bacterial growth. With only 20 patients involved, the authors recognized that the study was limited and further studies should be done to explore the possibility that honey, even with its acidic pH and high sugar content, may actually help prevent demineralization and gingivitis in patients when chewed. It would also be worthwhile for future

studies to look at how much of this initial success is due to the honey being chewed, which increases salivary flow rate, as well as, the buffering and clearing action of saliva. Singhal et al.'s study in 2018 examines this in an indirect way by comparing raw and manuka honey mouthwashes to chlorhexidine on plaque and gingivitis scores. All 135 cases showed reduced levels of plaque and gingivitis scores, with chlorhexidine having the best result, proving that honey-based mouthwashes have antimicrobial effects on the oral cavity [26].

4.4. Honey in mitigating malodor

Oral malodor (also termed: Fetor oris or Fetor ex ore) or halitosis, that is sensed during a person's speech has a very unpleasant odor. In the oral cavity, the posterior portion of the tongue's dorsum, subgingival areas (e.g., periodontal pockets and interdental spaces), faulty restorations (e.g., leaking crowns and bridges), dental implants, dentures, and abscesses, are most prone to harboring halitosis-causing elements. Furthermore, transient oral dryness, brought about by a temporary reduction in saliva flow, also plays an important part in promoting this condition. With regard to honey, there is some evidence to show that it can combat the malodor of oral squamous cell carcinomas (Drain and Fleming, [27]), but this might be no more effective than silver-coated bandages [28,29]. The theory behind it is that manuka honey's antibacterial action combats bacterial colonization of healing wounds and provides nutrients for the bacteria such that they produce lactic acid during metabolism rather than malodorous gases [30]. Again, while available evidence is promising, more research is required on honey's positive effects against infections in the oral cavity.

4.5. Honey in oral cancer

Of all the ailments and diseases affecting the oral cavity, cancer is the most severe and dangerous. Recent reports from the GLOBCAN indicate that more than 550,000 cases of head and neck cancers, most of which are oral cancers, are reported annually [31]. Oral cancer is the sixth most common cancer in the world and two to four times more common in men than women [31]. Pathologically, more than 90% of all oral cancers are squamous cell carcinomas [32]. Conventionally, depending on the cancer stage, surgery, chemotherapy and radiotherapy, either alone or in combination are used to cure/control the tumor growth. In the early stage (I), when excisable, oral cancers are preferably treated with surgery and may be backed up with radiation [33]. In advanced stages (stage II and III) a combination of surgery and radiation/chemo-irradiation (60–74 Gy delivered in 2 Gy fractions 5 days/week) may be used. In stage 4, when the cancer has metastasized to a distant site, depending on the general health of the patient, radical surgery followed by post-operative radiation therapy or the use of palliative radiation therapy or chemotherapy may be used [34].

4.6. Honey as an anticancer agent

Honey has been investigated for its anticancer properties in various cultured neoplastic cell lines and reports suggest that it is effective [35–37]. Seminal studies by Ghasm and co-workers (2010) [38] have shown that treatment of oral squamous cell carcinomas (OSCC) with various concentrations of Tualang honey (1–20%) was effective in causing a dose- and time-dependent cell death [38]. The 50% inhibitory concentration (IC50) was observed to be at 4% and maximum inhibition of cell growth ($\geq 80\%$) was obtained at 15%. Morphological studies also showed that honey induced a time and dose-dependent inhibitory effect [38]. Although not in oral cancer cells, mechanistic studies indicate that

honey modulates inflammatory cascade, cell cycle, cell growth and proliferation, and induces apoptosis [5,39–41]. With limited evidence in this field (especially with oral cancer models), more research needs to be done to understand the usefulness of honey as an anticancer agent.

4.7. Honey in mitigating treatment-induced ill-effects

Radiation is a very useful tool in the treatment of head and neck cancers and can be used after surgery/chemotherapy or with small, weekly doses of chemotherapy (called chemoradiation, the chemotherapy drug often used is either cisplatin or carboplatin) to increase the number of tumor cells killed [42,43]. This use of radiation has proven effective at increasing 5-year survival rates [42,43], but with major side effects. Localized radiation to the head and neck causes mucositis, xerostomia and impairs wound healing in the area. When these side effects cause the need for treatment breaks, the therapeutic benefit of radiation is reduced, as is disease prognosis. Hence, the following sections of this review look at the effects of honey in preventing or improving mucositis, xerostomia, and refractory wound healing.

4.8. Honey protects against radiation-induced mucositis

Radiation-induced mucositis is arguably the most prominent side effect of curative radiotherapy and causes immense pain and morbidity [42,44]. Influential studies by Biswal and coworkers [45] showed for the first time that honey was effective in preventing radiation mucositis. Since then many studies carried out around the world have shown that honey was beneficial in reducing the incidence of radio/chemotherapy-induced oral mucositis, reducing treatment interruptions, weight loss, and delaying the onset of oral mucositis [46–56].

4.9. Honey is effective in preventing radiation-induced salivary gland destruction and xerostomia

The salivary glands are often irradiated during the radiation treatment of cancers of the head and neck. The damage reduces the volume and quality of patients' saliva and results in xerostomia [57]. Xerostomia can significantly reduce a patient's quality of life by affecting their taste, swallowing, and speech, leaving their oral mucosa dry and atrophic and predisposing them to mucosal ulceration and dental caries [58]. One study has shown that honey was effective in preventing radiation-induced xerostomia but it is the only study in that area [59]. The investigators observed that when compared to the placebo (saline) application of thyme, honey was effective in mitigating xerostomia, improving the overall quality of life, and reducing unbearable pain and dysphagia, 1 and 6 months following treatment completion [59].

4.10. Honey as an adjunct to conventional therapies: enhancing refractory wound healing

Several studies carried out previously have confirmed without doubt that wound healing in sites previously exposed to radiation is problematic and slow [60,61]. Historically, honey has been documented to be one of the most efficient wound healing agents and scientific studies have shown it to be effective in healing open wounds, diabetic wounds and burns [62,63]. A pilot study with four patients has shown that topical application of honey via hydro fiber rope and non-adhesive foam, respectively, was effective in enhancing wound healing, and in mitigating pain without causing adverse effects [64]. Subsequent studies with head and neck cancer patients, previously treated for their head and neck cancer, has conclusively shown that honey was effective in enhancing wound healing after

salvage surgery [65]. Additionally, studies have shown that Tualang honey is effective in enhancing post-tonsillectomy healing in children [66]. Based on these observations it can be inferred that honey is effective as a wound healing agent during and after radiation.

5. Conclusions

In conclusion, honey has been recognized as having great medical worth for thousands of years, and is now finding its place in modern medicine. Various studies have shown the benefits of honey against diseases of the oral cavity such as caries, gingivitis, and radiation-induced mucositis but more work is needed in these Table 1 and Fig. 1. Perhaps a more pressing need for research however lies in the uses of honey in head and neck cancers treated by radiation as it has been shown to be effective against xerostomia and wound healing, but evidence is not yet conclusive enough for honey application to become a standard practice in treating these patients. On the down side, studies have shown that the use of baby comforters with honey enhances the risk of developing caries [67]. These concerns have been raised by some investigators [68] and need to be studied. Honey has the potential to be of immense use in oral care against inflammatory ailments and bacterial infections, but only when gaps in the evidence base are bridged.

Conflict of interest

The authors declare that they do not have any conflict of interest regarding the study topic.

Ethical statement

The authors declare that they have abided with ethical guidelines regarding the study.

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