

**Review****Potential biochemical effects of honey in oral health care: a review**

<sup>1,2\*</sup>Qamar, Z., <sup>3</sup>Alghonaim, M. F., <sup>1</sup>Almohana, S. A., <sup>1</sup>Almohana, A. A. and <sup>4</sup>Zeeshan, T.

<sup>1</sup>Department of OMFS and Diagnostic Sciences, Faculty of Dentistry, Riyadh Elm University, Riyadh, Saudi Arabia

<sup>2</sup>Department of Oral Biology, Liaquat College of Medicine and Dentistry, Karachi, Pakistan

<sup>3</sup>Department of Oral and Maxillofacial Surgery, King Fahad Hospital, Hofuf, Saudi Arabia

<sup>4</sup>Department of Oral and Craniofacial Sciences, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia

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Honey is a natural flower extract rich in healthy components including fructose, glucose, and various oligosaccharides. In addition, it comprises of proteins, enzymes, trace elements, vitamins, and polyphenols. Honey has a long history for its uses in medicinal purposes. However, its benefits on oral health have been overlooked till date. The main aim of this review is to address the benefits of honey in oral cavity, which have been identified in previous studies to have anti-cariogenic and anti-plaque; and also, for the treatment of cancer-induced mucositis and xerostomia.

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**Introduction**

Honey is a natural product comprising of flower nectar produced by honeybees. Honeybees ingest extracts from various flowers which are later digested to produce fructose and glucose. The extract ingested by honeybees is later regurgitated and transferred into the mouth of another bees until honey is converted into raw form. The whole process takes approximately 20 minutes. Later, the raw form of honey is placed in the honeycomb cells, and sealed by flapping the wings (Nicolson and Human, 2008; Zhu *et al.*, 2016).

Chemically, honey is composed of 17 - 20% water with other contents including flavour and colour. Honey colour is dependent on the types of flowers from which the extract has been taken, and it can vary from being colourless, straw-like, or black (Ahmad *et al.*, 2017). Honeybees can obtain extract from one or many types of flowers. Depending on the number of flowers involved, honey can be classified as mono- or multi-floral (Ahmad *et al.*, 2017). Natural honey is thought to comprise of more than 200 compounds, with few having pharmacological effect on human health. Honey mainly comprises of four components: (i) sugary content of various types of approximately 90 - 95%, (ii) organic acids, (iii) minerals, and (iv) water as shown in Figure 1 (Ezz El-Arab *et al.*, 2006; Eteraf-Oskouei and Najafi, 2013; Gašić *et al.*, 2017; Ahmed *et al.*, 2018; Khan *et al.*, 2018).

Honey has a long history with both medicinal and food uses in various ancient civilisations such as Chinese, Egyptians, Indians, Romans, and Assyrians (Eteraf-Oskouei and Najafi, 2013). It has sweetened taste and high nutritional values as reported by Aristotle, Hippocrates, and Arabs; and further by Ayurvedic physician who reported its benefits against numerous disorders (Bansal *et al.*, 2005; Eteraf-Oskouei and Najafi, 2013). Keeping in view of the uses of honey in ancient times, and the increasing microbial resistance against anti-microbial drugs, scientists are investigating the potential role of honey for medicinal use. It has been reported that honey has many beneficial pharmacological effects for the treatments of various injuries and illnesses (Figure 2) (Bansal *et al.*, 2005; Eteraf-Oskouei and Najafi, 2013). Previous studies have been conducted to investigate the potential effects of honey in oral health care, and this is the main focus of this review.

**Oral health**

Oral cavity is the beginning of the gastro-intestinal system. It houses hard and soft oral tissues, saliva, and oral micro-flora, thus creating the oral environment. The environment is constantly affected by changing conditions associated with food intake and its processing - mechanical and biochemical, which is the beginning of its digestion. The oral cavity possesses a distinctive ecosystem as a host environ, and it supports the growth and establishment of a variety of

\*Corresponding author.  
Email: [zeeshan.qamar@gmail.com](mailto:zeeshan.qamar@gmail.com)

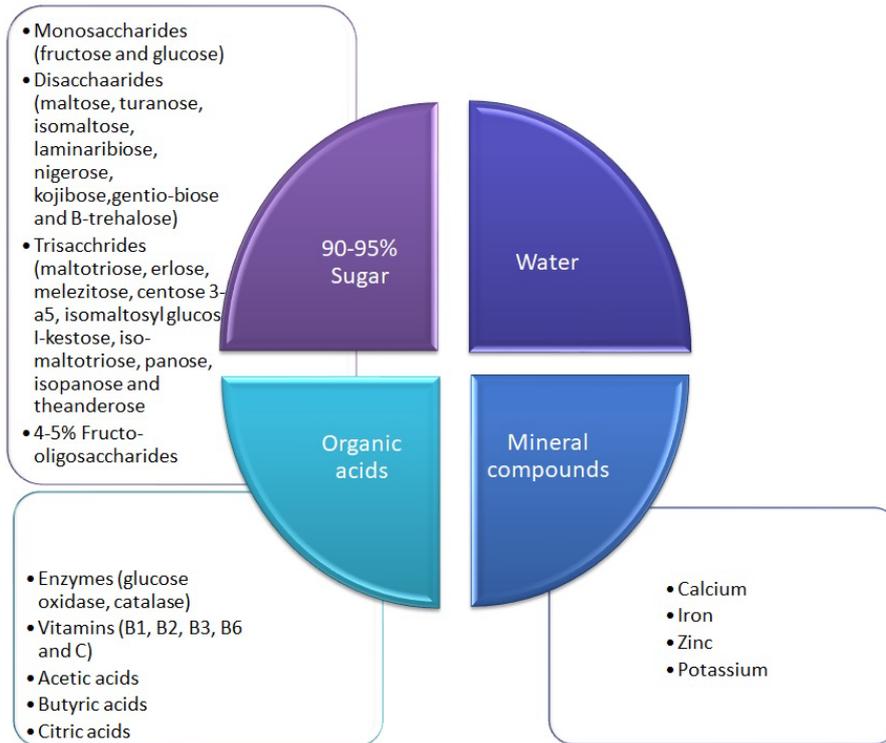


Figure 1. Composition of honey.

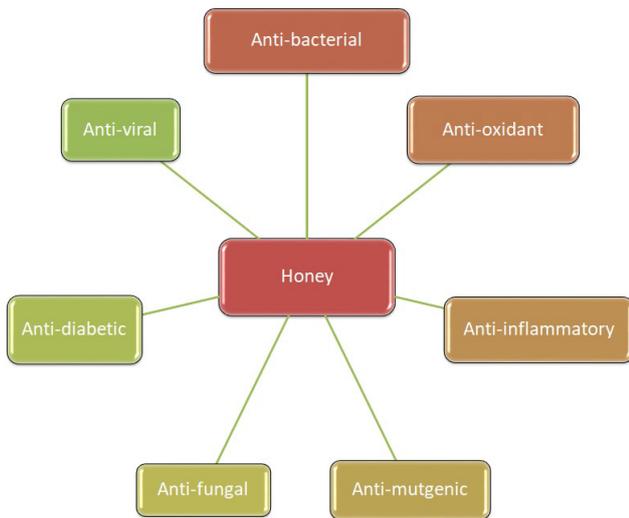


Figure 2. Pharmacological effects of honey.



Figure 3. Pharmacological effects of honey on oral health.

micro-flora. The hard and soft structures in oral cavity include cheeks, tongue, gingivae, and teeth which provide sites for the adherence and subsequently growth of microorganisms. The oral cavity plays vital role in relation to mental conditions, in particular with speech and chewing (Jin *et al.*, 2016). The effects of honey against some of the most common oral diseases are illustrated in Figure 3 (Baltas *et al.*, 2016; Kolayli *et al.*, 2016).

*Anti-microbial effect*

An extensive variety of bacteria

(approximately 500 - 700 species) inhabit and colonise the oral cavity (Marsh and Martin, 2009). Different populations of bacteria are concomitant with different sites within the mouth, and their compositions also rely on the anatomical locality. For instance, the bacterial consortium which colonises teeth is different to that which colonises the soft tissues like tongue and buccal mucosa (Mager *et al.*, 2003). The population of these commonly found bacteria with respect to their

anatomical location remains stable (Marsh and Martin, 2009) and non-pathogenic under normal conditions, until any discrepancy happens which leads to the impairment of the host's defences due to any underlying illness/pathology. In a healthy individual, higher count of simple Gram-positive bacteria is observed; whereas in unhealthy conditions, higher content of Gram-negative bacteria is observed (Scannapieco, 2013). Honey has been reported to be effective against approximately 60 bacterial species (Gram-positive, Gram-negative, aerobic, and anaerobic), including one of the most common active bacteria, *Streptococcus mutans* which is related to dental caries (Asadi-Pooya *et al.*, 2003; Bansal *et al.*, 2005; Beena *et al.*, 2018). The most important point pertinent to natural honey till date is that bacteria are not observed to develop resistance against honey, unlike against antibiotics commercially available in the market (Henriques *et al.*, 2011). The possible reason for continued sensitivity among the microorganisms towards honey could be that rather than acting on the bacterial cell wall or intracellular metabolism, honey has a bacteriostatic effect while having high sugar content and low pH (Emsen, 2007; Ajibola *et al.*, 2012). Furthermore, it is observed to have bactericidal effect attributed to the presence of hydrogen peroxide (Emsen, 2007; Mandal *et al.*, 2010; Ajibola *et al.*, 2012).

#### *Anti-plaque effect*

The dental hard tissue in oral cavity (tooth) plays a vital role in mastication of food. It has a suitable structure for the colonisation of oral microorganisms and oral biofilm formation. A natural tooth comprises of pulp, cementum, dentine, and enamel (Nanci, 2014; Fehrenbach and Popowics, 2015). Being the outermost layer of the tooth, "dental enamel" is the only part that is exposed to the oral environment under normal condition. Tooth offers surfaces such as pits and fissures that facilitate microbial growth and colonisation. The surface of tooth normally favours the habitation of aerobic, facultative, and anaerobic microorganisms (Samaranayake, 2002; Aruni *et al.*, 2015). Oral health maintenance can only be attained by taking an effective oral hygiene measures on regular basis. A toothbrush is the most used device or tool to eradicate the dental plaque. When performed with an adequate skill and duration of time, manual brushing is highly effective. However, for most reasons, neither of these criteria is fulfilled like in the case of pits, fissures, and interproximal spaces; while orthodontic appliances such as dental floss, toothpicks, mini brushes, and interdental brushes are used to compensate an improper brushing. Powered

toothbrushes with a rotating, oscillating, or sonic action are also available in the market, and efficiently remove plaque and reduce gingivitis (Tritten and Armitage, 1996; Ho and Niederman, 1997; Moritis *et al.*, 2002; Biesbrock *et al.*, 2008).

Chemotherapeutic agents have been formulated in order to contribute to the control of gingivitis and plaque, according to the established guidelines by The American Dental Association. Nayak *et al.* (2010) has demonstrated anti-plaque effect and reduction of acid production by the use of Manuka honey.

#### *Effect on gingivitis*

Inflammation of the gingival tissue due to microbial colonisation in the dental plaque is referred as gingivitis, with clinical features showing gingival bleeding, loss of "knife edge papilla", stippling, and orange peel appearance. Gingivitis if treated with good oral hygiene practice is considered as a reversible condition, but failure can lead to periodontal diseases leading to loss of alveolar bone and periodontal ligaments attachment. The microbial content from the dental plaque migrates towards the apex of the tooth, stimulating inflammation similar to that observed in wounds (Nayak *et al.*, 2010). Manuka honey when used on wounds has been observed to have rapid anti-bacterial effect, thus reducing inflammation (Nayak *et al.*, 2010). Previous study conducted a randomised controlled trial to evaluate the effect of chewable honey on pH, microbial count, and microbial growth in comparison to sucrose on 20 orthodontically treated female patients (Atwa *et al.*, 2014). It was observed that pH did not go below critical pH of enamel with respect to saliva (5.2 - 5.4). Furthermore, they also observed the bactericidal and bacteriostatic effects of honey (Atwa *et al.*, 2014). Later, another study was conducted to compare the effect of Manuka and raw honey with chlorohexidine mouthwash, and they reported a promising effect of naturally occurring honey-based mouth rinses on dental plaque and gingivitis (Singhal *et al.*, 2018).

#### *Effect on oral malodour (halitosis)*

The word halitosis is derived from Latin word for breath - "halitus"; and referred as oral malodour, "fedor ex ore", or "fedor oris"; and is a common condition. A most common disorder in various people is that they have an unpleasant oral odour (Scully and Felix, 2005). It is observed that nearly 8 - 50% of the world population have consistent recurrence of malodour. There are many factors playing vital role in microbial colonisation leading to oral malodour as described in Figure 4. There are previous studies

reporting the effect of honey in reducing oral malodour in patients suffering from oral squamous cell carcinoma (OSCC) (Drain and Fleming, 2015), but less than silver coated bandages (Lund-Nielsen *et al.*, 2011a; 2011b). In particular, Manuka honey is thought to have two pathways for reduction of malodour; (i) it has a bactericidal effect of reducing the bacterial load, and (ii) providing an alternative nutrition to microorganisms, which during metabolism tends to produce lactic acid rather than producing malodour sulphur compounds (Lusby *et al.*, 2002).

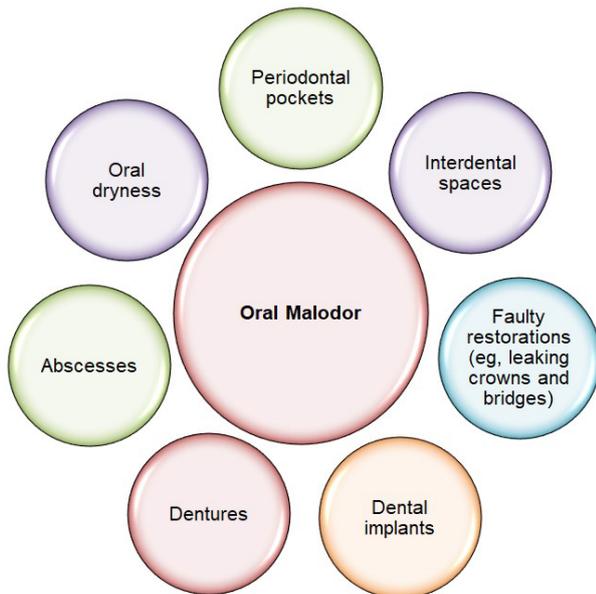


Figure 4. Potential factors for malodour.

#### *Anti-carcinogenic effect of honey*

As oral cancer is one of the most precarious diseases of the oral cavity, it is necessary to evaluate anti-cancer/anti-carcinogenic potential of various available natural products such as honey. As reported by GLOBCAN, lips and oral cavity are the most prevalent sites in head and neck cancer, which observe more than twice the ratio in men than women (Bray *et al.*, 2018). Approximately, there are more than 90% of all cancers in oral cavity, and OSCC is the most prevalent type (Scully and Bagan, 2009). Honey has been reported to have anti-carcinogenic effect on various cultured cell lines (Sela *et al.*, 1998; Molan, 2001; Al-Waili, 2003). A study on anti-cariogenic potential of Tualang honey in various concentrations (1 - 20%) reported that it was effective against OSCC (Ghashm *et al.*, 2010). In another study, it is stated that the cellular death was time- and dose-dependent (Ghashm *et al.*, 2010). Nearly 4% concentration of Tualang honey has demonstrated 50% inhibition in abnormal cell growth; whereas on increasing the concentration to 15%, approximately 80% inhibitory effect was observed (Ghashm *et al.*, 2010). Honey has

also been reported to regulate inflammation, cell cycle, cell growth, and cell proliferation. Furthermore, it also stimulates cellular apoptosis (Abubakar *et al.*, 2012; Ahmed and Othman, 2013; Jaganathan *et al.*, 2015; Ahmed *et al.*, 2018).

#### *Effect of honey in radiation-induced disorders*

Radiation therapy is commonly used for cancer treatment in post-surgery/post-chemotherapy, or used in combination with chemotherapy in order to increase the effectiveness to kill carcinogenic cell line (Sonis, 2013; Sroussi *et al.*, 2017). However, this tends to lead to various side effects which include xerostomia and mucositis, leading to immense pain (Elad *et al.*, 2013; Sonis, 2013). A study reported that patients treated for head and neck cancer with radiation therapy in combination with tropical honey tend to show more than 55% better prevention from mucositis than the control group (Biswal *et al.*, 2003). As honey reduces the prevalence of radiation-induced mucositis, it also reduces the treatment-breaks and further weight loss (Abdulrhman *et al.*, 2012; Maiti *et al.*, 2012; Jayachandran and Balaji, 2012; Samdariya *et al.*, 2015; Co *et al.*, 2016; Jayalekshmi *et al.*, 2016; Kobya Bulut and Güdücü Tüfekci, 2016; Xu *et al.*, 2016; Al Jaouni *et al.*, 2017; Charalambous *et al.*, 2018).

Furthermore, in radiation therapy for head and neck cancer, the salivary secretory units are damaged thus reducing the salivary flow, leading to dryness of mouth/xerostomia (Radvansky *et al.*, 2013). This compromises the lifestyle of an individual by disturbing the taste sensation, speech, swallowing, and digestion of food. Due to the decrease salivary flow, an individual is prone to mucosal infections and rampant caries (Guchelaar *et al.*, 1997). Charalambous *et al.* (2017) compared the effect of saline with thyme honey in patients with radiation-induced xerostomia. They reported that thyme honey is effective in uplifting the overall quality of life, and also reduces pain and dysphagia (Charalambous *et al.*, 2017).

#### *Honey enhances wound healing*

Honey has shown good effects in wound healing as reported by previous studies (Kumar and Jagetia, 1994; 1995). It has also shown excellent effect against open wounds, diabetic wounds, and burns (Cooper, 2016; Saikaly and Khachemoune, 2017). In a pilot study demonstrated by Robson and Cooper (2009), tropical honey application by hydro-fibre rope and non-adhesive foam enhances wound healing without any adverse effects (Robson and Cooper, 2009). Rothmeier *et al.* (2014) demonstrated that patients' undergone surgery for head and neck cancer in post-operative treatment with honey showed wound

healing at a faster pace in comparison to the control group (Rothmeier *et al.*, 2014). Furthermore, studies have reported that Tualang honey when used in patients of post-tonsillectomy, resulted in potent enhancement in wound healing (Mat Lazim *et al.*, 2013). Thus, honey is considered as an efficient agent for wound healing.

## Conclusion

To conclude, honey has countless medicinal benefits against oral diseases such as gingivitis, malodour, plaque, cancer, radiation-dependent xerostomia, and mucositis. Although benefits of honey have been widely reported, further investigations are required to determine the mechanism of honey in modulating the oral diseases.

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