

REVIEW ARTICLE

THE LOCAL EFFECTS OF HONEY ON DIABETIC FOOT DISORDER

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Both the *Qur'an* and *Hadith* refer to honey as a healer of many health disorders in humans. The use of honey to treat and prevent many disorders has been well documented highlighting antioxidant, antimicrobial, immune-stimulation, anti-inflammation and anti-tumour mechanisms. Moreover, local applications of honey in the treatment of different types of wounds have showed very promising outcomes. Diabetic foot disorder is a major complication in diabetic patients. It is the main cause of morbidity and disability. It often leads to amputations of foot. The potential benefits of honey in the treatment of diabetic foot disorder have been under study by researchers worldwide. The aim of this review is to summarize the reported local effects of honey on diabetic foot disorder and its possible mechanisms. The scientific findings indicate that honey can accelerate wound healing in diabetic foot disorder through its antimicrobial, anti-ulcerous and anti-inflammatory pathways in a clinical setting thus enhancing the quality of life in diabetic patients. However further research is needed to evaluate the molecular mechanisms of action and to standardize the use of honey in Diabetic foot disorder.

Keywords: antioxidant, antimicrobial, immune-stimulation, anti-inflammation, anti-tumour and Diabetic foot disorders

INTRODUCTION

Both holy Qur'an and sayings of Prophet Muhammad (Peace Be Upon Him) refer to Honey as a healer of diseases. It has been mentioned in Qur'an "And your Lord inspired the bee, saying: *"Take your habitations in the mountains and in the trees and in that what they erect; Then eat of all fruits, and follow the ways of your Lord, made easy [for you]. There comes drinks from their bellies, of varying colour where in is healing for mankind. Verily, in this is indeed a sign for people who think. (Al-Nahl, verse:68-69).*"¹

Honey was mentioned also in another place among the image of the gardens promised to those who keep their duty to Allah will be rivers of honey of undiluted purity. (*Muhammad, Verse: 15*).¹ According to Qur'an, our messenger Muhammad (peace be upon him) has informed us that honey has cure for many health problems, include Gastrointestinal tract.²

Honey is one of the drinks (others being propolis, wax, pollen, venom and royal jelly) that comes from bellies of bees as mentioned in *Al-Nahl*. Honey was considered an oldest wound dressing long before even discovery of bacteria, it dates back to ancient medical writings of Egypt, Greece and parts of India.³

These days honey is receiving a great attention as an alternative prophetic treatment in modern medicine especially after the very promising results observed when honey was applied as local dressing for infected wounds. In such treatment, the wounds become sterile within few days.⁴

Diabetic foot disorder manifests itself by one or more of manifestations that include chronic ulcers, infected in-growing toenails, open wounds, and skin cracks.⁵ It is one of the major complications of diabetes.

It is a leading cause of hospitalisation and non-traumatic amputation (80% of lower limb amputations).⁶

Bream *et al* reported a series of multiple mechanisms that contribute to lack of healing. These include decreased cell and growth factor response that leads to diminished peripheral blood flow and decreased local angiogenesis.⁷

The local application of honey in Diabetic foot disorder is increasing rapidly. Al-zahrani and Bakhotmah have reported that honey is the most commonly used dressing to topically treat Diabetic foot disorder in Saudi diabetic patients.⁸ There is an increase in reported and successful usage of honey recently as a wound dressing. This paper examines the literature that highlights the benefits of the application of honey on Diabetic foot disorder and reviews the clinical and experimental findings that have been published so far.

Composition of Honey

Honey is a mixture of natural products of very high nutritive value gathered, modified and stored in the honeycombs by honeybees from the natural sugar solutions called nectar (floral) and sweet deposits from plants (non floral).⁹ As mentioned in the Holy Quran '*Honey colour varies*', it had been documented that this variation in the colour depends on the botanical source, environmental and climatic conditions as well as processing influences. All of these factors affect its composition and properties. As a result the quality of honey is affected accordingly and thus can influence the efficacy of honey with respect to management of health problems.¹⁰

The major components of honey are monosaccharides (fructose and glucose) with low quantities of disaccharides (sucrose) and it includes a small amount of enzymes, acids, minerals and

unidentified substances.¹¹ Moreover, there are different quantities of minerals (potassium, calcium and sodium) and trace minerals (iron, copper, zinc, and manganese)¹² that are important for the general metabolism, circulatory system, reproduction and germination¹³ which indicate that honey has a significant effect on healing and prevention of illness.

Unfortunately, honey might be contaminated with pesticides, residues of antibiotics, minerals and toxic heavy metals above permitted levels. Therefore, the production of honey free of harmful chemicals is necessary.¹⁴ Heavy metals, such as mercury, cadmium, aluminium and lead, can be particularly dangerous if maximum permissible levels are exceeded.¹⁵ Many researchers however detected heavy metals in low levels in the honey. A study conducted in Saudi Arabia¹⁵ found that, the heavy metal contents of local honey were either comparable to or less than the internationally reported values and could be regarded as safe for human consumption. That is why honey is considered as an excellent monitor of contamination in their environment that reflects the concentrations of pollutants over both time and large spatial areas.¹⁶

Honey also contains choline which is essential nutrient that serves as precursor for acetylcholine and phospholipid. Many potential physiological roles for cardiovascular and brain function as well as for cellular membrane composition and repair have been proposed for honey.^{17,18} Honey contains aroma which depends on its botanical origin. Aroma is known as antioxidant through many researches, it has more than 500 different volatile compounds that were identified in different types of honey.¹⁹ Other important antioxidant compounds are polyphenols mainly flavonoids, phenolic acids and phenolic acid derivatives.²⁰

Antimicrobial Effect

The antimicrobial activities of honey have been extensively studied. It was reported that honey exhibits an inhibitory effect to around 60 species of bacteria including gram-positives, gram-negatives, aerobes and anaerobes,²¹ and Methicillin-Resistant *Staphylococcus aureus*.²² Moreover, honey is found to be very useful in the treatment of oral ulcers in comparison with the use of Triamcinolon acetonide (kenalog in orabase), without any side effect.²³ In addition, honey has showed fungicidal activity (against different types of dermatophytes)²⁴, antiviral activity²⁵ and antiparasitic²⁶ activity as well.

The antimicrobial activity of honey varies and depends on the geographic and botanical origin of honey.²⁷ The antimicrobial activity of honey has been attributed to certain factors including high hydrogen peroxide and non-peroxide components, osmolarity and acidic pH. Honey has both peroxide and non-peroxide antibacterial action, with different non-peroxide antibacterial substances involved, acidic, basic or

neutral.²⁸ In addition the osmotic effect of honey is a poor environment for microbial growth.²⁹ Honey has phytochemicals mostly consisting of complex phenol and organic acids that further serve an antibacterial function³⁰, and reduce the oxidative damage in the tissue³¹.

Anti-ulcer Effect

Wound healing process is a complex and highly regulated process that can be compromised by both exogenous factors (micro-organisms) and endogenous factors (pathophysiological). For diabetic foot disorder, the wound healing process is very important since it is considered the major cause of morbidity and disability in diabetic patients, which frequently leads to lower extremity amputations.³²

Jennifer *et al* applied honey in the treatment of a 79-year-old man with type 2 diabetes mellitus who lost two of his toes and refused below-the-knee amputation. He was informed by the surgical teams that without this surgery he would likely die. The honey was smeared on gauze and placed on heel ulcer that was then wrapped. The recommended therapy, included antibiotics selected by infectious disease consultants, and topical therapies directed by a wound care expert were discontinued but otherwise treatment was unchanged. It was observed that, dressing became painless and the serum glucose remained in excellent control due to the medicines that he was taking. Granulation tissue appeared within 2 weeks; and in 12 months the ulcers resolved. In the two years follow-up the ulcers did not recur and the patient was ambulatory with a walker and reported improved quality-of-life.³³

The local application of honey on wounds is one of the most widely used natural product and many evidence from animal studies and trials have suggested that honey may accelerate wound healing.³⁴ Makhdoom *et al*³⁵ have observed excellent results in treating diabetic wounds with dressings soaked with natural honey, and they concluded that, the disability of diabetic foot patients was minimised by decreasing the rate of leg or foot amputations by using honey dressing and thus enhancing the quality and productivity of individual life. It acts as a barrier preventing wounds from becoming infected³⁶, and preventing cross-infection³⁷.

It was reported that sloughs, gangrenous tissue and necrotic tissue are rapidly replaced with granulation tissue and advancing epithelialisation when honey is used as a local dressing.³⁸ It stimulates the growth of fibroblasts that replace connective tissue of the deeper layer of the skin and re-growth of epithelial cells that form the new skin cover over a healed wound, formation of new blood capillaries (angiogenesis) and produce the collagen fibres that give the strength to the repair.³⁹

Improvement of nutrition of wounds has been observed and the sloughs, necrotic and gangrenous tissue under honey dressing, quickly and easily separated so that they could be lifted off painlessly.³⁶

Honey has also been documented as a deodorisation of offensively smelling wounds through its strong osmotic action which draws exudates and lymph fluid from the wound out towards the surface to add the moisture needed for autolytic debridement.^{4,40}

An interesting observation about honey is promoting the formation of clean healthy granulation tissue.⁴¹ Increased blood flow has been noted in wounds making wounds suitable for suturing.⁴² It also allows early grafting on a clean clear base⁴³ and it reduces the incidence of skin graft areas.⁴⁴ It has been reported that dressing wounds with honey minimizes scarring.⁴⁵

Many scientists recommend the honey dressings as a safer alternative dressing for diabetic foot disorder, as they improve wound healing, prevent superadded infection and save cost.⁴⁶

Anti-inflammatory Effect

Anti-inflammatory property of honey has been reported by many investigators in human and experimental models. The anti-inflammation effect is very important in diabetic foot disorder because it improves circulation and delivers more oxygen and nutrients to help the tissue repair and heal.⁴⁰ It was documented that, honey reduces the signs of inflammation including oedema, heat, redness and exudation within 10 days.⁴⁷ Bilsel *et al* have referred the anti-inflammatory effect of honey to either its antibacterial properties or direct action.⁴⁸

The acidic composition of honey can be considered as another factor that serves for increased oxygen release from the haemoglobin in the wound bed, which, in turn, increases the rate of granulation.⁴⁹

Other benefits of honey dressings are easy application and removal.⁵⁰ There is no adhesion to cause damage to the granulating surface of wounds³⁶ and no bleeding at removal of dressings.⁵¹

Tonks *et al* found that, the proliferation of peripheral blood B and T-lymphocytes as well as activation of phagocytes in cell culture are stimulated by honey at low concentrations. It can also stimulate monocytes to release cytokines, interleukin, IL-1, IL-6 and tumour necrosis factor alpha, which activate the immune response to infection.⁵²

CONCLUSIONS

As the incidence of diabetes mellitus and its complications including diabetic foot disorder is increasing, it is important to find effective alternative strategies both to minimise amputation rates and improve quality of life. Honey is very effective and extremely cost effective. It also decreases antibiotic use and chances of resistance. Further research is needed to study the active principles from honey to understand the

molecular mechanism of action and to standardise the use of honey as local therapy in human diabetic foot disorder.

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