



Wound healing with Apitherapy: A Review of the Effects of Honey

Michael Malone, Gary Tsai

Penn State Department of Family and Community Medicine, USA.

Address for correspondence:

Michael Malone,
Penn State Department of Family and Community Medicine, USA.
mmalone@hmc.psu.edu

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ABSTRACT

Recent studies have shown potential benefits of medical-grade honey in the treatment of burns or wounds due to its various antibacterial and anti-inflammatory properties, which enhance wound healing. Wounds have been shown to not only heal faster compared to conventional treatments, but also have decreased inflammation and reduced scar formation. As a result, honey has been used for the treatment of partial thickness burns, post-operative wounds, and diabetic-related ulcers, with favorable results. Besides being cost-effective, it is overall safe and has good tolerability. Although further studies are warranted, honey appears to be a low-risk therapy for wound management.

KEY WORDS: Honey, Apitherapy, Wound, Healing, Diabetic ulcer, Burn

INTRODUCTION

Honey is a viscous substance derived from nectar and modified by honey-bees. It has wound-healing and antibiotic properties that shows promise as an inexpensive option for moist wound-dressings for a variety of wounds. Throughout history, there have been records of many civilizations such as those in ancient Egypt, India, and Greece that have utilized honey as medicine and current medical literature indicates that there may be benefits in treating burns or wounds with honey[1]. This article will review and discuss the literature pertaining to the use of honey in wound management, to determine whether there is a place for honey in the treatment of this condition.

HONEY'S ANTIBACTERIAL AND WOUND-HEALING PROPERTIES

The broad spectrum antimicrobial activity of honey has been demonstrated in various studies. A systematic review by Vandamme et al in 2013, concluded that evidence is strong for antibacterial and healing properties[2]. Honey reportedly exerts both bacteriostatic and bactericidal activities and it inhibits bacterial growth[2,3,4]. Honey has been shown to have antibiotic properties to a wide range of bacteria, including MRSA, without causing injury to the wound tissue[5].

Honey's antibacterial properties are multifactorial, so resistance to its effect is not highly probable. It is believed that the properties of honey with its high osmolarity, low pH (3.5-5), and hydrogen peroxide, are effective in wound healing and inhibiting bacterial growth[6]. The hyperosmolarity of honey appears to inhibit bacterial growth by drawing fluids from wounds and causing bacterial

dehydration and death[7]. The presence of phenolic acid and flavonoids in honey may also contribute to the antibiotic properties of honey and offer anti-oxidant effects[6].

Besides having antibacterial properties, honey has been shown to decrease inflammation, bring about rapid autolytic debridement, and stimulate the immune response for healing[8]. Studies have shown that manuka honey upregulates tumor necrosis factor-alpha, interleukin-1b, interleukin-6, and prostaglandin E2 production, which in turn stimulate the production of monocytes, leading to wound healing with the removal of debris and formation of blood vessels[9].

While there is a good deal of evidence in regards to honey's antibacterial action, the mechanisms in how honey modulates the immune system is not as well characterized. A research article published by Majtan in 2013, showed that honey can stimulate or inhibit certain immune factors such as proinflammatory cytokines and matrix metalloproteinase-9 during the inflammatory and proliferative wound healing phase[10]. However, it can also prolong healing if the wound environment is infected and inflamed as well by suppressing the same immune modulators[10].

Long exposure to light or the heating of honey above 37°C should generally be avoided since its enzyme content is easily destroyed by exposure to both heat and light[11]. It is suggested to avoid storage of honey at a cool temperature and to avoid the use of plastic containers as chemicals may diffuse and contaminate the honey[12].

IS ALL HONEY THE SAME?

Because bees have different nutritional behavior and collect the nourishments from different and various plants, the

produced honeys have different compositions[1]. Therefore, different types of honey have different medicinal value leading to different effects on wound healing[1]. There are many types of honey, depending on the type of plants they are made from and may be raw, commercial, and medical grade. Raw honey is the least processed and has been used in the majority of case reports, although processed honey is regulated by the FDA and available in the supermarket[13]. Medical-grade honey approved by the FDA for wound healing is a little more expensive, about \$2 per ounce, but is often gamma-irradiated to inactivate spores[13]. Formulations have been sold as sterilized medical-grade honeys that are combined with other compounds to make one-time use dressings[9].

Many types of honey have been used help facilitate wound healing, although honey from different sources have varying antibacterial and anti-inflammatory properties. Manuka honey, from the *Leptospermum* tree genus, have been specifically targeted for their bactericidal properties. Manuka honey has an advantage over other honeys for the medicinal treatment of wounds[8]. This is because, in most honeys, the antibiotic activity due to hydrogen peroxide is inactivated by the enzyme catalase that is present in blood, serum, and wound tissues. In Manuka honey, however, the activity is due to methylglyoxal which is not inactivated[8]. Therefore, the Manuka honey's antibiotic effect is maintained despite dilution with substantial amounts of wound exudate[8].

USE IN WOUND HEALING

Given its potential to stimulate healing and antimicrobial properties, honey and bee products are promoted as appropriate alternative treatment for wounds. Honey also has the potential ability to minimize the odor of offensive-smelling wound[4,14]. The number of studies regarding the use of honey for wound healing is growing, although evidence for treating wounds is still limited. Therefore, future research will likely determine whether there is a significant place for its use in wound healing.

According to expert recommendations, when using honey as a wound dressing, honey should be evenly applied on the dressing pad rather than directly onto the wound[13]. If a non-adherent dressing is used, it should be porous enough to allow the diffusion of honey into the wound[15]. To debride hard eschar, dressings soaked in diluted honey can be applied to allow better diffusion of honey until debridement is achieved[3].

The required dosage of honey on the wound depends on the amount of exudates present. The frequency of dressing change is also generally determined by the amount of exudates and there is little evidence available to suggest an optimum frequency of dressing changes[7]. The beneficial effects of honey will be reduced if it is diluted by exudates. Therefore, the dressing must be changed whenever it is moist with exudate, which is typically multiple times per day. However, when the amount of drainage decreases, the

dressing can be left on for longer periods (4–7 days) between dressing changes[16].

EVIDENCE

Evidence for Overall Wound Healing

There have been reports of some case studies and clinical and randomized controlled trials which provide considerable evidences indicating the effectiveness of honey in wound healing. A 2013 multi-center prospective study involving 104 patient wound cases from 10 hospitals over 2 years, concluded that the honey dressings stimulated wound healing, reduced pain with subsequent dressing changes, and led to enhanced wound debridement[17]. Hypertrophic scar formation during wound healing may also be reduced or alleviated by honey[3]. A 2016 review and meta-analysis noted that compared with topical agents such as hydrofiber silver or silver sulfadiazine, honey is more effective in the elimination of microbial contamination, reduction of wound area, and the promotion of re-epithelialization[1]. In addition, honey improved the outcome of wound healing by reducing excessive scar formation[1].

Based on a 2013 systematic review, honey's effect on venous, arterial, pressure and diabetic ulcers, are inconclusive, but have shown reduction in wound size in at least 50% of the studies[2]. In a 2015 Cochrane review, honey appeared to heal infected post-operative wounds more quickly than antiseptics and gauze[18].

Evidence for Treatment of Burns

In animal studies, an ointment of honey, milk, and aloe vera (HMA) ointment increased the wound closure rate, blood vessel counts, and collagen fiber density in rats with second-degree burns[19]. It also reduced the wound secretions, inflammation, and scar formation[19].

A 2013 study looked at the management of burn wounds in human models by comparing the use of silver sulfadiazide cream to a medically formulated compound consisting mainly of honey also containing lanolin, vitamin C, E and polyethylene glycol[20]. In this study, the honey compound showed increased re-epithelialization compared to silver sulphadiazine cream, although it required an increased frequency of application[20].

A 2015 systematic review and meta-analysis of honey for burn wound healing concluded that honey was significantly more efficacious for wound healing than silver, as measured in the number of days needed for wounds to heal (CI -0.29 to -0.11, $p < .001$)[21]. A 2015 Cochrane systematic review noted that honey appears to heal partial thickness burns more quickly than conventional treatment (which included polyurethane film, paraffin gauze, soframycin-impregnated gauze, sterile linen and leaving the burns exposed)[18].

A retrospective analysis of 108 burn patients, with first and second degree burns of less than 50% of the total body surface area, concluded that honey dressings make the wounds sterile

in less time, enhance healing, and have a better outcome in terms of hypertrophic scars and postburn contractures, as compared to silver sulfadiazine dressings[22].

Evidence for use with Diabetic foot ulcers

Honey has some unique natural features as a wound healer, and may be even more effective on diabetic wounds than on normal wounds[7]. Although a small placebo-controlled trial showed a lack of honey’s effectiveness for the healing of diabetic ulcers, other studies have shown some improvement of diabetic ulcers with honey[23]. A small 30 patient prospective study to compare the effect of honey dressing for Wagner’s grade-II diabetic foot ulcers with controlled dressing group (povidone iodine followed by normal saline) showed a non-significant improvement in healing time for the honey group[24]. The study concluded that diabetic ulcer healing was not significantly different with honey compared to a povidone iodine dressing and honey dressing is a safe alternative dressing for Wagner grade-II diabetic foot ulcers[24].

A small study of the management of diabetic foot ulcers with natural honey showed excellent results in treating diabetic wounds with dressings soaked with natural honey. The disability of diabetic foot patients was minimized by decreasing the rate of leg or foot amputations and thus enhancing the quality and productivity of individual life[25]. A prospective observational study of 172 patients showed that honey wound dressings significantly reduced rate of amputation and improve wound healing when used for wound dressing in chronic diabetic foot ulcers[26].

TOLERABILITY AND PATIENT ACCEPTANCE OF HONEY FOR WOUND TREATMENT

High patient comfort and tolerability has been reported for the use of honey in wound treatment[7,27,28,29]. Studies have also shown no local or systemic atopic reactions to honey[7]. The most common side effect of honey is a burning or stinging sensation due to its low pH[15]. The sticky nature of honey may also be bothersome to patients. Besides being generally well tolerated, honey dressings also appear to offer cost savings, compared to alterative wound dressings[27].

Key Points:

- _____
- Honey has antibiotic and anti-inflammatory properties.
- _____
- Manuka honey is likely to be superior to other honey for medicinal wound healing.
- _____

Clinical Treatment Key Points:

| Clinical Recommendation | Strength of Recommendation (SORT) |
|---|-----------------------------------|
| Honey appears to heal partial thickness burns more quickly than conventional treatment | B |
| Honey appears to heal infected post-operative wounds more quickly than antiseptics and gauze. | B |
| Honey may help heal diabetic ulcers and may reduce amputation rates | B |

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