



Review

Biological properties and therapeutic activities of honey in wound healing: A narrative review and meta-analysis



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Abstract For thousands of years, honey has been used for medicinal applications. The beneficial effects of honey, particularly its anti-microbial activity represent it as a useful option for management of various wounds. Honey contains major amounts of carbohydrates, lipids, amino acids, proteins, vitamin and minerals that have important roles in wound healing with minimum trauma during redressing. Because bees have different nutritional behavior and collect the nourishments from different and various plants, the produced honeys have different compositions. Thus different types of honey have different medicinal value leading to different effects on wound healing. This review clarifies the mechanisms and therapeutic properties of honey on wound healing. The mechanisms of action of honey in wound healing are majorly due to its hydrogen peroxide, high osmolality, acidity, non-peroxide factors, nitric oxide and phenols. Laboratory studies and clinical trials have shown that honey promotes autolytic debridement, stimulates growth of wound tissues and stimulates anti-inflammatory activities thus accelerates the wound healing processes. Compared with topical agents such as hydrofiber silver or silver sulfadiazine, honey is more effective in elimination of microbial contamination, reduction of wound area, promotion of re-epithelialization. In addition, honey improves the outcome of the wound healing by reducing the incidence and excessive scar formation. Therefore, application of honey can be an effective and economical approach in managing large and complicated wounds.

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1. History and background

Throughout history, honey has been well used for medicinal applications. Islamic traditions, ancient Egyptians, ancient Greek, Chinese and other countries and nations have used honey as a remedy for every illness [1]. In modern history and in World War I, honey was used for repair of battle wounds. For the first time in 1892, antimicrobial properties of honey were noted by Van Ketel. The role of honey in healing of infected wounds was first reported in Europe and USA in the mid-20th century [2,3]. However in the last decades and by development, introduction and wide application of modern antibiotics, the application of honey was reduced in a modern medicine. Advent antibiotic-resistant bacteria and the potent activity of honey against them renewed interest for its medical application [3]. Since then, many studies have shown that honey has several medicinal properties. For instance, honey is an anti-microbial agent, promotes autolytic debridement, stimulates growth of wound tissues to hasten healing and healing process in dormant wounds and finally initiates anti-inflammatory activity that rapidly reduces pain, edema and exudate production [4,5].

In this review, an overview of the current knowledge on the healing properties of honey has been illustrated and the mechanisms of action and therapeutic properties of honey in wound healing have been discussed in detail. In addition, the most recent and valuable clinical trial studies used honey for treating various wounds have been reviewed and discussed in order to find out whether honey is a valuable option for wound healing, modeling and remodeling.

2. Therapeutic properties of honey

Honey, due to its antimicrobial, anti-inflammatory and antioxidant activities, boosting effect on immune system, debridement action and stimulating role in wound regeneration, significantly contributes in wound healing processes (Fig. 1, Table 1). Below, these beneficial biological properties have been discussed in detail.

2.1. Antimicrobial activity

The use of substances produced by honey bees (*Apis mellifera*), including propolis, honey, wax and venom in wound management has a long history which belongs to many centuries ago [6–8]. When the body's immune response is unable to

clear infection, antimicrobial therapy is considered [9]. Silver dressing has been used for managing wound infections particularly in the burn wounds because of its antibacterial properties; however components such as silver sulfadiazine may delay wound healing [10]. So far, many compounds have been evaluated for their antibacterial properties [11–13]. It is believed that honey can be used as a suitable alternative option for managing various infected wounds [14,15]. However, it should be kept in mind that bees with nutrition of various plants create different types of honeys [1,16]. The compositional differences of honeys can influence their medicinal value. Brudzynski et al. [17] analyzed bactericidal activity of eight honeys (six varieties of buckwheat, blueberry and manuka honeys). They suggested that the dose of honey is important in its bactericidal efficacy and the maximal bactericidal effect occurs with degradation of bacterial DNA. The manuka and buckwheat honey showed bactericidal effect at the range of concentrations between 6.25% and 50% v/v, while bactericidal effect was observed only at the highest concentration tested (50% v/v) for blueberry honey. Finally, they concluded that honeys of buckwheat origin, dose dependently possess powerful bactericidal effect [17].

In the recent years, much more interests are seen for evaluating the effects of honey on the antibiotic-resistant organisms. Indiscriminate use of antibiotics and advent resistant strains has a considerable effect on patient's morbidity and mortality [16,18,19]. The emergence of antibiotic-resistant microbial strains can be an alarm that wound infections may once again become uncontrollable. Honey is a realistic antimicrobial in the treatment of infections. Theoretically, the increased use of honey can promote honey resistance, but to date, no honey resistant microbial strain has emerged and a possible explanation for this might be due to the multifactorial nature of the antimicrobial properties of honey that affects more than one target site [20–22]. Compared with other antimicrobial agents, honey produced a unique expression signature on the gene expression of *Escherichia coli*. Most of the genes upregulated by Medihoney, are involved in stress responses and the majority of downregulated genes encoded for products, are involved in protein synthesis. These findings confirm that honey works by a different mode of action than the other conventional antibiotics [23].

It has been shown that biofilm biomass that was treated with manuka honey increased bacterial resistance, which is possibly due to the appearance of small colony variants within the microbial

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