Honey in Advanced Wound Care

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The clinical considerations in wound-healing management include preventing and controlling the infection and/or contamination, maintaining the adequate moisture environment, treating edema, and preventing further injury. Conventional chronic wound care involves debridement to remove non-viable tissue and bacterial biofilms, followed by wound dressing. The common wound dressings consist of a standard cotton bandage or highly absorbent dressings, such as collagen and alginate, or hydrocolloids; however, this procedure of wound care is often ineffective.

Keywords: honey ; wound-healing ; antioxidant ; antimicrobial ; hydrogels ; dermal repair ; hydrogel

1. Introduction

Prolonged chronicity of wounds is normally related to a bacterial injured-tissue colonization, which can progress into a bacterial resistance to topical and systemic antimicrobial agents, or into biofilm development, which complicates, in both cases, their treatment [1]. In the end, this type of wound can cause sepsis and inflammation in organs and lead to increased morbidity and mortality.

Several case studies and randomized controlled trials provide considerable evidence of the effectiveness of honey in healing different types of wounds, such as amputation wounds, burns, skin grafting sites, skin lesions, or skin ulcers including leg, varicose, malignant, diabetic, and sickle cell ulcers [2][3][4][5].

However, the use of honey by itself might present some limitations which are being overcome with the development of different honey formulations and honey wound dressings.

This encyclopedia entry aims to highlight the mechanism of honey's action in wound healing and gather the literature available regarding the use of honey and modern engineering templates for promoting modern solutions for wound and skin healing and regeneration.

2. The Mechanisms of Honey in Wound and Burn Healing

Several studies have demonstrated, in vitro and in vivo, the efficacy of different varieties of honey against a broad spectrum of bacteria, including those that commonly caused wound and burn infections, such as Staphylococcus aureus , Pseudomonas aeruginosa , Escherichia coli , Acinetobacter baumannii , or Staphylococcus epidermidis [1][5][6][7][8][9]. In addition, honey has also been demonstrated to be effective against antibiotic-resistant bacteria [10][11][12][13], as well as against biofilms by preventing the formation and the development of the biofilm [14][15][16][17][18], by reducing the metabolic activity of already formed biofilms [15][19], or by altering the gene expression of different genes related to the formation and the development of biofilms [19][20], and is related to the bacterial quorum sensing [20][21].

Another advantage of the anti-inflammatory action of honey is the decrease in edema, thus reducing the pressure on the microvasculature of wound tissue that allows the availability of oxygen and nutrients required for growth of tissue and wound repair [22]. This effect also allows the control of the wounds' exudate with an appropriate moisture balance, which is still a constant challenge in the healing processes [8].

The anti-inflammatory activity of honey has been mainly attributed to phenolic compounds [23][24]. However, until now, no correlation was found between the level of anti-inflammatory activity in different honey samples and the phenolic compound content [25], which might be due to the distinct types of interactions that can occur among these compounds and other compounds present in honey.

On the contrary, another study has demonstrated the anti-angiogenic activity of honey is mediated by the modulation of prostaglandin E 2 and VEGF production [26]. This disparity among studies might be explained by the honey concentration tested, since the highest pro-angiogenic effect was found in a low concentration of honey, whereas higher concentrations demonstrated anti-angiogenic activity [27].

3. Safety of Honey Used for Topical Treatment

The extensive scientific evidence proves that honey may offer distinct advantages over the chemotherapeutic substances currently used in the wound- and burn- healing processes. However, this natural product shows a series of limitations, and is not completely free from adverse effects.

The composition of honey is rather variable, depending primarily on the botanical origin, and secondarily on other factors such as geographical origin, or harvesting, processing, and storage conditions [7][8]. This variability determines its bioactive properties, and consequently influences the therapeutic efficacy of the wound treatment [8]. In addition, the absence of standardization and the incomplete knowledge of the active components, and the mechanisms through which they interact and act in wound healing, are the major limitations for the application of honey in medicine. For this reason, is essential to select the more appropriate varieties of honey, and it is recommended to carry out a previous screening [7].

In addition, other considerations must be considered before honey application in wounds. The low pH, derived from the presence of organic acids in honey, may contribute to a stinging or burning sensation when it is applied to a damaged tissue [28]. Besides this unpleasant sensation, it is necessary to consider that, although minor, there is a risk of wound infection, mainly related to the presence of clostridial spores which have occasionally been found in honey [8][29]. This risk can be reduced by using gamma-irradiation, which inactivates the spores without modifying the original biological activity [30][31]. Nevertheless, no cases of wound infection due to clostridial spores related to the use of non-irradiated honey on wounds have been reported to date.

Furthermore, the honey used for medical purposes must be free of any chemical contamination, such as pesticides, herbicides, or heavy metals. In this sense, to guarantee the maximum purity, honey should be collected in areas that meet the requirements for organic production, as well as following rigorous quality, processing and storage standards [32][10]. In addition, is necessary to consider that some varieties of honey might present toxic active compounds originating from the nectar of species such as rhododendron, oleanders, mountain and sheep laurels, or azaleas. However, these effects have been described by honey ingestion [33][34].

4. Biomedical Application of Honey in Advanced Wound Care

The FDA-approved honey-based devices are indicated in the treatment of different types of wounds, such as low and moderate-to-heavy exuding wounds, diabetic foot ulcers, leg ulcers, pressure ulcers, burns, traumatic wounds, surgical wounds, chronic wounds, or colonized acute wounds, among other indications [5]. Despite the availability of these products, their use in medical practice is still limited, probably due to the misconception that there is no evidence to support the use of honey with therapeutic purposes, as well as the scarce promotion and diffusion of honey products for wound care [22].

The medical-grade honey, as well as the ointments and gels, is applied to the wound bed and requires a secondary conventional dressing (e.g., cotton wool bandage) to contain the honey in the wound bed environment, which on removal cause pain [35].

Tissue engineering has recently introduced wound dressings/scaffolds as an alternative treatment of wounds with advanced properties, suitable for keeping a moist environment while absorbing exudates, creating a barrier against pathogens, and facilitating drug delivery systems [36].

In addition, hydrogel wound scaffolds containing honey do not function merely as coverage to provide a clean, moist environment for healing, but also directly contribute to enhanced tissue regeneration and recovery [37].

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