Potential of Malaysian Stingless Bee Kelulut Honey in Wound Healing

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Abstract

Lower limb amputations due to non-healing persistent diabetic foot ulcers (DFU) are becoming more common due to poorly controlled diabetes, infection, antibiotic resistance, and the ineffectiveness of current treatment approaches. Diabetes-based foot complications have affected millions of patients worldwide and have become a financial burden to developing countries as the cost of treatment is expensive, lengthy, and require extensive hospital admissions. The development of alternative treatment was unquestionably necessary given the profound severity of DFU complications. One of the ancient remedies which have re-emerged of late is honey as it has been proven to contain antibacterial, inflammatory, and moisturizing properties to enhance healing in chronic wounds. Currently, medical-grade manuka honey is being used in healthcare settings for the treatment of burns and wounds. Despite better antioxidant capacity and similar therapeutic qualities, stingless bee honey has received less attention in the field of chronic wound management. Therefore, this study was conducted to determine the efficacy of local stingless bee kelulut honey in the treatment of DFU. Thirty adult diabetic patients with chronic DFU participated in this experimental study, which was carried out in a tertiary hospital. Kelulut honey was applied to the wound and covered with a sterile gauze dressing. The dressing was changed every other day and observed for a week. Wound size was measured at baseline and the end of the one week. The outcome demonstrated a statistically significant percentage reduction in the wound size after one week, with no adverse effects noted and no de-sloughing being necessary during the one week. Hence, kelulut honey was concluded as a potential wound dressing that could be explored further to improve healing outcomes in DFU and prevent foot complications.

Index Terms— amputation, foot ulcer, healing, honey, stingless.

1. Introduction

Diabetes-based foot complications can result in severe consequences such as infection, gangrene, and lower extremity amputation. are two of the most common causes of disability and death in diabetics [1], [2]. With 25% of diabetics developing DFU, this type of chronic wound not only impose a significant financial burden on patients but can also have a negative impact on their quality of life [3]. Intractable wounds caused by antibiotic-resistant microbial infections place a significant strain on global healthcare systems. An aging population, as well as rising diabetes and obesity rates around the world, have all contributed to the current

burden of chronic wounds [4]–[6]. Infected DFUs that do not heal can cause sepsis and increase morbidity and mortality. Moreover, the presence of biofilms in chronic wounds makes them more resistant to antibiotic therapy because the bacteria are protected by an extracellular polymeric barrier [7], [8]. The healing outcome of chronic DFU is very much related to the wound-healing process itself as chronic wounds do not follow the general process which includes hemostasis, inflammation, tissue proliferation, and regeneration. This type of wound gets stuck in the inflammatory stage, gets infected, becomes resistant to antibiotics, and takes a long time to heal [9]. To address the serious public health issue of antimicrobial drug resistance, the development of novel antimicrobial medications or novel therapeutic methods is critically required.

A variety of measures, including debridement, blood glucose control, advanced modern dressings, and infection prevention, have been used in the management of DFUs [10]. However, the clinical effectiveness of these methods was still unsuccessful in treating chronically resistant DFUs Technological advancements had brought forward new treatments for DFUs in the form of modern dressings in the past two decades [11]. A diverse range of modern dressings including alginates, hydro fiber, hydrogels, foams, and silver had been made available to the wound care field but there is not much choice available, as infection and chronic wounds dominate. Wound dressing with potential antibacterial properties had been accepted widely as an important part of managing DFUs as faster healing means preventing foot complications. Clinicians have increasingly recognized the importance of selecting suitable wound dressings which could inhibit microbe propagation and improve the healing rate [12]. The healing outcome of chronic DFU is very much related to the wound-healing process itself as chronic wounds do not follow the general process of hemostasis, inflammation, tissue proliferation, and remodeling [13]. If the healing process of acute wounds gets disrupted, then wounds get stuck in the inflammatory stage and turn chronic [14]. Therefore, interest has been resurgent for new alternative treatment modalities with more healing potential and antibacterial properties.

The search has certainly attracted many researchers worldwide and one such traditional remedy which made a came back is honey. It is one of the earliest natural biological remedies for wound healing and burns [15]. Due to its numerous antibacterial components and methods, honey is unlikely to cause bacterial resistance because it can destroy antibiotic-resistant bacterial strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) [16]. The ability of honey to promote angiogenesis, re-epithelialization, and the stimulation of skin and immune cells all contribute to its ability to aid in wound healing. The term "medical grade honey" refers to honey that has been sterilized using gamma irradiation, is produced by safety norms and standards, and is suitable for use in medicinal applications [17]–[19]. Medical-grade manuka honey produced by honeybees (*Apis mellifera*)from New Zealand has been used in the clinical treatment of burns and wounds and is potentially more effective than conventional dressings or antiseptics in post-operative, partial thickness burns and chronic wounds [20]. Despite available findings pointing to the efficacy of medical-grade manuka honey in some type of wounds, there was still insufficient significant findings for the treatment of DFU.

As each honey is unique, there is a need to explore less common honey with stronger wound-healing properties to treat foot complications in DFU. One such honey is stingless bee honey,

derived from the tribe Meliponini of the family Apidae, which included a varied range of highly sociable bees [21]–[23]. As their common name implies, stingless bees are so-called because they lack stingers, in contrast to *Apis mellifera* bees, which are known all over the world for producing conventional honey [24]. The color, flavor, and viscosity of stingless bee honey vary from that of the genus *Apis spp.* It was shown that honey from stingless bees has higher free acidity and moisture levels than *Apis mellifera* but lower pH than existing standards [25], [26]. These bees originated from Africa. Two distinct tribes of these bees included Meliponini, found only in the Neotropics and the majority of the stingless bees Trigonini tribe can be found in tropical and subtropical climates like Malaysia, Brazil, Mexico, Africa, Northern Australia, and Southeast Asia [27], [28]. The practice of beekeeping with stingless bees is well-known in tropical nations like Malaysia, Thailand, Mexico, Venezuela, Brazil, and Australia [25], [29]. Studies on kelulut honey have been less widespread despite demonstrating a strong body of shreds of evidence on anti-oxidant potency which could be utilized to improve wound healing outcomes[30], [31]. Moreover, stingless bee honey has similar therapeutic properties to honeybees [32]–[35]. Therefore, this experimental study was conducted to evaluate the efficacy of locally produced stingless bee honey from *Trigona itama* known as kelulut honey in the healing of DFU.

2. Methodology

This experimental study was conducted in one of the oldest tertiary teaching hospitals in Malaysia, University Malaya Medical Centre (UMMC) for 10 months. A total of 30 adult diabetic participants with DFU of more than one month with a SINBAD score of 3; no limitations to gender, age, or site of ulcer were enrolled in the study. Exclusion criteria included participants with sepsis, PAD, and ABI below 0.4. Kelulut honey produced by local stingless bee *Trigona itama* collected from Dinokelulut, in Kuala Pilah was used for honey dressing. The properties of this kelulut honey include a pH of 3.3, sucrose 4.4 mmol/l, fructose 5.5 mmol/l, glucose 5.2 mmol/l, and moisture of 30.7g. All participants with infected wounds were treated with appropriate oral antibiotics. Wound debridement was done with maggot debridement therapy before honey application. All the wounds were measured before kelulut honey application by the study team which included staff nurses and orthopedic doctors. The wounds were cleansed with normal saline and a thin layer of kelulut honey was spread over the wound and covered with sterile gauze and bandaged. If the wound is highly exudative, gamgee was used as a secondary dressing. Wound observation was done after one week and size was measured for all wounds. The percentage of wound size reduction was used as the benchmark to evaluate healing outcomes with kelulut honey dressing. If the chronicity of the wound worsened, such as increased infection, presence of more slough and necrotic tissue, and pus accumulation, and requires surgical debridement then intervention with kelulut honey dressing is considered ineffective.

3. Result

There were more males (60%), with an average age of 65 years old, and poorly controlled diabetes (HbA1c 8.0 mmol) with an average wound size of 30cm^2 in the study population. 240ml of kelulut honey was used for all the 30 participants in the study Wound measurement showed there was a size reduction of 20% calculated based on the differences in size after a week from baseline. The outcome of the study yielded a significant percentage size reduction with 80% of wounds showing positive outcomes (24 participants) whereas 6 participants

(20%) showed no changes. Healthy granulation without slough was observed in the wounds. Foul odor reduced in the one week of observation. None of the wounds worsened in terms of increased swelling, surgical intervention, and pain during the period of study.

4. Discussion

In this study, participants with SINBAD score 3 DFU were recruited as these were chronic, deep infected wounds that were at risk for amputation. Despite the chronicity of the DFU, the outcome of the study indicated that kelulut honey dressing was potentially effective in improving the healing outcomes of a chronic wound. The outcome of the study concurred with the pieces of evidence from previous studies on stingless bee honey which indicated a variety of therapeutic benefits for wound healing that was similar to medical-grade manuka honey [27], [28] which included antimicrobial, anti-inflammatory, but with higher anti-oxidant to overcome antibiotic resistance and positively useful in wound healing [21], [38], [39]. The high concentration of polyphenol chemicals in kelulut honey, in general, makes it effective in promoting cell division, safeguarding the cellular structure, and scavenging free radicals at the wound site as shown in several studies [40], [41]. Due to the acidic pH of kelulut honey, kelulut honey could be the potential dressing in the inhibition of bacteria and pathogenic organisms and enhance epithelialization for faster closure [42]–[45].

Moreover, the honey was able to keep the wound moist which befits the modern wound management concept, while preventing adherence to the granulating surface [46]. Hence, dressing change was done with ease and with less discomfort or pain. Given the osmolarity of kelulut honey, it could absorb water from surrounding tissues in the wound bed and stimulate local lymphatic drainage and improve blood circulation which could be the rationale behind the reduction of edema and pain in the study population.

5. Summary

It is common knowledge that almost all bee products include a wealth of nutrients and medicinal properties. Kelulut honey has gotten less attention than those from other honey producers especially honeybees as not all species of bees have been the subject of equal research. Despite the shorter duration of observation, the findings of this study could be a preliminary significant outcome in the evaluation of kelulut honey as a potential topical wound dressing in the treatment of DFU. Further research should be done with a bigger sample and a longer duration of the study. Kelulut honey should be explored for managing chronic, infected wounds and its cost-effectiveness in public healthcare settings. Moving forward, kelulut honey should be reframed and recognized as a potent wound dressing to manage antibiotic resistance, expedite healing and prevent the catastrophic impact of diabetes-based foot complications.

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