Wound-Healing Effect of Honey Gel and Film

Febriyenti Febriyenti, Henny Lucida, Almahdy Almahdy, Istianah Alfikriyah, Muhammad Hanif

Department of Pharmaceutical Technology, Faculty of Pharmacy, Universitas Andalas, Padang 25163, Indonesia

ABSTRACT

Background: Honey has been formulated into gel and film dosage forms for burn wound as previously reported. Aims: In this study, we evaluated the ability of honey gel and film to promote the healing of burns and incision wounds on the skin of Sprague-Dawley female white rats. Materials and Methods: Twenty-four female rats were divided into four groups, which were treatment groups (for honey gel or film), negative control, and positive control (treated with marketed product “B”), respectively. Burn and incision wound were created by the method previously reported with slight modification. Parameters such as the percentage of wound closure and the tensile strength of the incision wound were determined. Results: The experimental results showed that honey film has a greater effectiveness to accelerate the healing for burns and incision wound in comparison to the negative control. Conclusions: Two-way analysis of variance indicates the type of treatment group, and time has a significant effect on the burn wound ($P < 0.05$). Honey film shows the significant difference ($P < 0.05$) with other group on the incision wound.

KEYWORDS: Burn wound, honey film, honey gel, incision wound, wound healing

INTRODUCTION

Honey is a natural fluid produced by bees or wasps, which generally has a sweet taste and is used as a natural sweetener. Honey has also been used as a medicine for thousands years ago. Several studies reported that honey can be used to heal the wounds.[1-6] The glucose oxidase enzyme catalyzes the oxidation of glucose to gluconic acid, which causes a decrease in the honey pH so as to inhibit the growth of pathogenic bacteria. The end result of the glucose oxidase system is hydrogen peroxide; at low concentration, it is effective against various bacteria.[2,7,8] Honey is an antibacterial and antioxidant, and has a high content of nutrients such as carbohydrates that can inhibit the growth of microbes.[1,9] In a study in India, honey has been used in wound healing. It is mainly because honey provides a moist environment that promotes healing and stimulates tissue regeneration, and has a high osmolarity, high glucose levels, and some other organic components. Honey also has a similar composition to the substances needed by humans, thus it is not considered as a foreign object.[8,10]

Wound is described as destruction of normal anatomic structures of tissue, which can be divided into open and closed wounds. This condition can be caused by sharp objects or blunt trauma, extreme temperature, chemicals, explosion, electric shock, or animal bites.[11,12] Many methods have been developed for healing wounds such as wounds cleaning, suturing, using high-dose antiseptics, and also dressings using absorbent material. One of the methods for treatments of burns healing is a topical antibiotic therapy because the burns are extensive scar, thus facilitating the growth of bacteria. In this case, honey can act as an antimicrobial agent due to the high sugar content with relatively acidic pH and low protein content. Thus honey limits the amount of water available for microbial growth and can inhibit the growth of bacteria.[4,8,11]

Many dosage forms have been formulated to deliver the active ingredient to the wound and to function as

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Address for correspondence: Dr. Febriyenti Febriyenti, Faculty of Pharmacy, Kampus Limau Manis, Universitas Andalas (UNAND), Padang 25163, Indonesia.

E-mail: febriyenti@phar.unand.ac.id, febriyenti74@gmail.com

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wound dressing,[13-15] such as honey gel and film that have been formulated by Febriyenti et al.[16] In this study, we evaluate the effectiveness of the honey gel and film to accelerate the healing of burns and incision wound.

MATERIALS AND METHODS

Materials

Honey was bought from Madu Hutan Asli Fauzan Padang Sidempuan, Indonesia. Polyvinyl alcohol (PVA) was bought from VWR International, Belgium. Propylene glycol, glycerine, and methylparaben were acquired from RandM Chemicals (Essex, United Kingdom). Normal saline 0.9% was purchased from Widatra Bhakti, Indonesia. Ethanol 96% was bought from Brataco, Indonesia. Ether was purchase from Merck, Germany. Catgut was purchased from GEA Medical (Jakarta, Indonesia). All chemicals were used without further purification. Sprague-Dawley (SD) rats were provided by the Animal House of Andalas University (Padang, Indonesia).

Preparation of honey gel and film

The honey gel and film were prepared using the method that was described by Febriyenti et al.[16] PVA was used as polymer. Honey gel was prepared using propylene glycol as humectants. Glycerin was used as plasticizer for honey film.

Animals

The housing and handling of the rats followed the protocol described by Deacon,[17] Olfert et al.,[18] and Lansdown.[19] All the procedures included for the animals studies have been approved by the Animal Ethic Committee, Andalas University, with Ref. No. 035/KEP/FK/2015.

Burn wound model

Second-degree burn wounds were created using method of Priya et al.[20] and Laila et al.[21] with slight modification. The rats were anaesthesitized with ether by inhalation route. The test used 24 female SD rats, which were divided into 4 groups; each group consisted of 6 rats. Groups 1 and 2 were the treatment groups, which were given the honey gel and honey film, respectively. Group 3 was a negative control group (untreated). And group 4 was a positive control group (comparison), which was treated with marketed product “B.” Each group consisted of 12 rats. Honey gel, honey film, or marketed product “B” was applied every day. Rats were killed at intervals of 3, 6, 9, and 12 days after wounds creation, and tensile strength analysis was performed on the same day.[21,24] Tensile strength of wounds was calculated using the following formula:[28]

\[
\text{Tensile strength} = \frac{\text{Breaking load (force)}}{\text{cross-sectional area}}
\]

Where

Cross-sectional area = thickness \times width of skin strip.

Statistical analysis

Results of wound closure and tensile strength test were represented as mean ± SD. Two-way analysis of variance (ANOVA) for burn wound and one-way ANOVA (SPSS 16.0) for incision wound followed by Duncan post hoc test were used to identify differences between groups. It showed a statistical difference if \(P < 0.05\) was obtained.

RESULTS AND DISCUSSION

Incision wound model

Incision wounds were created using the method of Baie and Sheikh,[24] Mukherjee et al.,[25] Reddy et al.,[26] Singh et al.,[27] and Laila et al.[21] with slight modification. After wound creation, the rats were randomly divided into four groups. Groups 1 and 2 were the treatment groups, which were given the honey gel and honey film, respectively. Group 3 was a negative control group (untreated) and group 4 was a positive control group (comparison) that was treated with marketed product “B.” Each group consisted of 12 rats. Honey gel, honey film, or marketed product “B” was applied every day. Rats were killed at intervals of 3, 6, 9, and 12 days after wounds creation, and tensile strength analysis was performed on the same day.[21,24] Tensile strength of wounds was calculated using the following formula:[28]

\[
\text{Tensile strength} = \frac{\text{Breaking load (force)}}{\text{cross-sectional area}}
\]

Where

Cross-sectional area = thickness \times width of skin strip.

This study aimed to determine the ability of the honey gel and film to promote the healing of burns and incision wound on the skin of SD female white rats. The parameters observed in this study were percentage of wound closure for burn wound and tensile strength of wounded skin for incision wound.[21] There was no infection on the burn and incision wound, observed visually.

The average of wound area for all groups was measured on days 0–26. All animals tested on the honey gel group were healed and had 100% wound closure on the day 25, whereas the other group had not reached
Inflammatory phase had occurred on days 0–5, which was characterized by inflammation on the wound. But in the test group, the inflammatory phase did not affect the increase in the wound size. Inflammation serves to control bleeding, prevent bacterial invasion, remove debris from the injured tissue, and prepare to continue healing process. In this phase, honey film group experienced a higher percentage of wound closure compared with other groups (10.47% ± 4.38). It is because the honey film can prevent the invasion of bacteria into the wound by covering the wound surface as a wound dressing.

**Figure 1:** Photographs of burn wounds

![Figure 1: Photographs of burn wounds](image)

**Figure 2:** Percentage of wound closure

![Figure 2: Percentage of wound closure](image)
Honey contained in the film plays an important role in this phase to sterilize the wounds due to the production of hydrogen peroxide that is effective to kill the bacteria. Honey also stimulates the immune system by stimulating B lymphocytes and T lymphocytes and activates neutrophils, supplying glucose for respiration and the production of macrophages. Then, the proliferative phase at day 6 until day 21 was characterized by the movement of epithelial cells and fibroblasts into the injured area to replace the lost tissue and collagen synthesis. In this phase, the negative control group had the highest percentage of healing than other groups as seen at day 21 (81.78% ± 9.47). These results indicated that the administration of the honey gel, film, and marketed product had not significantly affected the promotion of the healing process. The last phase was the maturation phase that took place from day 21 until the wound was healed. This phase involved the formation of connective tissue and epithelial reinforcement. In this phase, the honey gel group had a greater percentage of wound closure compared to other groups. This is because honey in the gel stimulates the healing process by stimulating the promotion of granulation tissue, cell proliferation, and collagen synthesis induced by the nutritional content of honey such as protein, glucose, vitamins, and minerals.

Dosage form also affects the healing time. Gel dosage form with a hydrophilic base will induce drug penetration into the skin whereas the film dosage form serves as a wound dressing. Percentage of wound closure on day 1–13 was used for data analysis. It because the second-degree burns usually has healed after 10–14 days. In addition, acceleration of wound-healing effect of honey is more dominant due to the antibacterial properties of honey. The antibacterial property of honey is given by the presence of hydrogen peroxide resulted from the glucose oxidase enzyme activity. Hydrogen peroxide in honey prevents bacterial invasion, helps sterilizes, removes debris wounds, and stimulates macrophages, lymphocytes, and neutrophils, which accelerate the inflammatory phase of the wound. Hydrogen peroxide also stimulates angiogenesis and growth of fibroblasts and epithelial cells involved in the migration and proliferation phases.

The results of tensile strength test of the wounded skin could be seen in Figure 3. Data analysis using one-way ANOVA showed a significant result (P < 0.05) at day 6. Honey film gives the highest tensile strength followed by honey gel. It means that the honey film provides a good condition as wound dressing to promote the healing process. Honey film could provide good humidity at the surface of wound that promotes the movement of epithelial cells and fibroblast into the injured area to replace the lost tissue and collagen synthesis. Honey inside the film also could act as an antibacterial to prevent the infection.

**Conclusions**

Honey film has a greater effectiveness to accelerate the healing of burns and incision wound when compared to the negative control. The results of two-way ANOVA indicate the treatment type and time have a significant effect on the burn wound (P < 0.05). Honey film shows the significant difference (P < 0.05) with other group on the results at tensile strength test of the incision wounded skin.

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**Conflicts of interest**

There are no conflicts of interest.

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