The Efficacy of Topical Application of Sumbawa Forest Honey for Wound Healing: Study on Incision Wound of Balb/C Male Mice

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Abstract: Topical application of honey has a well-known effect for wound healing. The benefits of honey include preventing infection, moisturizing, reducing inflammation, and stimulating tissue regulation and repair. One of the largest sources of honey in Indonesia is Sumbawa Island. In vitro studies suggest that Sumbawa forest honey possess antioxidant activity and ability to inhibit the growth of *Staphylococcus aureus* in surgical wound infections. The purpose of this study was to determine the efficacy of topical application of Sumbawa forest honey on incision wounds of BALB/c male mice. This was a double blind randomized control trial. The subjects of this study were BALB/c male mice that met eligibility criteria. The study group was divided into 3 groups; treatment group with topical application of Sumbawa forest honey, control group with 10% povidone iodine solution and group with no treatment. From the statistical analysis, $p = 0.017$ was obtained. There was a significant difference between the mean of wound length of this 3 groups. In the Mann-Whitney Post-hoc test results, there was a significant difference between the mean of wound length in the treatment group and the control group ($p = 0.022$) also between the treatment group and untreated group ($p = 0.009$). The topical application of Sumbawa forest honey can accelerate the healing of incision wound on BALB / c male mice.

1 INTRODUCTION

Honey is a natural product produced by honey bees (Yaghoobi & Kazerouni, 2013). Honey has many health benefits, especially in wound care. Studies by Medhi (2008) and Ghaderi (2004) suggested that honey has significant efficacy in wound management. Topical application of honey can enhance wound healing by preventing infection, reducing inflammation, and stimulating tissue regulation and repair. In addition, it also does not require a sterile environment because honey has a bactericidal property. Honey also has a high viscosity, thus acting as a protective barrier and forming a moist environment that helps and accelerates wound healing (Ghaderi & Afshar, 2004, Medhi et al., 2008).

Honey is produced in various parts of Indonesia. One of the biggest sources of honey is the island of Sumbawa. Honey produced in Sumbawa island classified as forest honey. Sumbawa forest honey is a type of pure honey derived from *Apis dorsata* bees that cannot be cultivated. The potencials of Sumbawa forest honey is associated with the condition and typology of forests in Sumbawa. The highest potential honey in Sumbawa produced in forest with relatively good condition, typically damp tropical forests characterized by *Boan* trees (the name for tall trees that have beehives). This species of *Boan* tree covers 45% of the protected forest area in Sumbawa. Sumbawa forest honey were taken during the day and were still processed traditionally by the local community (Maryani et al., 2013; Julmansyat et al., 2009).

Sumarlin's study (2014) showed the presence of antioxidant activity in Sumbawa forest honey (Sumarlin et al., 2014). In addition, in vitro research by Zulhawa (2010) suggested that Sumbawa forest honey can inhibit the growth of *Staphylococcus aureus* in surgical wound infections. Therefore, this study aims to determine the efficacy of topical application of Sumbawa forest honey on healing of incision wound in BALB/c male mice.

2 METHODS AND RESULTS

This research used double blind randomized control trial. The subjects of this study were BALB/c male

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mice with inclusion criteria aged 2-3 months, weight 20-40 grams and had no physical disability. Exclusion criteria were mice with hyperglycemia and hemostasic disorders. This research was conducted in the Integrated Animal Laboratory, Faculty of Medicine, University of Mataram in September 2017. This research was approved by the Ethics Committee Faculty of Medicine, University of Mataram. This research was divided into 3 stages: (1) adaptation and intervention stages, (2) measurement of the remaining length of the wounds and (3) data analysis.

Before making an incision wound, 31 mice underwent adaptation stage. In this stage, they were fed with the same feed for one week. Afterwards, during the intervention stage, the back area of the mice was first shaved and body weight and blood glucose levels of mice were measured. The mice were then divided randomly into 3 groups: 12 mice in the treatment group with topical application of Sumbawa forest honey (KP), 12 mice in the control group with 10% Povidone iodine solution (KK) and 7 mice in the untreated group (KN). A two centimeters incision was made on each mice using a sterile scalpel, and after the bleeding was controlled, the treatment in each group was continued. The intervention in the three study groups was conducted once daily until the 21st day at the same hour. The time of incision and the first intervention was expressed as day 0.

The second stage is the measurement of wound length. This was done macroscopically on day- 0,1st ,3rd ,7th ,14th and day-21st , using a centimeter scale ruler and taken at the same hour.

The data analysis was performed by using non-parametric statistical test Kruskall-Wallis. Further, a Post-hoc Mann-Whitney test was conducted to see the significant difference between each of the two study groups

3 RESULT

The result of the measurement of the mean of length of remaining wound incision on day- 0,1st ,3rd ,7th ,14th and day-21st on 31 male BALB/c male mice can be seen in Figure 1 and Table 1.

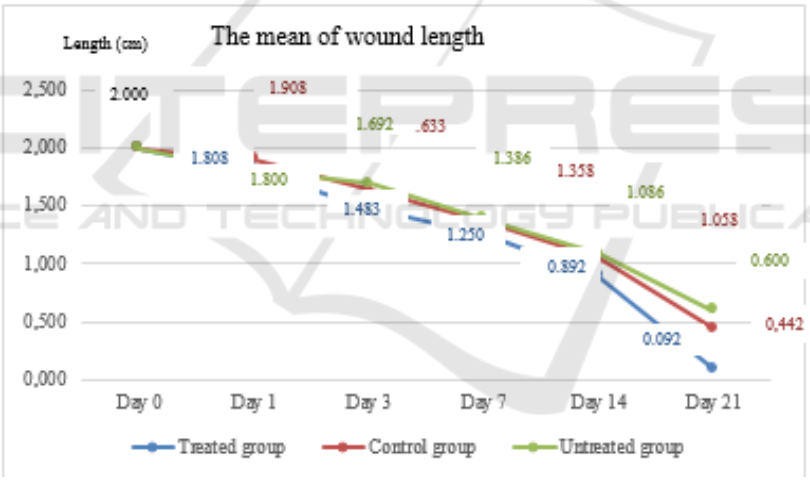

Figure 1. Graphic of mean wound length on day- 0,1st ,3rd ,7th ,14th and day-21st.

Table 1. The mean percentage of wound length.

Group	Number of mice	The mean of percentage of wound length (%)					
		Day 0	Day 1	Day 3	Day 7	Day 14	Day 21
KP	12	100	90,4	74,5	62,5	44,6	4,6
KK	12	100	95,4	81,65	67,9	52,9	22,1
KN	7	100	90	81,45	69,5	54,3	30

KP: Treatment group (Sumbawa forest honey). KK: Control group (povidon iodine 10%). KN: Untreated group.

Based on Table 1 and Figure 1, on day 21st, the mean percentage of wound length in the treatment group was smaller than the control group (4.6% vs. 22.1%) and untreated group (4.6% vs. 30%). Statistical analysis was performed using Kruskall-Wallis non-parametric test because the data was not distributed normally. From the Kruskall-Wallis test, $p = 0.017$ ($p < 0.05$) was obtained, demonstrating a significant difference in the mean of wound length between the treatment group, the control group, and untreated group. In the Mann-Whitney Post-hoc test results, there was a significant difference between the mean wound length of the treatment group and the control group ($p=0.022$; $p<0.05$) also the same result between the mean wound length of the treatment group and untreated group ($p=0.009$; $p<0.05$).

4 DISCUSSION

The efficacy of honey on acceleration of wound healing and antimicrobial properties of honey has been studied so far (Yaghoobi & Kazerouni, 2013). However, the efficacy of local Indonesian honey such as Sumbawa forest honey has not been widely studied. This study is important because the composition and function of honey are influenced by the different types of plants, climates, and environmental conditions within which the honey is produced (Sumarlin et al., 2014).

The results of this study indicate that from day 1st to day 21st, the mean percentage of wound length following topical application of Sumbawa forest honey is consistently smaller than the mean percentage of wound length in the group with application of povidone iodine 10% as well as in the untreated group. It can be interpreted that the wound closure occurred faster after topical application of Sumbawa forest honey. This is in line with Ghaderi's study (2004) which showed that the mean length of the wound edge of the group of mice smeared with honey were smaller than the control group (Ghaderi & Afshar, 2004). In the inflammatory phase that lasts between day 1 and 4, the application of honey provides an anti-inflammatory effect that reduces edema and necrosis, and decreases infiltration of polymorphonuclear (PMN) and mononuclear (MN) cells. In addition, previous studies have shown that honey can accelerate re-epithelization, stimulate angiogenesis and improve wound contraction by increasing collagen synthesis and the degree of cross-linking of collagen in granulation tissue in the proliferative phase (Yaghoobi & Kazeroune, 2013; Al-Waili et al., 2011).

There are three major properties of honey that play roles in accelerating wound healing. First, its high sugar content causes high osmolarity thus it inhibits bacterial and fungal growth in open wounds. Second, the presence of glucose oxidase enzyme that can convert into hydrogen peroxide, which acts as an antiseptic. Third, the content of various enzymes in bee pollen and propolis can stimulate the growth of new tissues. In addition, honey also contains essential oils, flavonoids and polyphenols and vitamin C that serve as antioxidants (Ghaderi& Afshar, 2004; Al-Waili et al., 2011; Molan & Rhodes, 2015).

It is necessary to observe the effects of Sumbawa forest honey on other aspects of wound healing such as microbiological and histological aspects. Further study is needed to determine the concentration of Sumbawa forest honey that is most effective for wound healing.

5 CONCLUSION

The topical application of Sumbawa forest honey can accelerate the healing of incision wound on BALB / c male mice.

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