Comparison of Healing Effects of Propolis to Silver Sulfadiazine on Full Thickness Skin Wounds in Rabbits

The effects of propolis and silver sulfadiazine (SS) on the wound healing were determined using qualitative and quantitative parameters and histopathological findings. A total of 30 full thickness skin wounds, 3 from each of 10 rabbits, were created on their dorsal aspects. Of these wounds, 10 were allocated to group 1 (propolis), other 10 group 2 (SS) and other 10 control. The skin wound in the 1, 2 and 3 groups were covered daily with 50% propolis cream, SS skin cream and bepanthane cream (control), respectively. Postoperatively the wound surfaces were macroscopically examined and the healing process and the rates of wound expansion, contraction and epithelialization processes were quantitatively analyzed. As a result, propolis was found in general to have a better wound healing feature than others.

Key words: Wound healing, propolis, silver sulfadiazine, rabbit.

Introduction

Propolis (bee glue-resinous material) is a mixture containing a number of plant products including flavonoids and is deposited in beehives by bees. Propolis has attracted the interest of many investigators because of its anti-bacterial (1, 2), anti-viral (3), anti-inflammatory, and immuno-stimulatory (4, 5) effects. Additional studies have shown propolis to be tumoricidal, antifungal, antiamoebic, and antipyretic (6, 7). It was found that propolis has therapeutic effect on wound healing. Silver sulfadiazine (SS) is the topical agent and is used universally today in wound healing. The purpose of this study was to compare healing rates of wounds treated with propolis or silver sulfadizine in rabbit model.

Materials and Methods

The dorsal aspects of 5 male and 5 female rabbits were clipped and prepared for aseptic surgery. All rabbits were anesthetized with intramuscular administration of 10 mg/ kg xylazine hydrochloride (Rompun, Bayer) and 50 mg/ kg ketamine hydrochloride (Ketanest-Ailke). On each animal, two cranially and one caudally located square (4 cm²) full-thickness skin wounds were created using a template prepared from an X-ray film. These wound sites were allocated to three groups and covered with 50% propolis cream (Turkish propolis), silver sulfadiazine skin cream and bepanthane cream (control), respectively. These applications were repeated every day. A wound site was considered macroscopically to be fully healed when its whole surface was covered with epithelium. The wound boundaries were traced on a transparent sheets were scanned and the areas of wound sites and epithelization fronts were measured with the help of the paintbrush (PB) computer program. The data obtained were calculated as described by Kilic et al. (8). Briefly; area (cm²) = P/K.M, where P is the value of a particular wound site obtained on the PB, K is a rate constant for expressing the value of the PB as cm², and M is magnitude of tracings after scanning. During the examination, the day wound contraction started, the rate of wound contraction, the day epithelization and the number of days in which wound fully completed were evaluated.
The statistical comparison was made with ANOVA. The result were considered as significant $P \leq 0.05$. Ten and 20 days later, the rabbits were anaesthetised and the skin tissue biopsy samples were collected from rabbits for histopathological examinations. The samples were fixed in 10% neutral buffered formalin, and were cut into 5 µm sections and stained with hematoxylin and eosin (H&E), and examined microscopically (9).

**Results**

No mortality was seen in the animals during the study. Macroscopically, in all treatment groups, no difference was detected with regard to inflammatory response: heat, redness, and swelling. All wound sites was healed completely 17 days after surgery. The wound contraction and wound healing rates of propolis were higher than treatment and control groups (Figure 1), (Table 1).

**Table 1.** Changes in wound sizes of three groups during the healing periods (n=10).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Days of Operation</th>
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<tbody>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Propolis</td>
<td>$3.5 \pm 0.4^b$</td>
</tr>
<tr>
<td>SS</td>
<td>$3.7 \pm 0.1^a$</td>
</tr>
<tr>
<td>Control</td>
<td>$3.8 \pm 0.3^a$</td>
</tr>
</tbody>
</table>

*a,b,c : Ayni sütunda farklı harfleri içeren grup ortalamaları arası farklar önemlidir ($P<0.05$)*

At the 10th day of experiment, histopathologically; there was inflammatory reaction including lymphocytes, macrophages and neutrophiles and fibroblastic loose connective tissue in dermis of all groups examined. The severity of the reaction in propolis group was lower than SS and control group. In control group, inflammatory cells were abundant and completely filled the gap of wound. Connective tissue between the wound margins and surface debris were also more voluminous in control and SS groups than propolis group. At the 20th day of experiment, the epithelial and dermal healing was completed in propolis group and better than both control and SS groups. Both dermis and epidermis were completely regenerated in this group (Figure 2). The appearance of the skin was completely normal except for the decreased epidermal thickness. In SS and control groups, the surface was covered by scab and epidermal regeneration was not completed (Figure 3). In control group; dermal and epidermal regeneration was also retarded as compared to SS and propolis groups (Figure 4).
Discussion

The wound healing process involves many complex factors. These may be classified as local factors, systemic factors and organ and species variability in response to injury. Topical medications should provide a specific desired effect during the appropriate stage healing (8). In this study, we adopted an experimental design including macroscopical and histological evaluations of the wound healing process. Propolis is a natural drug that has been employed extensively since ancient times (1, 5, 10, 11). Khayyal et al. (5), reported that aqueous propolis extract possesses significant anti-inflammatory properties and has successfully reduced oedema in both acute and chronic models of inflammation.

The propolis skin cream appears to have a beneficial effects on healing burn wounds (10, 13). It was also reported that propolis has a therapeautic effect on wound healing, inflammations of the skin and other skin lesions (1, 4). In this study, all wound sites was healed in 17 days after surgery. The wound contraction and wound healing rates of propolis were higher than other groups.

According to the results of the present study, including macroscopical, qualitative, and microscopical analyses propolis has a higher healing performance than other groups.

References

ERÖKSÜZ Y. ve Ark.

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