Fibroblast cell description of provision of sugar and honey in incision wound of domestic cat (*Felis domestica*)

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Abstract. This study aimed to observed the fibroblast cell description in incision wound of the domestic cat after treated by sugar and honey. Fifteen domestic cats (*Felis domestica*) were used in the research. The cats were divided into five treatment groups as follow, the negative control group (KK1) was normal wound healing (without any treatment), the positive control group (KK2) used Bioplacenton® ointment, group 1 (KP1) used sugar, group 2 (KP2) used honey, and group 3 (KP3) used a combination of sugar and honey. All preparations were given topically for 14 days. The sample collection of the skin was performed on the 4th, 9th, and 14th days. Histopathological preparation with hematoxylin-eosin staining was conducted on all skin samples. Treatment with a combination of sugar and honey showed a very high increase in fibroblast cells, and this also occurred in KP1, KK2 and KK1. Group treated with honey (KP2) showed low fibroblast cell level. This research revealed that the combination of sugar and honey showed a good influence on the process of fibroblast cell formation during the wound healing process.

1. Introduction

Function the skin as protection and its existence at the surface of the body causes the skin susceptible to trauma and of the injury. Wounds are a form of tissue damage to the skin caused by contact with heat sources, the results of medical procedures, and changes in physiological conditions [1]. The incision wound, for example, was caused by a wedge by a sharp instrument or due to the dissection [2].

The healing of a sore is the result of the process for repair of tissues that occurs in a complex manner. To replace and improve the structure of the cells and a layer of tissue of loss or damage [3]. The process of healing of a wound was divided into three phases, the inflammatory, the formation of new tissue, and the remodeling phase [4]. One of the important components in the healing process is the fibroblast. Fibroblast cells are the most common cells found in connective tissue and synthesize several extracellular matrix components (collagen, elastin, reticular) [5], as well as multi-adhesive
GAG, proteoglycans, and glycoprotein consisting of basic ingredients that play an important role in the wound healing process [6], to support the process needed drugs or alternatives that can accelerate the wound healing process. Recently, traditional medicine has been widely used in the process of wound healing. Some natural ingredients that can be used in wound healing are sugar and honey.

2. Materials and method

Fifteen male cats were used in the study and divided into five groups for 14 days of treatment. The negative control group (KK1) was normal wound healing (without treatment), the positive control group (KK2) used Bioplacenton® ointment, group 1 (KP1) used sugar, group 2 (KP2) used honey, and the group 3 (KP3) used a combination of sugar and honey. All preparations were given topically.

Experimental animals were anesthetized by injecting ketamine at a dose of 10 mg/kg of BW and xylazine dose of 2 mg/kg of BW intramuscularly (IM). The cats were placed in a dorsoventral position. After being anesthetized, a rectangular incision was made with a size of 2 cm × 1 cm. The skin sampling process was carried out on days 4, 9, and 14 after treatment in each group. The incised skin was then isolated and rinsed with physiological NaCl and put in a 10% formalin solution before histological preparations with hematoxylin-eosin (HE) staining.

3. Results and discussion

Histopathological scoring parameters for fibroblasts density were shown in table 1. Table 1 showed that on the 14th day, fibroblast cell production experienced a significant increase in treatment group 3 (KP3) with a high number and density of fibroblast cells was scored 3. Similar finding occurred in the treatment group 1 (KP1), positive control group (KK2), and negative control group (KK1) with the number and density of fibroblasts quite high in the injured area. In treatment group 2 (KP2) showed a non-significant increase with the results of observations, number and density of fibroblasts in the wound area were scored 2.

| Group                  | 4th day | 9th day | 14th day |
|------------------------|---------|---------|----------|
| KK1 (Without treatment)| 0       | 1       | 3        |
| KK2 (Bioplacenton®)    | 1       | 2       | 3        |
| KP1 (Sugar)            | 1       | 2       | 3        |
| KP2 (Honey)            | 0       | 1       | 2        |
| KP3 (Sugar + Honey)    | 1       | 2       | 3        |

Score 0 = No fibroblast cells were found in the injured area
Score 1 = Low fibroblasts in the injured area, low density, dominated by cells inflammation
Score 2 = moderate fibroblasts in the injury area, moderate density
Score 3 = high fibroblasts in the injured area, high density

Honey had hygroscopic properties that allow bacterial dehydration, which caused the bacteria to be inactive; without water, the bacteria could not survive so that it can accelerate the healing of wounds [7]. Sugar can increase the migration of keratinocytes and fibroblasts to damaged tissue, the formation of new extracellular matrix (ECM), re-epithelization, and formation of granulation tissue [8]. Osmolarity possessed by sugar was higher than plasma so that it can reduce local edema quickly. This strong osmotic pressure can stimulate the growth of granulation tissue and cleanse the injured area [9]. Honey and sugar had an essential role in the process of wound healing by affecting the process of fibroblast cell formation.
Figure 1. Histopathological features of cat skin in group 3 (KP 3) used sugar and honey of topical administration of the 4th day (A), 9th day (B), and 14th day (C). Inflammatory cells (a), fibroblasts cells (b), and collagen fibers (c). HE staining, 40×10 magnification.

Treatment group 3 (KP3) on day 4th showed a low fibroblast density, inflammation cell proliferation, which predominates with moderate density and low-density collagen fibers (figure 1A). Sugar had antibacterial properties and had a strong osmotic effect capable of attracting macrophages into wounds. Macrophage cells functioned to secrete pro-inflammatory and anti-inflammatory cytokines [10]. On the 9th day, observations showed inflammatory cells with low density, while fibroblasts and collagen fibers were found with moderate densities (figure 1B). Honey had hygroscopic properties that attracting water from the surrounding environment, thus creating an environment with low water concentration with a high osmotic effect so that it could attract macrophages. Macrophages will attract fibroblasts to the wound area to start collagen synthesis [11]. On the 14th day, observations showed a significant increase in fibroblasts with a fairly high density and were surrounded by collagen fibers, which were quite dense (figure 1C). The content of sugar in honey induced TGF-β while granular sugar contains TGF-α. TGF-β was involved in extracellular matrix (ECM) reorganization and collagen deposition. At the same time, TGF- α was then activated by integrin α and β receptors, which functioned in fibroblast proliferation and collagen synthesis. TGF- α, as an EGF receptor, acts as an EGF activator to synthesize collagen, thus accelerating wound healing [12].

4. Conclusion
Sugar and honey administered to incision wounds of domestic cats (Felis domestica) as an alternative drug influenced the formation of fibroblast cells. The combination of sugar and honey showed good results as well as giving only sugar. In contrast, wound healing with honey alone shows more prolonged healing and formation of fewer fibroblast cells.
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