

## **Difference Of the Wound Healing At Buccal and Oral Labial Mucosa After Giving Aloe Vera Extract (*Aloe Vera Linn*)**

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*Aloe vera is one of the plants that often used as traditional medicine. Aloe vera contains bioactive substances such as alkaloids, flavanoids, glycosides, saponins, and tannins which act as anti-inflammatory and antioxidants that influence the healing process of wounds. The purpose of this study was to determine the effect of 100%, 50% and control groups (untreated) aloe vera extract on wound closure with intentional incision wounds from the first day to the tenth day in white rats. This research is a pure experimental design with a post test-only design with control design. This study used 21 white rats divided into 3 groups of 100% aloe vera extract group, 50% aloe vera extract group, and control group (not treated). One-way Anova and Post-hoc LSD test results showed significant differences in wound closure ( $p < 0.05$ ) between the 100% aloe vera extract group and 50% aloe vera extract group compared to the control group (not treated). The results of the T-Test showed a significant difference ( $p < 0.05$ ) in wound closure in white rats between the buccal mucosa and the labial mucosa. Conclusion: This study of aloe vera extract has an effect in accelerating wound healing in the oral mucosa.*

**Key Words:** *Aloe Vera Extract, wound healing, long wound, oral mucosa*

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### **I. Preliminary**

Aloe vera plant has an anti-inflammatory and immunostimulant effects that play a role in helping the wound healing process. The compound content in aloe vera plant generally consists of one or more compounds, including alkaloids, flavanoids, glycosides, saponins, and tannins. Aloe vera leaves contain vitamins, enzymes, proteins, carbohydrates, minerals (calcium, sodium, magnesium, zinc, iron) and amino acids that act as anti-inflammatory.<sup>1</sup>

The oral mucosa contains two layers, epithelium and connective tissue (lamina propria). The oral epithelium is the outermost layer of the mucosa which serve as a protection for the underlying layer. While the lamina propria is a layer of fibers that are mutually bound and function to provide strength to the epithelial layer. Epithelial cells are mostly different keratocyte cells with lamina propria, which is a loose connective tissue formed under the epithelium consisting of fibroblast cells, lymphocytes, macrophages, eosinophilic leukocytes, mast cells and plasma cells, small blood vessels and glands.<sup>2</sup>

If the cells are mature, epithelium cells begin a maturation process and will be pushed towards the surface. Epithelial regeneration originates from mitosis which occurs in epithelial cells, pushed to the uppermost layer and ultimately has no nucleus, also the cells are thinner.<sup>1,2</sup> The process of mitosis in epithelial cells occurs continuously. The number of cells lost in the superficial layer are generally balanced with the number of new cells produced by mitosis from basal cells. Epithelial cells experience regeneration every 14-21 days starting from the cuboidal basal cell, maturing upwards over more polygonal shapes, namely spinosum cells, lifted up more flat, and granules and the core disappears into dead cells without nucleus called horn cells. Horn cells are continuously released from the surface of the skin called desquamation.<sup>3</sup>

Injury at the oral mucosa is the loss or damage of a portion of mucous tissue caused by physical or chemical actions. Wounds will trigger a healing reaction that is the body's mechanism to restore damaged tissue integrity. At least, there are 3 phases in wound healing, which are inflammatory phase, vasoconstriction and formation of blood clots occur. When bleeding stops, platelets release cytokines to attract inflammatory cells and release vasoactive substances to increase vascular permeability. In the proliferative phase, granulation tissue is formed and the tensile strength of the wound is increased. Then, remodeling phase occurs to reshape the new

network. Wounds are healed if the surface can be reunited, obtained by the strength of the tissue that reaches normal, does not interfere with its normal function, and all signs of inflammation have disappeared.<sup>4</sup>

Saliva has an important role in the biological processes that occur in the oral cavity as a lubricant for mastication, ingestion of food, cleaning and protection from dental caries. Saliva function will run maximally if the saliva flow rate increases. The saliva flow rate can be in the form of masticatory activity while the chemical process in the form of a casting effect such as acid, sweet, salty, and bitter. Saliva contains growth factors such as Epidermal Growth Factor (EGF) which is believed has function as a wound healing factor in the oral cavity so that the wound healing is faster than the wound on the skin.<sup>5</sup>

According to the research of Moch AK Budiyanto, the results of aloe vera extract with a concentration of 100% and 50% in the wound can occur healing in the mucosa. At a concentration of 100% healing is faster than the concentration of 50%.<sup>6</sup>

This study aims to see differences in the healing of buccal and labial parts.

## II. Research Methodology

This type of research is true experimental design with a *post test only design with control design*. This study used 21 white rats divided into 3 groups, namely 100% aloe vera extract group, 50% aloe vera extract group, and control group (not treated).

Aloe vera extract was made at USU's Pharmaceutical Phytochemical Laboratory. Identification and testing of samples was carried out in the Sunggal Rat Housing. To calculate the sample size, this study used the Federer formula.

Data from the results of this study are processed computercially. The analysis used in this study is the *Saphiro-Wilk* test, because it is more effective and valid to use for small numbers of samples and using the homogeneity test. After that, this study also using *Levene's test* because it is used to test the similarity of variance from several populations. Statistical significance is obtained if the value is  $p < 0.05$ . Followed by Post-Hoc LSD (*Least Significance Different*) analysis to find out which groups showed significant differences. Then using the t-independent test to determine the difference in mean wound healing between the buccal mucosa and labial mucosa per concentration group, namely a group of 100% aloe vera extract, 50% aloe vera extract group, and a control group.

### Making Aloe Vera Extract

Before making aloe vera extract, aloe vera is washed first using running water, then cut into small pieces. Then the aloe is dried at 40°C for 48 hours using the oven. The dried aloe vera is soaked with 96% ethanol to yield an ethanol 1 cm above the surface of the sample. Soaking is done for 3x24 hours while stirring occasionally, and soaking again for 2x24 hours. Then evaporated with a vacuum rotary evaporator with a heating temperature of 40-50°C, until the extract is thick. The ethanol-free test was carried out by weighing the heated extract and the cooled extract. If the weight of the extract was the same, it could be concluded that the extract had been free of ethanol..

## III. Research Result

In this study, the collected data was tabulated, then the normality test using Saphiro-Wilk was carried out, and homogeneity tests using *Leven's test*. The Sapjiro-Wilk test results for all groups showed a value of  $p > 0.05$ , which meant the distribution of data was normal. Data analysis continued using One-Way Anova analysis showing the value of  $p = 0,0001$  ( $p < 0.05$ ) which showed a significant difference between treatments so that the Post-hoc LSD analysis was conducted to determine which groups showed significant differences. Then continued the data analysis using the Independent T Test analysis showed a value ( $p > 0.05$ ) which showed a significant difference between treatments.

Table1 Post-Hoc LSD Analysis Result  
White Rats Buccal Section

Number	Groups	Amount of Sample	Mean Difference	Value p
1	Treatment 100%-Control	7	1,44 mm	0,000
2	Treatment 50%-Control	7	1,15 mm	0,000
3	Treatment 100%-50%	7	0,28 mm	0,011

Based on the Post-hoc LSD analysis, the 100% aloe vera extract group showed a significant difference from the 50% aloe vera extract group and the control group. It was seen that there was an acceleration of wound healing with a visible reduction in the length of the wound.

In table 1, at the buccal, a concentration of 100% is the most effective for wound healing, as seen from the difference between the average closing wounds, which is 1.44 mm. Then, followed by a concentration of 50% with a difference in mean wound closure of 1.15mm. From these results, it can be seen that the concentration of Aloe vera extract is 100%. The faster the wound heals, which may be caused by the more active content of the extract with a lower concentration.

**Table2 Post-Hoc LSD Analysis Result White Rats Labial Section**

Number	Groups	Amount of Sample	Mean Difference	Value p
1	Treatment 100%-Control	7	1,25 mm	0,000
2	Treatment 50%-Control	7	1,00 mm	0,000
3	Treatment 100%-50%	7	0,25 mm	0,008

Based on the Post-hoc LSD analysis, the 100% aloe vera extract group showed a significant difference from the 50% aloe vera extract group and the control group. It was seen that there was an acceleration of wound healing with a visible reduction in the length of the wound

In table 2,in the labial section, it can be seen that the 100% concentration that is most effective in healing wounds is seen from the highest difference in the average wound closure, which is 1.25 mm. Then followed by a concentration of 50% with a difference in mean wound closure which is 1.00 mm. From these results, it can be seen that the concentration of Aloe vera extract is 100%. The faster the wound is heals, which may be caused by the more active content of the extract with a lower concentration.

**Table 3 T-Independent TestAnalysisResultConcentration 100%on 10<sup>th</sup>days buccal and labial section**

Groups	Amount of sample	Diameter of wound closure x ± SD	Value p
Buccal Mucosa	7	8,97 mm ± 0,20 mm	0,001
Labial Mucosa	7	8,51 mm ± 0,15 mm	

It can be seen (Table 3) that the concentration 100% showed a difference of wound healing between the buccal mucosa and the labial mucosa section, where the wound healing of the buccal mucosa was faster, as seen from diameter of wound closure, which is 8,97 mm.

**Table 4 T-Independent Test AnalysisResultConcentration 50% on 10<sup>th</sup> days buccal and labial section**

Groups	Amount of sample	Diameter of Wound Closure x ± SD	Value p
Buccal Mucosa	7	8,68 mm ± 0,16 mm	0,000
Labial Mucosa	7	8,25 mm ± 0,17 mm	

It can be seen (Table 4) that the concentration 100% showed a difference in wound healing between the buccal mucosa and the labial mucosa section, where the wound healing of the buccal mucosa was faster, as seen from diameter of wound closure, which is 8,68 mm.

**Tabel 5 T-Independent TestAnalysisResultcontrol group on 10<sup>th</sup> days buccal and labial section**

Groups	Amount of Sample	Diameter of Wound Closure x ± SD	Value p
Buccal Mucosa	7	7,52 mm ± 0,18 mm	0,12
Labial Mucosa	7	7,25 mm ± 0,15 mm	

It can be seen (Table 5) that the concentration 100% showed a difference of wound healing between the buccal and labial mucosa, where the wound healing of the buccal mucosa was faster, as seen from diameter of wound closure, which is 7,52 mm.

#### IV. Discussion

Laboratory experimental studies of aloe vera extract (Aloe Vera Linn) for healing oral mucosal wounds in white rats are to prove that aloe extract has a long healing effect on wounds, the role of saliva in wound healing. This study was also conducted to analyze the effects of aloe vera extract on the long healing of internal wounds (buccal mucosa) and the outside (labial mucosa). This research is a laboratory experimental study that uses 21 male white rats whose purpose is only for research, not for diagnostic or therapeutic purposes.

Based on the study of the effect of aloe vera extract on decubitus wound healing in rats, to determine the effect of aloe vera extract on the length of wounds in white rats by measuring the length of the wound. The concentration used is 50%, 75%, and 100%, indicating that the concentration is 100% faster than other concentrations.<sup>6</sup>

In the research conducted, the results of 100% concentration of aloe vera extract were the most effective for healing wounds. The same study conducted in Manado regarding the effects of Aloe vera L on rabbit skin incision wound healing showed that the administration of aloe vera extract had the effect of accelerating the healing of incisional wounds on rabbit skin.<sup>7</sup> The same study was conducted in Lampung regarding the influence Aloe vera extract concentrations of 25%, 50%, 75%, and 100% of the number of macrophages in oral mucosal inflammation of male white rats spraguedawley strain. This study used aloe vera extract with a concentration of 25%, 50%, 75%, and 100%. In this study, the concentration of Aloe vera extract was 100% the most effective as an anti-inflammatory in inflammation of the oral mucosa.

The concentration used in this study is 100% and 50%. The choice of concentration and research procedures used this study was less guided by previous studies conducted by Malang by Nurul, Ajeng, and Hardani regarding the effects of aloe vera extract on decubitus wound healing in white mice. This study was also conducted to determine the effect of aloe vera extract on the length of wounds in white rats by measuring the length of the wound. The concentration used is 50%, 75%, and 100%. This study showed that the concentration of 100% healed faster than other concentrations.<sup>6</sup>

A concentration of 100% in some herbal studies does look more effective than lower concentrations. For example, a study conducted in Banjarmasin on the effect of citronella extract (*Cymbopogon citaratus*) on the labial mucosal length of rats clinically to determine the effect of citronella extract on the length of labial mucosal wound rats clinically by measuring wound length. In this study showed that the concentration of 100% healed faster than the concentration of 50% and concentration of 25%.<sup>9</sup>

Research conducted in Kupang regarding the effect of concentrations of propolis extract on the effects of burning of burns on the skin of the Newzealand rabbit stage using concentrations of 50%, 75%, 100%, negative controls, and positive controls. In this study showed that the most effective healing effect of burns was 100% propyllic extract<sup>10</sup>

Aloe vera extract with a concentration of 100% and 50% can accelerate the healing of incisional wounds in the oral mucosa of male white rats when compared to mice not given treatment because aloe vera extract has bioactive substances in aloe vera such as alkaloids, flavanoids, glycosides, saponins, and tannins which play a role in the phases of wound healing because they trigger various responses to inflammation and the immune function as a signaling mechanism for redox regulation. Aloe vera leaves contain vitamins, enzymes, proteins, carbohydrates, minerals (calcium, sodium, magnesium, zinc, iron), and amino acids that act as anti-inflammatory.<sup>2</sup>

Flavonoids function as anti-inflammatory can through several pathways :inhibiting the activity of cyclooxygenase and lipoogenaseenxymy, inhibiting leucocyte accumulation, inhibiting histamine release. The content of flavonoids is believed to have benefits in the process of wound healing.<sup>11,12</sup>

Saponin compounds also have antibacterial activity in which the active substance can increase membrane permeability so that cell hemolysis occurs. If the saponins interact with bacterial cells, the bacteria will rupture or lysis. Saponin can be antibacterial because the surface active agent is similar to detergent or soap. As a result, saponin will reduce the surface tension of bacterial cell walls and damage membrane permeability. Injuries can be accelerated. Tanin can shrink the cell wall or cell membrane so that it disrupts the permeability of the bacterial cell itself. Due to disruption of permeability, bacterial cells cannot carry out living activities so that growth is stunted or even dead. The antibacterial effects of tannins include reaction with cell membranes, enzyme inactivation, and destruction or inactivation of the function of genetic material. Tanin is a water-soluble phenolic compound which also has the potential as an antioxidant that protects against oxidative damage such as cancer, arthris and aging. The content of tannins is useful for stopping bleeding, accelerating wound healing and inflammation of mucous membranes, and regenerating new tissues. In addition, the content of tannins can accelerate wound healing with a number of cellular mechanisms, namely cleaning up free radicals and reactive oxygen, increasing wound closure, and increasing capillary blood vessel formation as well as fibroblasts.<sup>15,16</sup>

The research conducted showed that aloe vera extract with a concentration of 50% can also heal wounds. This study was supported by a study conducted in Sukoharjo regarding the effectiveness of *Aloe vera L* extract on incisive wound healing in the male rat (*Mus musculus*) Swiss strain. This study uses a concentration of 12.5%, 25%, and 50%. In this study, 50% concentration was more effective in healing wounds in mice. *Aloe vera* contains a lot of bioactive substances that are useful in accelerating wound healing, including saponins, flavonoid, tannins, and polyphenols.<sup>17</sup> The same study was conducted in Mataram regarding the formulation of aloe vera extract ointment as a wound medicine in 10%, 30 %, and 50% concentration of white mice showed there was a difference in effectiveness of 50% *Aloe vera* extract on wound healing in white rats compared to the negative control group which was only given ointment base treatment and the positive control group, which was given betadine (*Povidone Iodine*).<sup>18</sup>

Other herbal studies issued for wound healing as those conducted in Banda Aceh regarding the effect of tapakdara leaf extract (*Catharatus rosues*) on the number of fibroblast in the wound healing process in the labial mucosa of wistar rats (*Rattus norvegicus*). The study used tapakdara leaf extract on the number of fibroblast in the concentrate of 6.25%, 12.55%, 50%, 100%, and the control group give distilled water. In the study showed that tapakdara leaf extract with concentration with tapakdara leaf with a concentration of 50% had an effect on the number of fibroblast in the wound healing process in the labial mucosa of wistar rats.<sup>19</sup>

Research conducted in Mataram regarding the optimization of dosage of lamtoro leaf extract (*Laucaena Galuca*) was effective against healing burns in mice. This study used lamtoro leaf extract with a concentration of 15%, 30%, 50%, positive control given bioplacenton, and negative controls given by Vaselin album. In this study showed that the concentrations of 30% and 50% were the most effective in healing burns in mice. Wound healing can occur because lamtoro leaves contain flavonoids, alkaloids, saponins, and tannins. Flavonoids are active compounds that can play a role in healing burns because they can inhibit bacterial growth, increase the number of fibroblasts. Besides saponins and tannins can trigger angiogenesis.<sup>20</sup>

Research using saliva on wound healing in cutaneous rats showed that saliva can accelerate wound healing, so saliva with EGF content can be a new source of medicine for wound healing.<sup>22</sup> This study proves that saliva also plays a role in wound healing compared to injuries that are not affected saliva.

Based on the research that has been done, it can be concluded that *Aloe vera* extract with a concentration of 100% and 50% can affect the wound healing process. The buccal wounds coated with saliva heal faster than the external wounds. It is hoped that further studies of the effect of aloe vera extract to see wound healing by histopathology, phytochemical tests on aloe vera extract to find out more about its active compounds. It is necessary to carry out toxicity and other further tests to be used as a treatment for human oral mucosa.

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