

Effect of Andaliman Fruit Extract (*Zanthoxylum Piperitum*) On the Healing Process of Post-Tooth Decays Wounds in Wistar Rats

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ABSTRACT

The healing post-tooth decaying wounds is a vital tissue regeneration stage involving fibroblast cell activity. Andaliman fruit (*Zanthoxylum piperitum*) contains bioactive compounds such as flavonoids and terpenoids that can accelerate healing through anti-inflammatory effects and stimulation of tissue regeneration. This study aims to determine the impact of andaliman fruit extract with a concentration of 30% and 60% on the number of fibroblasts in the healing process of wounds after tooth extraction in Wistar rats. Thirty-two male Wistar mice were randomly divided into two treatment groups using a post-test-only control group design. The extract was given as much as 0.05 ml for five days in the area of tooth extraction, and then histological observations were carried out using hematoxylin-eosin staining. The results showed that the group with a concentration of 60% had a higher number of fibroblasts (63%) than the group of 30% (19%), and the Chi-Square test showed a significant relationship between the concentration of the extract and the number of fibroblasts ($p = 0.024$). Thus, Andaliman fruit extract has a concentration of 60% more effective in accelerating the healing of post-tooth decays through increased fibroblasts.

Keywords: andaliman, fibroblasts, post-tooth wounds, wound healing, *Zanthoxylum piperitum*.

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I. Introduction

Andaliman, also known as Batak pepper (*Zanthoxylum acanthopodium* DC), is a typical plant only found around Lake Toba. This plant has an essential role in supporting the development of the Toba Caldera Geopark, as determined by UNESCO. Andaliman grows naturally in the Lake Toba area and its surroundings, as mentioned in Presidential Regulation Number 81 of 2014. In addition, andaliman also has a close relationship with the Batak people, especially as a spice in traditional dishes such as *arsik*, *natinombur*, and *sangsang* carp (Siregar & Lubis, 2020). Andaliman is also known by different names in various regions, such as "Sinyarnyar" in South Tapanuli, "Itir-itir" in Tanah Karo, and "Tuba" in Simalungun (Sinaga et al., 2019). These plants contain bioactive compounds such as terpenoids that have the potential to be antioxidants, antimicrobials, and immunostimulants (Hutapea et al., 2021).

Tooth extraction is a standard surgical procedure that can cause injury to the alveolar bone in the oral cavity. Based on data from the 2018 Basic Health Research (RISKESDAS), the prevalence of tooth extraction in Indonesia is relatively high, with a national DMFT index of 4.6, and the most significant component is 3.1 missing teeth per person (Ministry of Health of the Republic of Indonesia, 2018). Post-tooth extraction wound healing involves three main phases: an inflammatory phase that lasts within the first three days after injury, a proliferation phase characterized by the formation of new blood vessels within 3-24 days, and a remodeling phase that lasts more than a year, depending on the depth and extent of the wound (Hidayat & Lestari, 2021). Fibroblasts play an essential role in wound healing, particularly in synthesizing collagen that strengthens damaged tissue (Putri et al., 2022). Research at the Dental and Oral Hospital (RSGM) in 2019 reported several post-tooth extraction complications, such as crown fractures (15.2%), root fractures (12.8%), dry sockets (5.1%), and bleeding and pain (2.4%) (Rahman et al., 2019).

The use of herbs in the medical world is growing, with evidence showing that herbal medicines are effective for a wide range of health care with lower side effects than synthetic medicines (Handayani et al., 2021). The World Health Organization (WHO) supports using traditional medicines, including herbs, for health maintenance, disease prevention, and treating chronic and degenerative diseases (WHO, 2020). The "back to nature" lifestyle trend is increasingly encouraging people to use herbal medicines because they are considered safer and more economical than chemical drugs (Yusuf et al., 2023). Based on this, this study aims to examine the effectiveness of andaliman fruit extract (*Zanthoxylum piperitum*) with a 30% and 60% concentration in accelerating the healing of post-tooth extraction wounds in Wistar rats.

II. Research Methods

This is a laboratory experimental study with a *post-test-only control group design*, where subjects are randomly divided into treatment and control groups without any initial measurements. An evaluation was carried out after treatment to assess the effectiveness of the intervention by minimizing bias. The research was conducted at the Laboratory of Pharmacology and Traditional Medicine, Faculty of Pharmacy, and the Laboratory of Anatomical Pathology, Faculty of Medicine, University of North Sumatra, in January 2025. The study subjects were 32 healthy male Wistar rats aged 2–3 months, weighing 200–250 grams. The mice were divided into two groups, each receiving an extract of andaliman fruit (*Zanthoxylum piperitum*) with concentrations of 30% and 60%, respectively, to compare its effectiveness in wound healing after tooth extraction.

The inclusion criteria included healthy male mice of the appropriate weight and age, while the exclusion criteria included sick mice who had an infection or a physical disability. Primary data were collected through post-extraction tissue histological observations. The tools used include labeled cages, extraction tools, syringes, microscopes, and histology devices. The ingredients include Andaliman fruit extract, ketamine, 10% formalin, alcohol, cotton pellets, and Hematoxylin-Eosin (HE) coloring reagents. The extraction of andaliman fruit is carried out through the maceration method using water solvent; the results are evaporated until pure extract is obtained and diluted to a concentration of 30% and 60%. The treatment procedure was carried out after the rat adaptation period for one week. The rats were anesthetized with ketamine, then tooth extraction. The extract treatment is given daily, as much as 0.05 ml, to the extraction scar area. On the fifth day, the rats were sacrificed, and their jaws were taken for histological analysis of fibroblasts using a microscope. The fibroblast scoring parameters consist of four categories, ranging from none to the number of fibroblasts large (30–60%).

The independent variable in this study was the concentration of andaliman fruit extract (30% and 60%), while the bound variable was the wound healing process after tooth extraction. The operational definition includes andaliman fruit extract as a source of flavonoids measured in ml, and the wound healing process is assessed by the number of fibroblasts in histological preparations. Data was analyzed using the SPSS 16 program with the Chi-Square test. This study aimed to identify significant differences between treatment groups in supporting wound healing.

III. Results and Discussion

The distribution of data and frequency of the number of fibroblast tissue per field of view in Wistar rats after tooth extraction of the group given 30% and 60% of Andaliman Fruit (*Zanthoxylum piperitum*) extract can be seen as follows:

Table 1 Data on the Distribution and Frequency of the Number of Fibroblast Tissue Per Post-Tooth Extraction Field of View

NO	Number of Fibroblasts	Buah Andaliman (<i>Zanthoxylum Piperitum</i>)			
		Concentration 30%		Concentration 60%	
		n	%	n	%
1	No fibroblast tissue was found	0	0	0	0
2	Low number of fibroblasts (less than 10% per field of view)	8	38%	2	13%
3	Moderate fibroblast tissue count (10%-30% per field of view)	5	31%	4	25%
4	The number of fibroblast tissues is large (30%-60% per field of view).	3	19%	10	63%

Based on Table 1, the distribution of the number of fibroblast tissue per field of view after tooth extraction in Wistar rats showed a difference between the groups given Andaliman Fruit extract (*Zanthoxylum piperitum*) with concentrations of 30% and 60%. No fibroblast tissue was found in either group. In the group given the extract with a concentration of 30%, as many as 8 (38%) had a small number of fibroblasts (less than 10% per field of view), while in the group with a concentration of 60%, only 2 (13%) showed the same category. Moderate fibroblast tissue count (10%-30% per field of view) was found in 5 (31%) in the 30% group and 4 (25%) in the 60% group. Meanwhile, the number of fibroblast tissue (30%-60% per field of view) was more dominant in the group given 60% extract, which was as many as 10 (63%), compared to the 30% group, which was only 3 (19%).

These results show that administering Andaliman Fruit extract with a concentration of 60% tends to increase the number of fibroblast tissues, which is more than that of a concentration of 30%. These findings indicate that extracts with higher concentrations have the potential to speed up the healing process of wounds after tooth extraction through an increase in the number of fibroblasts, which play a role in the process of tissue

regeneration.

Table 2 Relationship of Fibroblast Tissue Count Per Field of View in Wistar Rats After Tooth Extraction with Administration of Andaliman Fruit Extract (*Zanthoxylum piperitum*) Concentrations of 30% and 60%

Number of Fibroblasts	Buah Andaliman (<i>Zanthoxylum Piperitum</i>)		p
	Concentration 30%	Concentration 60%	
1. No fibroblast tissue found	0	0	0,024*
2. The number of fibroblasts is small (less than 10% per field of view)	8	2	
3. Moderate fibroblast tissue count (10%-30% per field of view)	5	4	
4. The number of fibroblast tissues is large (30%-60% per field of view).	3	10	

Significant $p < 0.05$. Uji Chi-Square

Table 2 shows the relationship between the number of fibroblast tissue in Wistar rats post-tooth extraction with the administration of Andaliman Fruit (*Zanthoxylum piperitum*) extract at concentrations of 30% and 60%. The results showed that in the 30% concentration group, most mice (38%) had few fibroblasts (less than 10%), while in the 60% group, only 13% showed a small number of fibroblasts. In contrast, the 60% group was more dominant in having multiple fibroblasts (30%-60%), i.e. 63%, compared to the 30% group (19%). The Chi-Square test showed a $p = 0.024$ value, which showed a significant relationship between extract concentration and the number of fibroblasts, which play a role in post-tooth extraction wound healing.

This study aims to evaluate the effectiveness of Andaliman Fruit extract in accelerating post-tooth extraction wound healing in Wistar rats. The results showed significant differences in the number of fibroblasts between the two treatment groups. The group with 60% extract tended to have more fibroblasts, indicating that increased concentration of the extract accelerated the proliferation of fibroblasts that are important in wound healing. Based on observations, no fibroblasts were found in either group at the beginning of the study. However, after the administration of the extract, there is a difference in the number of fibroblasts that develop. The 60% group showed more fibroblasts (63%) than the 30% group (19%). These results suggest that extracts with higher concentrations can stimulate fibroblast proliferation, which plays a role in collagen synthesis and wound healing (Masir et al., 2012).

Statistical analysis with the Chi-Square test strengthens the hypothesis that Andaliman Fruit extract increases the number of fibroblasts ($p = 0.024$). The phytochemical content of Andaliman Fruit, such as flavonoids, tannins, alkaloids, and saponins, is believed to have a therapeutic effect in accelerating wound healing by stimulating fibroblasts and increasing collagen synthesis (Anggraeni, 2020; Saragih & Arsita, 2019). The study also found obstacles in the tooth extraction procedure, such as the risk of tooth fractures and limitations in checking the vitamin C levels in the extract. Overall, Andaliman Fruit extract with a concentration of 60% is more effective in accelerating wound healing than 30%. This study proves that Andaliman Fruit extract has excellent potential as a natural therapeutic agent in post-tooth extraction wound healing, which can be developed for applications in dentistry and regenerative medicine.

IV. Conclusion

The conclusions of this study showed that andaliman fruit extract (*Zanthoxylum piperitum*) with a concentration of 60% was more effective in accelerating the healing of post-tooth extraction wounds in Wistar mice compared to a concentration of 30%. A significant increase in the number of fibroblasts ($p = 0.024$) in the group with a concentration of 60% indicates the critical role of this extract in the tissue regeneration process. These results strengthen the potential of andaliman as a natural therapeutic agent in dentistry and regenerative medicine. The suggestion for future research is to test higher concentrations of the extract and use other animal models to reinforce the findings. Long-term research is also needed to evaluate its safety and potential side effects. In addition, identifying bioactive compounds in the extract is essential to determine the optimal concentration that plays a role in wound healing and improve tooth extraction procedures in test animals to avoid fractures that can affect the study results.

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