The Effect Of Aloe Vera And Manuka Honey On IL-1 Level In Periodontitis Rats

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Received 2 July 2025; Accepted 22 August 2025; Published online 22 August 2025

Keywords:

Periodontitis;IL- 1

ABSTRACT

Background: *Periodontitis is a chronic inflammatory disease that occurs as a result of the immune system's response to bacterial infection of the gums and surrounding tissues. This condition is caused by chronic inflammation and increased levels of proinflammatory mediators associated with chronic infectious conditions. Periodontitis can trigger inflammation by increasing the level of interleukin-1 (IL-1), which plays a role in the inflammatory response. Aloe vera (Aloe vera) and manuka honey are known to have anti-inflammatory properties and inhibits the production of pro-inflammatory cytokines, including IL-1. Purpose of this research to determine the effect of Aloe Vera and Manuka Honey on IL-1 level in periodontitis rats..*

Method: *30 rats were randomly divided into four groups; control group, Aloe vera groups, Madu manuka group, combination of Aloe Vera and Manuka Honey group. Aloe vera and Manuka Honey were injected at doses 150 uL in the gingival. At the 5th day after treatment, all rats were terminated and Elisa from gingival tissue was performed to identify the level of IL-1.*

Result: *The results a significant decrease of IL-1 in combination of manuka honey and Aloe Vera group($p<0.000$) compared to control group*

Conclusion: *The combination of Aloe Vera and manuka honey significantly decreased on IL-1 level.*

DOI: http://dx.doi.org/10.30659/medali.7.2.109-114
MEDALI Jurnal: Media Dental Intelektual accredited as **Sinta 4 Journal**
(https://sinta.kemdikbud.go.id/journals/profile/13665)
2337-6937/ 2460-4151 ©2025 National Research and Innovation Agency

How to Cite: *Muchaeroni et al*. The Effect Of Aloe Vera And Manuka Honey On Il-1 Level In Periodontitis Rats. MEDALI Jurnal: Media Dental Intelektual, v.7, n.2, p.109-114, August 2025.

INTRODUCTION

Periodontitis is a chronic inflammatory disease that occurs due to the immune system's response to bacterial infections in the gums and surrounding tissues.[1] Bacterial colonization will trigger the release of cytokines such as IL-1a and ß, IL-6, IL-8 and TNF-a, and PMN in inflammation.[2] This condition is caused by chronic inflammation and increased levels of proinflammatory mediators associated with chronic infection conditions.[3] Based on Basif Health Research of 2018 data, the percentage of periodontitis cases in Indonesia reached 74.1%.[4]

The Interleukin-1 (IL-1) cytokine family plays a major role in inducing and maintaining this inflammatory response. Among the IL-1 family members, IL-1α and IL-1β are key in driving inflammation in periodontitis which contributing to tissue damage and bone degeneration.[1]

Herb that are known to have anti-inflammatory effects namely aloe vera and manuka honey. Aloe vera is a plant that contains various bioactive compounds, such as polysaccharides, flavonoids, saponins, and vitamin E. Those bioactive compound can reduce blood glucose levels and inhibit the production of pro-inflammatory cytokines, including IL-1, IL-6, and TNF-α.[5] Aloe vera has been used in traditional medical practice for many years due to its various benefits. Aloe vera gel contains various bioactive components that provide therapeutic effects, such as antibacterial, anti-diabetic, anti-ulcer, anti-inflammatory, antioxidant, hemostatic, and anticarcinogenic properties.[6]

Manuka honey is a type of honey that comes from the nectar of the Leptospermum scoparium plant, which has a high methylglyoxal (MGO) content. MGO is a compound that can inhibiting the growth of periodontitis-causing bacteria, as well as reducing blood glucose levels and cytokine expression including IL-1.[7] However, the therapeutic potential of targeting the cytokine IL-1 to manage periodontitis has not been fully explored.

MATERIAL AND METHOD

Processing of Aloe Vera Juice

The stages of making aloe vera juice begin with washing the aloe vera stems with water to remove dirt. Then the Aloe vera peeled to get the aloe vera flesh. The aloe vera flesh that has been peeled from its skin is washed using flowing water. Furthermore, the aloe vera flesh is pureed using a blender at medium speed for 3 minutes to obtain aloe vera juice. The juice is stored in a cool container and protected from the sun.[8]

Periodontitis Induction

Rat (Rattus Novergicus) were adapted to laboratory conditions for 7 days. On the 7th day before being induced with periodontitis, rats were anesthetized by injecting ketamine HCl intramuscularly into the hamstring muscle at a dose of 0.2 ml/200 grams of body weight.[9] Periodontitis induction with P. gingivalis bacteria in the distobuccal and distolingual gingival sulcus of the lower left incisor teeth at dose of 0.05 ml. Inducction was carried out in every 3 days for 14 days using a tuberculine syringe and a 30 gauge needle. The time required to make rat into periodontitis models is 14 days. Rats are said to have periodontitis characterized by the formation of periodontal pockets, alveolar bone resorption and inflammation such as swelling and redness of the gingiva.[10]

Treatment in Rat

Rats were divided into 4 groups. The First group is negative control group given distilled water, second group given aloe vera as much as 0.2 cc/gram body weight, third group given manuka honey as much

as 0.2 cc/gram body weight, and the fourth group given aloe vera and manuka honey as much as 0.2 cc/gram body weight. Therapy was given by injecting aloe vera and manuka honey into gingival rats for 4 days. Thereafter rats were terminated by being placed in an airtight box and given chloroform for 10-30 minutes until the rats died. Then the jaw rat was separated with a scalpel and scissors, then the gingival organ was taken around the anterior teeth.[11] The next step is to process the gingival to obtain homogenate tissue that will be used to measure IL-1 (Interleukin 1) level. Gingival tissue was cut into small pieces and placed in a micro tube containing an appropriate buffer, such as phosphate buffer or PBS, to maintain the stability of the protein in the tissue. Furthermore, the tissue is crushed using a homogenizer or mortar and pestle to obtain a homogenate, which functions to release the proteins in the tissue, including IL-1. After the tissue was crushed, the sample was centrifuged to separate the insoluble component until the supernatant containing soluble proteins, including IL-1, can be separated and ready for further analysis.

Detection of IL-1

Examination of interleukin-1 serum was performed using an ELISA tool (Human Interleukin 6 ELISA kit Cat.No E0090Hu and Elisa reader PHO MO Autobio) which is an immunoserology examination tool. The interleukin-1 examination procedure was performed using the SOP *Bioassay Technology Laboratory - Human Interleukin 1* ELISA kit Cat.No E0090Hu, sensitivity 1.03 ng/L, with a size of 96 wells. This research is conducted in Laboratory of the Center for Food and Nutrition Studies, Gajah Mada University in December 2024.

RESULT

The results of the ELISA reading provide data on IL-1 levels as follows :

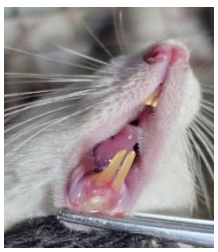
Table 1. Mean and Standard Deviation of IL-1 amount

Number	Group	Mean±Standar Deviasi
1	Aquades	128±5.17
2	Aloevera	47±2.36
3	Manuka Honey	63.16±3.61
4	Aloevera + Manuka Honey	40±3.39

Based on table 1, the group given distilled water showed the highest average number of IL-1, which was 128 ± 5.17, indicating that distilled water was not effective in reducing IL-1 levels. The manuka honey group had an average of 63.16 ± 3.61, indicating a decrease, but it still has high level. Meanwhile, the group given aloe vera showed an average of 47 ± 2.36, indicating potential in reducing IL-1. The group that received a combination of aloe vera and manuka honey had the lowest value, namely 40 ± 3.39, indicating that this combination is more effective in reducing IL-1 levels compared to another group.

Picture 1

Periodontitis Rat



Treatment Aloe vera+manukaHoney

The next step is conducting normality and homogeneity tests to adjust the test that will be used:

Table 2. Normality and Homogenity Test

Number	Group	Shapiro-Wilk	Lavene
1	Aquades	0.670	
2	Aloevera	0.739	0.361
3	Manuka Honey	0.988	
4	Aloe vera+Manuka Honey	0.515	

The type of normality test used is the Shapiro-Wilk test because the number of data in this study is less than 50. As shown in table 4.2, all data are normally distributed with a p value > 0.05. Furthermore, Levene's homogeneity test is used to test the data, and the significance value obtained is 0.361 (p > 0.05), which indicates that the data is homogeneous. Therefore, the next step is to conduct a One-Way ANOVA parametric test because the data are homogeneously and normally distributed and meet the requirements for a parametric test. The purpose of this test is to determine whether there is a significant difference in the amount of IL-1 between each group tested.

Table. 3 One Way Annova Test

Number	Group	Sig
1	Aquades	
2	Aloevera	0.000
3	Manuka Honey	
4	Aloe vera+Manuka Honey	

Based on table 3, the results of the One-Way ANOVA test show a significance value of p = 0.000 (p < 0.05), which indicates a significant difference in the amount of IL-1 among the four groups tested, namely distilled water, aloe vera, manuka honey, and a combination of aloe vera with manuka honey. This very low p value indicates that at least one group has a significantly different average compared to the other groups. Thus, these results provide strong evidence that the treatment received by each group affects IL-1 levels. Further exploring and determine specific differences between each group, the next step is to conduct a post hoc LSD (Least Significant Difference) test. This test will help identify which groups differ significantly from each other, providing a deeper understanding of the effects of each treatment on IL-1 levels.

Table.4 Post Hoc LSD Test

Treatment Group	Aquades	Aloevera	Manuka Honey	Aloevera+ Manuka Honey
Aquades	-	0.000	0.000	0.000
Aloevera	0.000	-	0.000	0.044
Manuka Honey	0.000	0.000	-	0.000
Aloe vera+Manuka Honey	0.000	0.044	0.000	-

The results of the LSD post-hoc test, the comparison between the aquades group and the aloe vera group showed that there was a significant difference in IL-1 expression with a p value of 0.000 (p < 0.05). In addition, there was a significant difference in IL-1 expression between the aquades group and the manuka honey group with a p value of 0.000 (p < 0.05). However, the comparison results between the aloe vera group and the manuka honey group did not show a significant difference in IL-1 expression with a p value of 0.044 (p < 0.05). These results indicate that both aloe vera

and manuka honey have different effectiveness in reducing IL-1 expression in periodontitis therapy.

DISCUSSION

Based on the results of the One Way ANOVA and post hoc LSD tests shown in tables 3 and 4, it is known that the treatment of aloe vera and manuka honey is effective in reducing IL-1 expression compared to the negative control group. This can be seen from the decreasing of IL-1 level. The findings of this study are in line with research before which explained that the use of aloe vera can reduce inflammation by stimulating prostaglandin synthesis and increasing leukocyte infiltration[12]. This study is supported by the results of a study conducted by Yazdani et al (2022) which showed that aloe vera can significantly reduce inflammatory factors such as IL-1, TNF-α, TGF-β, and IL-6.[13]

Manuka honey contains phenolic and flavonoid compounds, peroxide groups, and compounds such as GO, 3-DG, and MGO which have antibacterial activity. In addition, manuka honey is also known to be able to inhibit bacterial growth.[14] In another study, regarding the effects of two concentrations of Manuka honey (0.5% and 3% v/v) on the release of cytokines from neutrophils, it was found that a concentration of 0.5% reduced the release of IL-1β, which has the potential to accelerate wound healing by reducing inflammation. Conversely, at a concentration of 3%, although most cytokines decreased, TNF-α actually increased, indicating a complex effect on the inflammatory response. These findings indicate that manuka honey has dose-dependent ability to modify cytokine release.[15]

Furthermore, the research before showed that topical aloe vera gel, combined with SRP, significantly reduced IL-1β levels in gingival crevicular fluid in chronic periodontitis patients.[16]

CONCLUSION

Combination of Aloe Vera and Manuka Honey showed a significant decrease in IL-1 level compared to the control group, aloe vera group and manuka honey group. These results conclude that the combination of Aloe Vera and Manuka Honey is devastating as an anti-inflammatory agent in reducing IL-1 levels in periodontitis.

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