



EFFECTIVENESS OF *CENTELLA ASIATICA* EXTRACT ON IL6 AS A BIOLOGICAL MARKER OF WOUND HEALING POST-OPERATIVE METHODS IN PERIORBITA REGION

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Abstract

Centella asiatica is the most effective herbal remedy for wound healing as it stimulates the release of growth factors and cytokines, including interleukin-6 (IL-6), from inflammatory cells. These cytokines serve as indicators of the progress of the wound healing process, and can be measured through the production of protease enzymes, such as matrix metalloproteinase (MMP). Therefore, this study aimed to determine the effectiveness of *Centella asiatica* (Lanakeloid) on IL-6 levels as a biological marker of postoperative wound healing in the periorbita region. The Double-Blind Randomized Clinical Trial study was conducted on patients after the first day of periorbital surgery was undertaken at Dr. Mohammad Hoesin Central General Hospital from March 2022 to June 2022. A total of 30 post-periorbital surgery patients who met the inclusion criteria were involved. The Wilcoxon test was used to analyze the effectiveness of *Centella asiatica* (Lanakeloid) and placebo, while the Mann Whitney test was used for the comparison of effectiveness between Lanakeloid and placebo on SPSS version 22.0. The results showed that there was no significant difference in age, gender, and IL-6 levels before treatment between the Lanakeloid and placebo groups, as indicated by $p > 0.05$. Furthermore, there was a decrease in IL-6 levels before and after Lanakeloid treatment ($p = 0.005$) and an increase before and after placebo treatment ($p = 0.031$). After the intervention, the results showed that there were differences in IL-6 levels between the Lanakeloid and placebo groups, as indicated by $p = 0.004$. In conclusion, there was a difference in IL-6 levels after systemic treatment of *Centella asiatica* (Lanakeloid) with placebo on wound healing in the first week after surgery in the periorbita region.

Keywords: *Centella asiatica*, interleukin-6, periorbita, placebo, wound healing

Introduction

A wound can be defined as an injury to the normal structure and function of the skin and its underlying soft tissues. Wounds are generally classified into two categories: acute and chronic. Acute wounds are easily identifiable and typically result from trauma, while chronic wounds develop from acute wounds that do not heal or take longer than normal to heal. Surgical wounds, on the other hand, are a form of controlled acute wound that occur during surgical procedures in the operating room¹

The wound healing process stimulates the release of cytokines and growth factors from inflammatory cells. These cytokines include interleukins (IL-1 and IL-6), tumor necrosis factor-alpha (TNF- α), platelet-derived growth factor (PDGF), and fibroblast growth factor-2 (FGF2). These growth factors and cytokines, together with the production of protease enzymes such as matrix metalloproteinase (MMP), can be used as markers or biomarkers of the wound-healing process.²

Centella asiatica, which belongs to the Apiaceae family, has been widely used for both medicinal and culinary purposes in East Asia for centuries. Its extract is recognized for its ability to enhance wound healing and is commonly found in skincare products (Almaida & Saputra, 2021). The plant's antioxidant

activity allows it to help form collagen and restore damaged tissue, leading to improved skin tightness, elasticity, and protection from UV rays. While the exact molecular mechanism of *Centella asiatica*'s wound healing properties is not known with certainty, many studies have reported its successful use. Topical therapeutics using *Centella asiatica* are used to treat skin ulcers, hypertrophic scarring, keloids, impaired wound healing, and venous lymphatic disorders. 3, 4

Many studies have been published regarding the efficacy and effects of *Centella asiatica* on wound healing due to burns or surgical scars. However, studies in the periorbital region of post-operative patients have not been carried out worldwide⁵

Therefore, this study aims to further explore the effect of *Centella asiatica* on wound healing in post-operative periorbital region patients. The formulated hypothesis includes:

H₀: There was no significant difference in effectiveness between *Centella Asiatica* and placebo in reducing IL-6 levels after administering *Centella* by signing an informed consent form.

H_a: There is a significant difference in IL-6 levels after administration of *Centella Asiatica* systems and placebo on wound healing in the first week after surgery in the periorbital region

Research Method

This study was conducted at the Central General Hospital Dr. Mohammad Hosein Palembang from March 2021 and continuing until the required sample size was reached. It was a randomized, double-blind, controlled clinical trial and involved all willing patients who had undergone periorbital surgery. All eligible subjects who met the inclusion criteria were included in the study(Sugiarti & Rusmana, 2022).

Nisa and Hutagalung (2022) The inclusion criteria are (a) The first day of post-periorbital surgery patients who were treated at Central General Hospital Dr. Mohammad Hoesin Palembang, (b) Patients aged > 20 years, (c) The general condition of the patient is good, and (d) the willingness to participate by signing an informed consent. The exclusion criteria used were (a) Patients with allergy to *Centella Asiatica*, (b) Patients with liver disease, (c) Patients with oral/topical steroid use, (d) Patients with infections, (e) History of surgery in the periorbital region within the last 6 weeks, and (f) Patients with chronic diseases.

Samples were collected by matching sampling based on the size of the wound. Patients who met the inclusion criteria were taken as samples until they reached the specified number(Hutamya, Marham, Alisyahbana, Arisah, & Hasan, 2021). Furthermore, simple randomization is used to assign participants to the *Centella asiatica* extract or placebo groups(Lestari, 2023). The sampling technique was a pilot study, where 10 patients were treated with the *Centella asiatica* extract and 10 with a placebo. The definitive sample size is calculated with the paired numerical analytic test formula.

Result and Discussion

Comparison of the Effectiveness of Lanakeloid and Placebo Interventions against IL-6 levels

Table 1. Comparison of IL-6 Levels of Research Subjects After Intervention

Asiatica systems with placebo for wound healing in the first week after surgery in the periorbital region.

Variable	Intervention		P Value
	Lanakeloid (n=15)	Plasebo (n=15)	
IL-6 After Intervention (pg/mL)			
Average ± SD	3.39 ± 1.85	6.01 ± 3.37	0.044*
Median	2.96	5.33	
(Min-Max)	(1.5-7.08)	(1.5-0.81)	

Mann Whitney, * $p < 0,05$

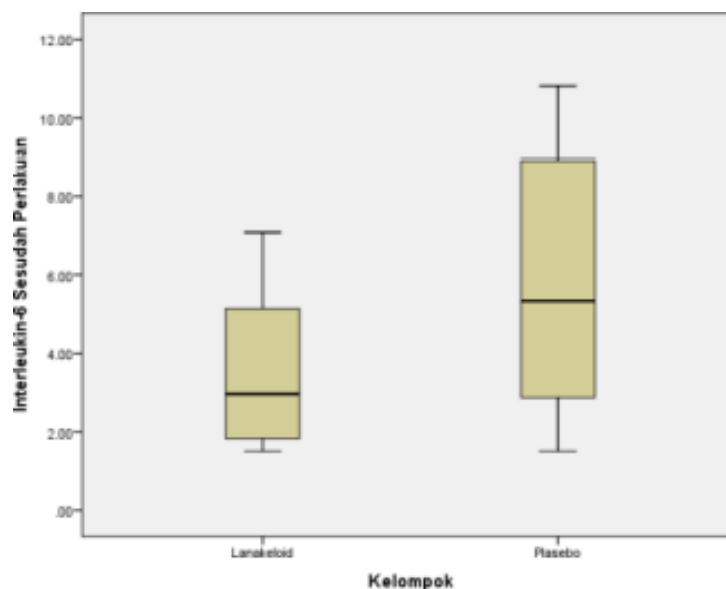


Figure 1. IL-6 levels after intervention

IL-6 levels of both groups were assessed after the next intervention. The average IL-6 level after the intervention in the Lanakeloid group was 3.39 ± 1.85 pg/mL with a median of 2.96, ranging from 1.5 to 7.08 pg/mL. In the placebo group, the average level after the intervention was 6.01 ± 3.37 pg/mL, with a median of 5.33, ranging from 1.5 to 10.81 pg/mL. The Mann-Whitney test showed a significant difference in IL-6 levels after the intervention between the Lanakeloid and placebo groups, as indicated by $p = 0.044$ and $p \geq 0.05$.

In this study, a sample of 30 post-operative periorbital patients was collected and divided into Lanakeloid and placebo groups. Lanakeloid tablet contains 17.5% *Pegagan* extract in each caplet^{2,7}. Meanwhile, *Centella asiatica* belongs to the Apiaceae family, and it is recognized for its ability to enhance wound healing and has also been used in skincare.



Figure 2. *Centella asiatica* (Pegagan) [5]

Centella asiatica can help form collagen and restructure damaged tissue due to its antioxidant properties, thereby restoring tightness, skin elasticity, and protection from UV rays. Its molecular mechanism of

action for wound healing is not known with certainty, but many studies have mentioned its success as a topical therapeutic agent for the treatment of skin ulcers, hypertrophic scarring, keloids, impaired wound healing, and venous-lymphatic disorders 8, 9

In this study, *Centella asiatica* and placebo extract are administered in the same shape and size and administered in the form of 30 mg tablets with a dose of 3 times daily after the first day of surgery for 1 week¹⁰. The administration of Lanakeloid showed a decrease in IL-6 levels in 12 patients after administration for 1 week. In contrast, after the administration of a placebo, an increase in IL-6 levels was observed in 11 patients. The mean IL-6 level in the group that received Lanakeloid was lower than the placebo^{11, 12}

In four clinical trial studies, *Centella asiatica* was reported to improve wound healing due to increased angiogenesis and showed anti-inflammatory effects, which were observed by decreasing Interleukin-1 β (IL-1 β)^{13,14}. (Mas'adah, Asngadi, & Hirmantono, 2021) Previous results and discussion concluded that there were significant differences in IL-6 levels after the administration of *Centella asiatica* systemic treatment with placebo on wound healing in the first week after surgery. Therefore, H₀ was rejected, and H_a was accepted.

Conclusion

The conclusions made from this study include the following:

1. IL-6 levels in the first week of wound healing following regional surgery periorbital was 3.39 ± 1.85 , with a range of 1.5 and 7.08, after administration of systemic *Centella asiatica*.
2. IL-6 levels in the first week of wound healing following regional surgery periorbital was 6.01 ± 3.37 , with a range of 1.5 and 10.81, after administering a systemic placebo.
3. There is a significant difference in effectiveness between *Centella asiatica* and placebo in reducing IL-6 levels after administration of systemic *Centella asiatica* with placebo in the first week after regional surgery periorbital.

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