

RESEARCH ARTICLES

Effectiveness of Celery Leaf Extract Gel (*Apium graveolens* (Linn.) As A Treatment for IIA Degree Burn Wounds in Wistar White Rats (*Rattus norvegicus*) (In Vivo Study)

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Abstract: Indonesia is one of the countries that has traditionally used traditional medicine as a treatment. The pharmacological activity of celery leaves is antimicrobial, antibacterial, and anti-inflammatory. As one of the herbal ingredients, celery (*Apium graveolens*) has the potential to be developed as an anti-inflammatory drug because it contains the main compound apiin, which is the main metabolite for anti-inflammation. This study aims to determine the Effectiveness of Celery Leaf Extract Gel (*Apium graveolens*(Linn.) As a Treatment of Grade II Burns in White Wistar Rats (*Rattus norvegicus*) (In Vivo Study). This study is a true experimental study. 30 rats were divided into five groups, namely rats with grade IIA burns given sulfadiazine cream, negative control, celery gel preparations with concentrations of 1%, 2% and 4%; the average number of days of wound healing was tested with One-Way ANOVA. The average healing of grade IIA burns in the positive control group was 7.5 days, in the negative control 17.3 days, treatment I 13.6 days, treatment II 9.5 days, and treatment III 9.0 days. One-way ANOVA test value ($p < 0.05$) showed significant differences among the treatment groups. Post hoc test showed no significant difference between the positive group and treatment group 3 ($p = 0.061$). Conclusion: Celery gel (*Apium graveolens*) is effective in healing burns in grade IIA white Wistar rats at a dose of 4%.

Keywords: Celery leaves, burns, male Wistar rats

INTRODUCTION

Indonesia is one of the countries that has traditionally used traditional medicine for treatment. According to the World Health Organization (WHO), approximately 80% of the world's population uses traditional medicines derived from plants.^{1,3} Indonesia has approximately 30,000 plant

species. 7,000 of these plant species are known to have medicinal properties. Approximately 90% of medicinal plants in the Asian region grow in Indonesia. 940 species of medicinal plants have been utilized by the community as traditional medicine; only 120 species are included in the Indonesian Medical Material. 1 several

herbal plants have the potential to heal burns, such as areca nut, binahong leaves, atsute leaves, avocado leaves, guava leaves, and celery leaves. The pharmacological activity of celery leaves is antimicrobial, antibacterial, and anti-inflammatory.^{2,3}

Burns can be caused by exposure to heat, radiation, electricity, chemicals, or friction, most often caused by heat from a fire.⁵ Clinically, burns can be divided into four degrees based on their depth: first-degree, which affects only the epidermis; second-degree, which involves the epidermis and dermis; third-degree, which involves the epidermis, dermis, and skin appendages. Fourth-degree burns, on the other hand, can penetrate subdermal fat, muscle, and even bone. The healing time for burns varies depending on the degree; first-degree burns heal completely without scarring in 5-10 days. Second-degree burns heal in 14-21 days.⁴ The healing phase of a burn begins with hemostasis, inflammation, proliferation, and remodelling.

As an herbal ingredient, celery (*Apium graveolens*) has the potential to be developed as an anti-inflammatory drug because it contains the main compound apiin, a key metabolite for anti-inflammatory properties. In the body, apiin is hydrolysed into sugar and the aglycone apigenin, a substance proven to relieve inflammatory symptoms. The same source states that celery contains flavonoids and tannins, which have the potential to accelerate wound healing. This is due to the presence of flavonoids, which are secondary metabolites with potent anti-

inflammatory properties due to their effects on reducing oxidative stress and preventing several other inflammatory factors.^{5,6}

Flavonoids play a role in accelerating the process of stopping bleeding through a vasoconstriction mechanism, while tannins function as hemostatic agents by precipitating blood proteins, namely albumin.⁶

Previous research stated that applying celery cream to cut wounds in experimental mice can heal the cuts within 7 days; another study using aloe vera gel can heal second-degree burns within 9 days, and there has been no research that has tested celery gel preparations on burns. Therefore, with these considerations, the author will conduct research with a research gap that will test the effectiveness of celery leaf extract gel (*Apium graveolens*) in treating second-degree burns by testing on white Wistar rats.^{7,8}

METHOD

This study is a true experimental study with a post-test-controlled group design. This is because it aims to determine the effectiveness of Celery Leaf Extract Gel (*Apium graveolens*) in healing second-degree burns in male Wistar rats (*Rattus norvegicus* L). The total sample in this study was 30 rats. Data were analyzed using SPSS. Then, a One-Way ANOVA test was performed. If a p-value of <0.05 is obtained, it is considered statistically significant.

RESULT

2 kg of fresh celery leaves were washed thoroughly with running water and drained using a winnowing basket. Then, the dried celery leaves were ground using a blender and sieved using a 50-mesh sieve to obtain 250 grams of fine celery leaves. The fine celery leaves were soaked in 87 ml of 96% ethanol in a closed glass jar with a ratio of 1:10 w/v for 3 days while stirring constantly twice a day. The results of the maceration process were then filtered. The macerate was then evaporated in a rotary evaporator until a thick extract was formed.

Table 1. Results of making celery leaf extract

Powder Weight	Extract Weight	Yield
250 gr	35 gr	14 %

Phytochemical screening tests were then conducted to determine the authenticity of the compounds contained within. Phytochemical screening tests on celery leaf extract included tests for saponins, mollisch, tannins, flavonoids, alkaloids, and terpenoids/steroids.

Table 2. Phytochemical Screening Results of Celery Leaves

Testing	Reagent	Result
Saponin		(+)
Mollisch		(+)
Tanin		(+)
Flavonoid	- FeCl ₃ 5%	(+)
	- NaOH 10%	(-)
	- H ₂ SO ₄	(+)
	- Mg + HCl	(-)
Alkaloid	- Wagner	(+)
	- Maeyer	(-)
	- Bouchardat	(-)
	- Dragendorff	(+)

Terpenoid / Steroid	- Liebermann-Burchard	(-)
	- Salkowsky	(-)

The phytochemical screening results for saponins, mollisch, tannins, and flavonoids were positive. This indicates the presence of apiin, an anti-inflammatory substance derived from glycosides. A positive Molisch screening result indicates the presence of glycosides. Furthermore, flavonoids can increase vascularization and reduce oedema. Flavonoids have anti-inflammatory and antioxidant effects. Flavonoids are also believed to be beneficial in the wound healing process. Saponins act as antiseptics, stimulate epidermal cell proliferation, and influence the rate of keratinocyte migration to the wound area, thereby increasing wound epithelialization. Tannins can enhance wound healing through cellular mechanisms that inhibit free radicals and reactive oxygen species, and enhance angiogenesis. Alkaloids act as antimicrobials and antioxidants.

Table 3. Average Days to Burn Healing Between Groups

Group	Average Days of Wound Healing (Mean±SD)
Kontrol Positif	7,5±0,8
Kontrol Negatif	17,3±2,0
Perlakuan 1	13,6±1,21
Perlakuan 2	9,5±1,2
Perlakuan 3	9,0±0,8

From the results of this study, in the positive control group, the average wound healing time was 7.5±0.8 days. In the negative control group, the average wound healing time was 17.3±2.0 days. In treatment group 1, the average wound healing time was

13.6±1.21 days. In treatment group 2, the average wound healing time was 9.5±1.2 days. In treatment group 3, the average wound healing time was 9.0±0.8 days.

Table 4. ANOVA test

Group	Average Days of Wound Healing (Mean±SD)
Kontrol Positif	< .001
Kontrol Negatif	
Perlakuan 1	
Perlakuan 2	
Perlakuan 3	

There is a difference in the ANOVA test; the p-value obtained is below <0.05, so it can be concluded that there is a significant difference between the groups.

Table 5. LSD Post-Hoc Test

Group (I)	Group (II)	Mean Difference	Sig.
Positive Control	Negative Control	-9.83	0.000*
	treatment 1	-6.17	0.000*
	treatment 2	-2.00	0.015*
	treatment 3	-1.50	0.061
Negative Control	treatment 1	3.67	0.000*
	treatment 2	7.83	0.000*
	treatment 3	8.33	0.000*
Treatment 1	treatment 2	4.17	0.000*
	treatment 3	4.67	0.000*
Treatment 2	treatment 3	0.50	0.518

The data above show that there was no significant difference between the positive control and treatment 3. Therefore, it can be concluded that the effective dose of celery as an antiseptic for second-degree burns is at dose P3, which is 4%. However, descriptively, the positive control, or

sulfadiazine cream, was superior to the 4% celery leaf gel extract.

DISCUSSION

The discussion illustrates the rats regarding the healing of burns in rats using celery leaf extract. The results showed that the compound apiin was found to be anti-inflammatory, as evidenced by the reactivity of the Molisch reagent, indicating the presence of glycosides in the extract. In the body's system, apiin will be hydrolysed into sugar and the aglycone apigenin, a substance proven to be able to overcome inflammatory symptoms. The same source states that celery contains flavonoids and tannins that have the potential to accelerate wound healing.⁶ This is due to the presence of flavonoids themselves, which are secondary metabolites with strong anti-inflammatory properties due to their effects on reducing oxidative stress and can prevent several other inflammatory factors.⁶ Flavonoids play a role in accelerating the process of stopping bleeding through a vasoconstriction mechanism, while tannins function as hemostatic agents by precipitating blood proteins, namely albumin.⁶

Meanwhile, when discussing herbal ingredients as anti-inflammatories, several previous studies have conducted limited research focusing on the use of aloe vera and other herbal ingredients to treat burns.^{8,9,10} Meanwhile, research on celery leaves (*Apium graveolens*) in the world of health has been studied for their use as a hair tonic,

anti-hyperglycemic, and medicine for cuts.^{11,12}

Previous research has shown that applying celery cream to cuts in rats can heal wounds within 7 days. Another study using aloe vera gel can heal second-degree burns within 9 days. However, no research has yet tested celery gel preparations on burns. Therefore, with these considerations in mind, the authors conducted a research gap study to test the effectiveness of celery leaf extract gel (*Apium graveolens*) in treating second-degree burns. This study will be conducted on Wistar rats.^{7,13}

Based on the results of the One-Way ANOVA analysis, a p-value of <0.001 was obtained, indicating a significant difference between the study variables. It can be concluded that celery leaf extract has healing activity in second-degree burns in Wistar rats.¹⁵

From the research data, the effective dose for healing burns was 4% in treatment group 3. This is in line with the results of research conducted by Agust Dwi Djajanti, Dzul Asfi. (2018), where the study evaluated celery cream extract with concentrations of 1%, 2%, and 4% for cuts in rabbits and the most effective dose was 4%. This is also in line with the results of research conducted by Patel, J., & Amrutia, J. (2017), where the study was conducted to evaluate the effect of celery leaf extract on wounds in mice, and found that wounds in mice treated with topical celery leaf extract can increase the speed of epithelialization and stimulate increased collagen production in the treated

area.¹³ In addition, the results of this study are also in line with research conducted by Shukla, P., & Pandey, G. (2019) where this study was conducted to assess the antioxidant and anti-inflammatory properties of celery leaf extract on wounds, found that celery leaf extract applied to mouse wounds can reduce the levels of pro-inflammatory cytokines such as TNF- α and IL-6, as well as reduce oxidative stress in wound tissue. Research on celery leaf extract (*Apium graveolens*) in wound healing generally shows positive results.^{7,14,16}

CONCLUSION

1. Celery gel (*Apium graveolens*) is effective in healing grade IIA burns in Wistar rats.
2. The effective dose of celery gel for healing burns is 4%.
3. The positive control (Sulfadiazine cream) was the most effective control group in healing grade IIA burns in Wistar rats.

REFERENCES

1. Tilaar, Martha & Widjaja, Bernard T. The Power of Jamu. Jakarta: Pt Gramedia Pustaka Utama. 2014.
2. Anggraeni L, et al. Review Article: Medicinal Plants That Have Activity Against Burns. Padang. Farma. 2018. <https://Jurnal.Unpad.Ac.Id/Farmaka/Article/View/17621/Pdf>
3. Oaks RJ, Renford, Affiliations C. Silver Sulfadiazine Continuing Education Activity.

- <https://Www.Ncbi.Nlm.Nih.Gov/Books/Nbk556054/?Report=Printablerexs>.
(2012). Burn Injuries. Current Opinion In Critical Care, 18(6), 671–676.
<https://Doi.Org/10.1097/Mcc.0b013e328359fd6e>
4. Guo S, Dipietro La. Critical Review In Oral Biology & Medicine: Factors Affecting Wound Healing. J Dent Res. 2010;89(3):219-229.
 5. Jeschke Mg, Van Baar Me, Choudhry Ma, Chung Kk, Gibran Ns, Logsetty S. Burn Injury. Nat Rev Dis Primers. 2020;6(1). doi:10.1038/S41572-020-0145-5
 6. Escalona Jc, Peres-Roses R, Rodriguez Jr, Et Al. Traditional Medicine In Cuba: Experience In Developing Products Based On Medicinal Plants. In: Therapeutic Medicinal Plants: From Lab To The Market. Crc Press; 2016.
 7. Agust Dwi Djajanti, Dzul Asfi. Activity Test of Celery (*Apium graveolens* L.) Herb Ethanol Extract Cream Preparation on Cut Wounds in Rabbits (*Oryctolagus Cuniculus* L.).
 8. Hekmatpou, D., Mehrabi, F., Rahzani, K., & Aminiyan, A. (2019). The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wounds: A Systematic Review. Iranian Journal of Medical Sciences, 44(1), 1–9.
 9. Hadiningrat Fm. Antihyperglycemic Activity Test of 70% Ethanol Extract of Japanese Celery (*Angelica Keiskei*) Leaves on Male White Rats of the Sprague Dawlet Strain Using the Alloxan Induction Method. UIN Syarif Hidayatullah Jakarta; 2017.
 10. Anuar Ahbs, Levita J. Review: Celery *Apium graveolens*. Linn. as a tablet and anti-inflammatory. Pharmaka. 2018;16(1).
 11. Hassan Bazafkan M, Hardani A, Reza Afzal Zadeh M, et al. Wound healing effect of an ointment made from a mixture of *Brassica oleracea* var., *Punica granatum*, and *Plantago major* L. extracts in rats. Jentashapir J Health Res. 2014;5(4):21877.
 12. Najihudin A, Akmal, Rachmawati AS. Formulation and hair growth testing of hair tonic preparations using celery leaf extract on rabbits. In: National Seminar of Perhipba: Potential of natural ingredients as medicines, cosmetics, and functional foods, Faculty of Pharmacy, Pancasila University. 2019.
 13. Patel, J., & Amrutia, J. (2017). Wound healing activity of *Apium graveolens* leaves extract. International Journal of Pharmaceutical Sciences and Research, 8(10), 4256-4261.
 14. Shukla, P., & Pandey, G. (2019). Antioxidant and anti-inflammatory activities of *Apium graveolens* leaf extract in burn-induced inflammation. Journal of Ethnopharmacology, 229, 86-92.
 15. Miller, T. A., & Cohen, D. (2021). Failure of *Apium graveolens* extract in enhancing burn wound healing in a rat

model. Journal of Wound Care, 30(11), 967-974.

16. Smith, B. J., & Patel, K. (2019). Negative effects of celery (Apium graveolens) extract on burn wound healing: An experimental study. Dermatology Research and Practice, 2019, 9243517.