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The Effect of *Apium graveolens* (Linn) Extract on Reepithelialization of Incision Wounds: In Vivo Study

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ABSTRACT

Background: A wound is a disorder of the continuity of the epithelial layer of the skin or mucosa and can result from physical or thermal damage. Proliferation and remodeling processes are important phases in incision wound healing. Celery is believed to have the potential to regulate the inflammatory phase and accelerate the process of proliferation and remodeling of wound tissue. This study aims to evaluate the potency of celery extract (*Apium graveolens* (Linn)) on incision wound healing in vivo.

Methods: This study was an in vivo experimental study. A total of 24 rats were used in this study and divided into 4 treatment groups (2 control and 2 treatment groups). Analysis of epithelial thickness ratio and epithelial length was performed using SPSS using univariate and bivariate. **Results:** The control group had the lowest epithelial thickness ratio, followed by 50% extract, 75% extract, and finally, the gentamicin group. The length of newly formed epithelium in wounds treated with *Apium graveolens* (Linn) extract group 70% (mean 1.461 mm) was similar to that treated with gentamicin 0.1% (mean 1.457 mm) and much better than those treated without extract (0.869 mm). **Conclusion:** Celery extract (*Apium graveolens* (Linn)) has the potential to accelerate the process of reepithelialization of incision wounds in vivo studies.

1. Introduction

A wound is a disorder of the continuity of the epithelial layer of the skin or mucosa and can result from physical or thermal damage. It is usually formed as a result of human activity. Any stimulus that breaks the physical continuity of functional tissue can create a lesion. The stimuli that cause the lesion can be external or internal, as well as physical, chemical, electrical, or thermal. The mechanism of the wound

healing process consists of four interacting phases, namely the coagulation, inflammation, proliferation, and remodeling phases. These four processes can take place smoothly as long as there are no certain conditions that hinder the proliferation and remodeling process. Proliferation and remodeling processes are important phases in incision wound healing. Infectious conditions and certain medical conditions, such as diabetes mellitus, nutritional

disorders, chemotherapy, and stress conditions, are believed to play a role in inhibiting the healing process of incision wounds. Disturbances in the processes of wound proliferation and remodeling lead to the prolongation of the inflammatory phase. The inflammatory process that takes place chronically causes activation of the death receptor, where activation of the death receptor will trigger the process of cell death or apoptosis. Apoptotic conditions will greatly complicate the wound-healing process. Inflammatory conditions are believed to be a key phase for optimal intervention processes to accelerate the wound healing process.¹⁻⁵

Current medical interventions also focus on intervening in relation to this inflammatory process. The use of antiseptic compounds, such as povidone-iodine, is believed to be able to reduce the bacterial load in wound tissue. However, the use of povidone-iodine is not without problems. Some studies show that these compounds cause allergic conditions in some individuals. In addition, it is necessary to clean the wound using gauze and bandages, which need to be changed three times a day. Of course, this really interferes with individual mobility and performance and really requires much money. Various existing problems related to the management of wound care a problem that needs to be pursued by a strategy and further exploration to be developed into a new therapeutic modality for incised wound conditions.^{6,7}

Indonesia is a country with the second-largest biological wealth in the world. This condition is an opportunity for Indonesia to take advantage of various existing biological potentials for the greatest prosperity of its people, including the potential to be developed as new drugs. Celery (*Apium graveolens* (Linn)) is one of the native plants of Indonesia, which is well known to the public and has been widely used as a cooking spice. Celery has been widely used as a therapeutic modality in Indonesian society. Celery has been widely used as a health drink for metabolic disorders, such as diabetes mellitus, hypercholesterolemia, and gout disorders. Celery is rich in various secondary metabolites, such as flavonoids. One of the main

flavonoids in celery is apigenin. Flavonoid compounds are believed to be useful in the regulation of oxidative stress. Oxidative stress is a condition that activates the inflammatory process. The presence of oxidants under conditions of oxidative stress causes an inflammatory process, and vice versa. Inflammation also causes oxidative stress. Celery is believed to have the potential to regulate the inflammatory phase and accelerate the process of proliferation and remodeling of wound tissue.⁸⁻¹² This study aimed to evaluate the potency of celery extract (*Apium graveolens* (Linn)) on incision wound healing in vivo.

2. Methods

This study was an in vivo experimental study with a post-test-only approach with a control group design. Twenty-four rats (*Rattus norvegicus*) were used in this study. The rats used in this study met the inclusion criteria in the form of male Rats, aged 8-12 weeks, with a body weight between 150-200 grams, and rats in good health. Rats were grouped into 4 groups (6 rats each), namely C1: negative control group, where the rats were treated with incised wounds. C2: positive control group, where white rats received gentamicin ointment, T1: treatment group 1, which received ointment 50% celery extract and T2: treatment group 2, which received 75% celery extract ointment, where the treatment was given for 7 days. This study was approved by the medical and health research ethics committee at the Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia.

Celery extract was prepared by maceration method from celery simplicia. The thick extract was then carried out by the cream preparation process with a concentration of 50% and 75%. The efficacy of celery extract in wound healing was assessed by measuring the length of the epithelial tissue formed with a digital caliper in millimeters and assessing the epithelial thickness ratio. Data analysis was carried out using SPSS software version 25 in a univariate and bivariate manner. Univariate analysis was performed to present the frequency distribution of each test variable. Bivariate analysis was performed to determine

differences in the mean epithelial tissue length and epithelial thickness ratio between the test groups with a p-value <0.05.

3. Results

Figure 1 shows the mean epithelial thickness ratio between groups. Groups T1 and T2 had a higher mean

epithelial thickness ratio than group C1, which was statistically significant. However, the average epithelial thickness ratio was not as optimal as the C2 group. These results indicate that celery extract has potential in the process of reepithelialization of incision wounds, although it is not as optimal as using gentamicin.

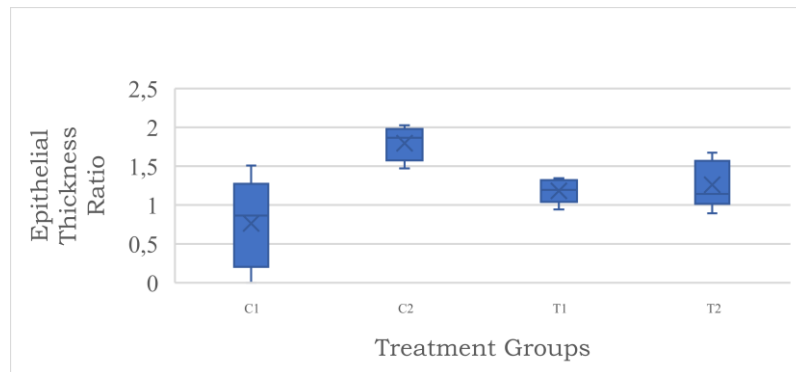


Figure 1. Comparison of mean epithelial thickness ratio between groups.

Figure 2. shows the comparison of newly formed epithelial length between groups. Groups T1 and T2 showed a mean length of newly formed epithelial length that was longer than group C1, even though they were not statistically significantly different. Although the mean of newly formed epithelial length

for the T1 and T2 groups was not as optimal as the newly formed epithelial length means for the C2 group. The results of this study indicate the potential of celery extract in optimizing newly formed epithelial length in incisions.

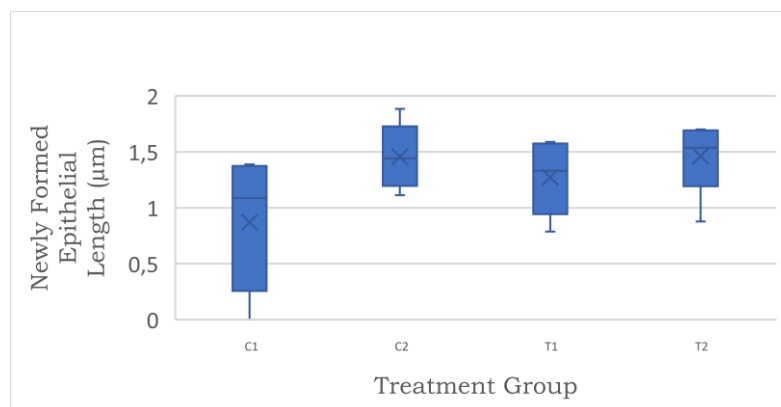


Figure 2. Comparison of newly formed epithelial length between groups.

4. Discussion

This study is one of the first studies to assess the effect of *Apium graveolens* (Linn) extract on reepithelialization of the incision wound healing after 7 days of treatment. The control group had the lowest

epithelial thickness ratio, followed by 50% extract, 75% extract, and finally, the gentamicin group. The 75% and gentamicin extract groups both had statistically significant differences compared to the control (p = 0.042 and p = 0.000, respectively), and the

50% extract group achieved a better ratio of epithelial thickness compared to the control group ($p = 0.080$). The fact that gentamicin cream group achieved a statistically significant difference compared to the control group ($p = 0.000$). To close the wound gap, the wound will heal faster horizontally than vertically. The length of the newly formed epithelium was completed to assess the speed of wound closure. However, this study found that the length development of newly formed epithelium in wounds treated with *Apium graveolens* (Linn) extract group 70% (mean 1.461 mm) was similar to that treated with gentamicin 0.1% (mean 1.457 mm) and much better than the non-extract treated (0.869 mm). A similar effect was also found in those who were given 50% *Apium graveolens* (Linn) extract (mean 1.273 mm). The results of this study indicate that the topical application of *Apium graveolens* (Linn) accelerates the rate of reepithelialization.

A reduction in the wound area after treatment with flavonoid-rich herbs was also found in previous studies. Injured rats treated with *Gynura procumbens* extract also had a better healing profile compared to those left untreated.¹³⁻¹⁶ Flavonoids (e.g., leuteolin, rutin, apigenin, catechin), found in *G. procumbens* and *Apium graveolens* (Linn), are known for their ability to initiate the wound healing process, especially for their antimicrobial properties, which appear to be responsible for wound contraction and increased rate of reepithelialization. Flavonoids also have the potential to control oxidative stress and inflammation. Reducing the process of oxidative stress and inflammation will accelerate the processes of epithelialization and remodeling as well as wound healing.¹⁷⁻²⁰

5. Conclusion

Celery extract (*Apium graveolens* (Linn)) has the potential to accelerate the process of reepithelialization of incision wounds in vivo studies.

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