

**Original Article****The Effect of *Lansium domesticum* Corr. (Duku) Seed Extract on Wound Healing**Tungki Pratama Umar<sup>\*1</sup>, Fernando Wijaya<sup>1</sup>, Junoretta Haviva Ernanto<sup>1</sup> and Theodorus Parulian<sup>2</sup><sup>1</sup>Department of Medicine, <sup>2</sup>Department of Pharmacology, Sriwijaya University, Palembang, IndonesiaArticle Received: 5<sup>th</sup> March, 2020; Accepted: 1<sup>st</sup> June, 2020; Published: 30<sup>th</sup> June, 2020DOI: <http://dx.doi.org/10.3126/jonmc.v9i1.29395>**Abstract****Background**

A wound is an injury caused by a cut, blow, or any else that typically involves laceration. For the treatment of infections and promoting wound healing, povidone-iodine is usually used but sometimes it can lead to irritation. The researcher would like to develop *Lansium domesticum* Corr. (duku) seed extract ointment to promote wound healing.

**Materials and Methods**

This experimental study was done on 30 rats which are divided into six groups namely negative control, positive control (povidone-iodine 10%), the experimental group with three different concentration of *Lansium domesticum* seed extract ointment (2.5%, 5%, and 10%) and followed for three days to assess wound size. Approval was acquired by the Research Ethics Committee of the Sriwijaya University Faculty of Medicine, Palembang, Indonesia. In vitro capacity of *Lansium domesticum* extract was also assessed by measuring inhibitory diameter.


**Results**

After three days of treatment, there is a significant difference in wound closure for all groups ( $p < 0.05$ ) except for the negative control group. The best wound closure was found in a 10% extract group with average wound size decreasing by 0.3 cm. For in vitro activity, only 10% *Lansium domesticum* seed extract ointment which is showing inhibitory zone at 3 mm of diameter.

**Conclusion**

*Lansium domesticum* Corr. seed extract ointment has the potency to promote wound healing on rats in addition to its small antimicrobial activity.

**Keywords:** *Phytochemical, Wounds and injuries, Wound healing*

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## Introduction

A wound is an injury caused by a cut, blow or any else that typically involves laceration or breaking of a membrane to the living tissue like skin and usually damage to underlying tissues. Wounds are classified according to their general condition, size, location, how the skin or tissue is broken, and the agent that caused the wound. Classification of wound comprises contusion, abrasion, puncture wounds, laceration, and avulsion defects. Lacerations are a torn ragged wound that results in an injury to the living tissue involving a cut or break in the skin. Simple lacerations are the most common type [1]. Injuries that are not treated seriously can get an infection that can make the treatment that needs to be done more difficult. Commonly, infections often occurs because of *Staphylococcus*, commensal bacteria in skin [2].

For the treatment of infections and promoting wound healing, ionophore-based formulations are often in the form of povidone-iodine which is used as antiseptics to boost wound heal process, this is evident with its efficacy [3], however, the use of povidone-iodine is also susceptible to infection reactions due to irritant substances [4-6]. Based on that, the basis of this research is to examine new alternative substances that can be used as a substitute for povidone-iodine. These alternative substances are plants that have potential as antiseptics, one of which is *Lansium domesticum* Corr. (duku), especially its seeds.

Duku is a seasonal plant that grows in the tropical area in South East Asia, especially in South Sumatera, Indonesia, and called "Duku Rasuan" or "Duku Komer" [7]. Its fruit flesh is consumed but the seeds are becoming the waste although it has many potentially useful substances such as flavonoids, alkaloids, and saponins which are useful in wound healing. Flavonoid content in various studies is effectively used as antiseptic and wound healing [8]. Saponins stimulate collagen formation, namely protein structure which plays a role in the process of wound healing [9]. Alkaloid content in duku seeds is useful as an antimicrobial that works by inhibiting proteoglycan synthesis in bacterial cell walls [10]. The potential of the duku seeds has not been used optimally as possible even though the content is very beneficial for various things, including for wound healing. The researcher aims to explore the efficacy of *Lansium domesticum* Corr. seeds extract ointment to promote wound healing.

## Materials and Methods

This experimental study was conducted on 30 Male Wistar Rats (*Rattus norvegicus*) between April to May 2019. All of the rats used were at the age of 20 weeks old and weighing 200-300 grams at the start of the study. Ethical approval was obtained from the

Research Ethics Committee of the Sriwijaya University Faculty of Medicine, Palembang, Indonesia. Before the experimental procedure, the rats were acclimatized, had *ad libitum* access to water and standard feeding with temperature about 22°C, 50-60% atmospheric humidity, and controlled light-dark cycle [11]. Animals were divided into five groups. All rats were inflicted with incision wounds, according to the method of Morton and Malone [12]. The first group was not given any treatment (negative control). In the second group, rats were applied 0.1 grams of povidone-iodine 10% ointment (Betadine®) as the positive control. The extract was obtained by macerating *Lansium domesticum* Corr. seed powder in ethanol (Merck®) at a ratio of 1:10 for 72 hours. *Lansium domesticum* Corr. (duku) seed extract ointment was made by mixing it with Vaseline (Merck®) and lanolin anhydrous (Merck®) until homogeneity is attained. Third to the fifth group of rats were applied 0.1 grams of *Lansium domesticum* (duku) seed extract with 2.5%, 5%, and 10% concentration, respectively. The topical application of ointment was carried out for 3 days and given 2 times daily, morning, and afternoon. Wound contraction is quantified by measuring the length of the wound on the third day. In vitro analysis of inhibitory activity against *Staphylococcus aureus* was evaluated using Mac Conkey (Merck®) blood agar plates. Results were determined by visual inspection of zones of growth inhibition. Data retrieval, tabulation, and statistical analysis were done using Statistical Package for Social Science (SPSS® version 25.0 for Windows). Data analysis was done using descriptive and analytic statistics (using the Mann-Whitney test for independent data and Wilcoxon test for dependent data). The significance level was settled at  $p$  value < 0.05.

## Results

After three days of treatment, the extract was found to show its effect to accelerate wound closure with a significant difference from the first day of treatment ( $p$  value < 0.05). Findings on the third day favor the potential curative effect of the *Lansium domesticum* Corr. seed extract. The mutual condition is also seen in the control treatment (Table 1).

**Table 1: Analysis of treatment effectiveness in wound closure**

Group	N	Pre test	Post test (Mean)	Δ closure	P value
Negative control	6	1 cm	0.88 cm	-0.12 cm	<b>0.138</b>
Positive control	6	1 cm	0.77 cm	-0.23 cm	<b>0.023</b>
Ointment (2.5%)	6	1 cm	0.82 cm	-0.18 cm	<b>0.030</b>
Ointment (5%)	6	1 cm	0.80 cm	-0.20 cm	<b>0.026</b>
Ointment (10%)	6	1 cm	0.70 cm	-0.30 cm	<b>0.016</b>

\*Wilcoxon,  $p$ -value < 0,05



We then compared the significance difference between each group using Mann Whitney U test. According to the analysis we found that all treatment had significant differences with negative control group ( $p < 0.05$ ). Extract group did not show any significant differences with positive control group ( $p > 0.05$ ) as shown on table 2.

**Table 2: Analysis of effectiveness between each groups**

	Control (-)	Control (+)	2.5% extract	5% extract	10% extract
Control (-)		0.026	0.240	0.038	0.014
Control (+)	0.026		0.310	0.038	0.014
2.5% extract	0.240	0.310		0.310	0.015
5% extract	0.038	0.584	0.310		0.004
10% extract	0.014	0.206	0.015	0.004	

\*Mann-Whitney,  $p$ -value  $< 0,05$

Inhibitory zone was measured on day 3 and it is evaluated that antiseptic activity of *Lansium domesticum* Corr. seed extract is small and only happening in 10% concentration ointment as compared with positive control Table 3.

**Table 3: Inhibitory zone diameter**

Group	Diameter (mm)
Positive control	26 mm
Negative control	0 mm
Ointment (2,5%)	0 mm
Ointment (5%)	0 mm
Ointment (10%)	3 mm

## Discussion

Wound healing is the process of repair that follows injury to the skin and soft tissues. This is a complex process involving inflammatory response due to local injury and activity of the cells below the dermis to increase collagen production. Then, there will be the regeneration of the epithelial tissue [13]. The process of wound healing in a simple way involving the acute inflammatory phase, proliferative phase, then followed by maturation and remodeling phase [14].

Topical application of *Lansium domesticum* Corr. seed extract showed the potential to improve the outcome of wound healing in Wistar rats. *Lansium domesticum* has many components that can be analyzed from phytochemical screening, including flavonoids, phenols, steroids, terpenoids, tannins, and saponins [15-16]. The component of *Lansium domesticum* extract is responsible for producing a better progression of wound healing. The flavonoid in *Sphaerant husamaranthoides* and *Martynia annua* showed an increase of hydroxyproline (a marker of collagen deposition) when compared to the control group [17]. Other flavonoids, such as Quercetin has good anti-inflammatory and antimicrobial activity that can

contribute to better tissue reorganization, re-epithelization, and thus giving some inhibitory effects of microbial growth [18]. Antioxidant activity of flavonoids that comes from *caffeic acid phenyl ester* (CAPE) is able to inhibit the oxidative process due to hyperinflammatory and hypermetabolism state by regulating NF- $\kappa$ B expression [19].

Saponins are triterpenoid or steroid glycoside that can be found on plant extract. It is functioning as an antioxidant and anti-inflammatory compound [20]. Saponin can lead to better progression of wound healing rate [21]. It was also reported to increase the expression of proliferative factors which is responsible for promoting epidermal cell proliferation besides increasing keratin cell migration [22]. *Panaxnoto-ginsengsaponin* was proved to accelerate wound healing and preventing scar formation by reducing fibroblast accumulation and hence  $\alpha$  SMA expression in wound tissue [23]. Another study found that saponin is related to an increase of fibroblast collagen synthesis and inhibiting expression of matrix metalloproteinase [24].

The phenolic compound is also abundant in *Lansium domesticum* seeds extract. Phenol has many actions to promote healing by decreasing the inflammatory process, accelerating contraction due to its interaction with myofibroblasts, accelerating crust detachment, and promoting the re-epithelization process [25]. The phenolic compound also mediates cell proliferation in wound tissue by increasing collagen synthesis and its maturation (related to attenuation of proinflammatory cytokine production) [26]. Another effect of phenol is as anti-bacterial which is believed by its action to change the permeability of the membrane [25].

Although there are potential effects of *Lansium domesticum* extract to promote wound healing, more examination is needed in the future. Examination of wound tissue with histopathological analysis is needed, therefore more time examination also needed to evaluate all stages of wound healing. Analysis of the phytochemical compound in our extract is also needed to validate more the mechanism of *Lansium domesticum* seeds extract activity.

## Conclusion

In conclusion, the results of our study showed that the ethanolic extract of *Lansium domesticum* Corr. seed can promote the natural healing process and could be used as an alternative wound healing agent. The ointment from *Lansium domesticum* Corr. extract can accelerate the wound closure process. Ethanolic extract of



*Lansium domesticum* Corr. seed also showed low antimicrobial activity. Further studies are needed to isolate the active compound(s) responsible for the wound healing process and more research is needed to develop the safety profile of that preparation.

**Conflicts of interests:** None

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