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The Effectiveness of Taro Leaf Stalk (*Colocasia esculenta* L.) Ointment Extract on Burn Wound Healing in mice (*Mus musculus* L.)

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Abstract: The purpose of this study was to determine the effectiveness of taro leaf stalk extract ointment (*Colocasia esculenta* L.) on the length of time for wound healing, burn diameter, and percentage of burn healing in mice (*Mus musculus* L.). Taro leaf stalk extraction using the Maceration method. This type of research is experimental with a completely randomized design (RAL) method with 20 male mice divided into 5 treatment groups, namely Negative Control (Ointment Base), Positive Control (Bioplacenton 10%), K1 (Taro Leaf Stalk Extract Ointment 4%), K2 (Taro leaf stalk extract ointment 6%) and K3 (Taro leaf stalk extract ointment 8%), each with 4 replications. Making burns on the backs of mice with hot metal coins with a diameter of 20 mm which were affixed for 2 seconds. Observation parameters are the length of healing time, wound diameter, and percentage of burn healing for 18 days. Data were analyzed using One Way ANOVA (*Analysis Of Variance*) (α = 0.05%) and continued with the LSD (*Least Significant Different*) test. The results showed that taro leaf stalk extract ointment with a concentration of 8% was more effective in accelerating wound healing with an average healing time of 16 days compared to positive control (16.5 days), 4% ointment (17.25 days), 6% ointment (17 days) and negative control (18 days). The diameter of the burn which was initially 20 mm the fastest was 8% ointment with a wound diameter of 0.37 mm and a high burn healing rate of 98.12% when compared to Bioplacenton 10% followed by taro leaf stalk extract ointment with a concentration of 6% and 4%.

Keywords: Extract Ointment, *Colocasia esculenta* L., *Mus mmusculus* L., Burn Healing.

Introduction

Biodiversity of medicinal plants owned by Indonesia is a natural resource that is quite potential to be utilized and developed by the community as raw materials for traditional medicines (Wehantouw et al., 2011). Knowledge about the use of traditional medicine has been passed down from generation to generation and is usually based on experience, traditions, and beliefs that exist in the community. Treatment with traditional medicine is one alternative to meet the basic needs of the community in the health sector (Dalimartha, 2005). One of the plants used by the community as medicine is the taro plant.

All parts of the taro plant can be used to cure various diseases such as purulent skin inflammation, ulcers, allergies, diarrhea, healing minor wounds, burns to bleed (Sangtam et al., 2012). All parts of the taro plant organ can be used as medicine, such as the taro leaf stalk which is often used by the community as a wound medicine (Dalimartha, 2006). Taro is a perennial herbaceous plant that belongs to the Araceae family which consists of 11 genera, namely Alocasia, Caladium, Colocasia, Cyrtosperma, Dieffenbachia, Homalomena, Lasia, Pistia, Rhapidopora, Syngonium, and Xanthosoma (March et al., 2017). This study used a type of taro from the genus Colocasia, species *Colocasia esculenta* L. with taro leaf stalks used that are round (teres) and green in color.

Taro contains alkaloids, flavonoids, tannins, phenols, triterpenoids, and saponins (Wadankar et

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al., 2011). Taro leaf stalks contain secondary metabolites of flavonoids, alkaloids, saponins, tannins, steroids, and terpenoids (Wijaya et al., 2014). The metabolite compounds that are suspected to have the potential for wound healing are flavonoids and saponins (Biren et al., 2007). Flavonoid compounds are anti-inflammatory so they can reduce inflammation and help reduce pain in the event of bleeding and swelling (Ruswanti et al., 2014). Saponin compounds function to trigger the formation of collagen which plays a role in the wound healing process. The content of saponins has the ability to an antiseptic against pathogenic microorganisms (Faure, 2002).

Burns are tissue damage that occurs on the skin caused by hot water or radiation, electric current, fire, friction, or contact with chemical compounds (Siahaan and Chan, 2018). Burns are expressed in degrees determined by the depth of the burn, a decrease in the area of the burn. The severity of the burn depends on the depth, extent, and location of the wound (Izzati, 2015). Physiologically, wound healing will naturally pass through several phases, namely the inflammatory phase, the proliferative phase, and the maturation phase (Negara et al., 2014).

Research on the use of taro plants as medicine has been widely carried out including Amarsya (2017) that taro leaf extract can heal wounds at a concentration of 15%. Wijaya et al (2014) stated that the ethanol extract of the taro leaf stalk (*Colocasia esculenta* L.) at a concentration of 20% had the potential as a medicine for cuts on rabbit skin. Nasution (2015) that the ethanolic extract of tubers (*Colocasia esculenta* L.) can accelerate wound healing at a concentration of 1%.

Research that uses taro leaf stalks for healing burns in the form of ointment preparations has so far not been widely carried out, so in this study, the results of taro leaf stalk extraction were made in ointment preparations. The choice in making ointments is intended to make a preparation that has good penetration power and long contact time with the skin, besides that it is also intended to protect the skin and can absorb drugs more quickly so that it can provide the maximum healing effect.

Materials and Methods

Materials

Materials used in this study include Mice (*Mus musculus* L.), taro leaf stem (*Colocasia esculenta* L.), vaseline album and adeps lanae, CP12 Mice Feed, Alcohol 70%, ethanol 70%, chloroform, aquades.

Experimental setting

Making Taro Leaf Stalk Extract Ointment

The ointment that will be used in this study is made in different concentrations, namely 4%, 6%, and 8% which is made as much as 25 grams. The manufacture of 25 grams is intended for use for 18 days of treatment of burns in mice. The formulation for making taro leaf stalk extract ointment is listed in Table 1.

Table 1. Formulation of Making Taro Leaf Stalk Extract Ointment (Agoes, 2008).

No	Ingredients	Concentration (%)		
		F1 (4%)	F2 (6%)	F3 (8%)
1	Taro leaf stalk extract	1 gr	1.5 gr	2 gr
2	Ointment base	24 gr	23.5 gr	23 gr
mf total ointment		**25 gr**	**25 gr**	**25 gr**

Information :

F1: Taro leaf stalk extract ointment with a concentration of 4%

F2: Taro leaf stalk extract ointment with a concentration of 6%

F3: Taro leaf stalk extract ointment with a concentration of 8%

The ointment base that has been made previously, is then added with ethanol extract of taro leaf stalk little by little according to the concentration of the formula to be made (4%, 6%, and 8%) while stirring until homogeneous. The finished ointment is then put into a container pot.

Test Animal Preparation

Before testing, mice (*Mus musculus* L.) were acclimatized for 7 days, the purpose of acclimatization was so that the test animals could adapt to their new environmental conditions. During the acclimatization process, a place for keeping the test animals was prepared, namely

cages, sawdust, feeding places, and drinking bottles for mice (Mus musculus L.). Provision of drinking using clear water given ad libitum (unlimited), feeding, and drinking to test animals was carried out 3 times a day.

Wound Making on Test Animals

The test animal mice (*Mus musculus* L.) which had been acclimatized were shaved in the back area until smooth and cleaned with 70% alcohol, then made burns on the back skin of mice (*Mus musculus* L.) using coins of Rp. 100 with a diameter of 20 mm which has been heated in a Bunsen flame and affixed for 2 seconds to the back of the mouse (*Mus musculus* L.) until a second-degree burn is formed which is marked by a reddish color and a bulla (water bubble) is formed on the back of the mouse (*Mus musculus* L.) (Ghofroh, 2017).

Giving Taro Leaf Stem Extract Ointment to Test Animals

The administration of taro leaf stalk extract ointment for burns of test animals in each of the 5 treatment groups was administered by applying it to the backs of mice with 3 times a day application of ± 0.347 grams per mouse with an interval of 5 hours each. Measurements were taken once a day before the last ointment was administered for 18 days to observe the effectiveness of each treatment group.

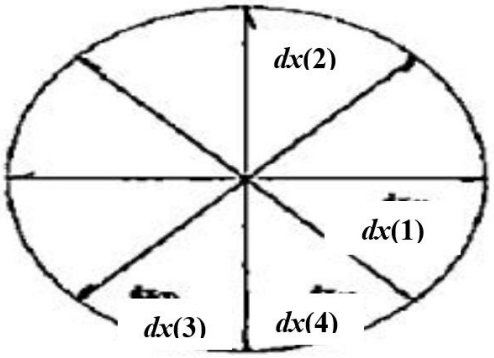
Measurement of Burn Diameter

The measurement of wound diameter was carried out using the Morton method, which was to measure four wound diameters from various directions, then the average value of the diameter of each measurement was calculated (Sumoza et al., 2014).

$$dx = \frac{dx(1) + dx(2) + dx(3) + dx(4)}{dx}$$

Information :

dx = wound diameter x day (mm)
$dx_{(1)}$ = Horizontal diameter (mm)
$dx_{(2)}$ = vertical diameter (mm)
$dx_{(3)}$ = Diagonal diameter (mm)
$dx_{(4)}$ = Diagonal diameter (mm)



Calculation of Burn Healing Percentage

Calculation of the percentage of burn healing is calculated by the following formula (Handayani et al., 2016):

$$\boldsymbol{P = \frac{L1 - Ln\ x\ 100\%}{L1}}$$

Information :

LFirst-day day burn diameter
Ln = Diameter of burn on day n

Data analysis

Analysis of the data using the application program Statistical Product Services Solution (SPSS) version 20.0. The data obtained in the form of wound healing time, burn diameter, and percentage of burn healing were then tested statistically one-way Anova with 95% confidence level, = 0.05. If there is a significant difference, then it is continued with the LSD test (*Least Significant Different*) to see which treatment gives a different effect.

Result and Discussion

Wound healing time

The effectiveness of taro leaf stalk extract ointment (*Colocasia esculenta* L.) on healing burns aims to determine the effect or effect on the length of time for wound healing and the diameter of burns in mice for 18 days of observation.

Table 2. Wound Healing Time.

Group	Wound Healing Time (Days)				Average±SD	*Wound Healing Time (Hours)
	1	2	3	4		
KN (-)	18	18	18	18	18±0[d]	432
KP (+)	16	16	17	17	16.5±0.57[ab]	396
K1	17	17	18	17	17.25±0.5[c]	414
K2	17	17	17	17	17±0[bc]	408
K3	16	16	16	16	16±0[a]	384

Information:
Numbers followed by different letters indicate that there is a significant difference in the level of confidence 95%
*Average result (Days) converted in hours (multiplied by 24 hours)
KP = Bioplacenton 10%
KN = Ointment Base
K1 = Taro Leaf Stalk Extract Ointment 4%
K2 = Taro Leaf Stalk Extract Ointment 6%
K3 = Taro Leaf Stalk Extract Ointment 8%

Based on the table above, it can be seen that taro leaf stalk extract ointment can accelerate the healing process of burns with the fastest wound healing time in the K3 group (8% taro leaf stalk extract ointment) with a healing average of 16 days. The results of this study are not much different from the research of Liling (2020), which used taro leaves formulated in ointment preparations with an average wound healing time of 16 days and faster than the Mawarsari study (2015) which used taro tubers formulated in cream preparations with an average wound healing for 20 days. The difference in the average results of this wound healing time depends on the base material that is formulated, where the ointment has the fastest effect compared to other base ingredients due to the ability of the ointment base material in the form of vaseline album to increase hydration of the skin where these properties are very beneficial because it can maintain skin moisture. According to Handayani *et al*., (2016), Vaseline album has moisturizing and emollient properties. Adeps lanae is the basic ingredient of absorption ointment whose use is intended so that during the healing process of infected wounds, this ointment base can help absorb fluid in the wound (Ansel, 1989).

The wound healing process in each treatment resulted in different variations of burn healing which were influenced by the amount of concentration given in the ointment preparation. Extracts with high concentrations of secondary metabolites will accelerate the wound healing process and extracts with low concentrations of metabolites will slow down the wound healing process. This is according to Candra et al., (2018) stated that the success of burn wound healing is strongly influenced by the concentration of secondary metabolites contained in the extract.

Burn Diameter

The effectiveness of taro leaf stalk extract ointment (*Colocasia esculenta* L.) on healing burns includes parameters for measuring burn diameter. The results of the measurement of the average burn diameter presented represent the stages of the burn healing process.

Table 3. Wound Diameter.

Group	Wound Diameter (Mean ± SD)			
	Day 1st	Day 6th	Day 12th	Day 18th
KN (-)	20	17.68±0.23	11.50±0.35	2.37±0.32[c]
KP (+)	20	17.37±0.14	10.12±0.59	0.62±0.25[ab]
K1	20	17.56±0.23	11.25±0.28	0.93±0.31[b]
K2	20	17.25±0.20	10.75±0.54	0.87±0.32[b]
K3	20	16.81±0.37	9.56±0.31	0.37±0.14[a]

Information:
KP = Bioplacenton 10%
KN = Ointment Base
K1 = Taro Leaf Stalk Extract Ointment 4%
K2 = Taro Leaf Stalk Extract Ointment 6%
K3 = Taro Leaf Stalk Extract Ointment 8%

After giving of taro leaf stalk extract ointment caused the diameter of the burn to decrease, this was shown mainly in the 8% ointment, which resulted in an average burn diameter of 0.37 mm. The higher the concentration of the treatment given can accelerate the shrinking of the wound diameter, this is in line with the research of Paputuangan et al., (2014), Wahyudi and Agustina (2018) that the more active compounds in the ointment preparations are made, the faster wound healing occurs. The reduction in the diameter of burns in mice is due to the presence of flavonoids in the form of quercetin and saponins contained in taro leaf stalk extract which can help the healing process of burns. According to to Horton et al., (2013) stated that one class of compounds that have the potential to treat burns is quercetin. Quercetin is one of the active substances in the flavonoid class of the flavonol group derived from various fruits and vegetables. Quercetin and its derivatives have the ability to anti-inflammatory, antioxidant, reduce histamine secretion from mast cells in various tissues and also from basophils (Hatahet et al., 2016). Saponin compounds can accelerate the formation of new epithelial cells and support the epithelialization process, causing a reduction in the size of the burn wound (Widyantoro and Sugihartini, 2015).

The reduction in the diameter of the wound occurs due to a reduced inflammatory reaction and the occurrence of a granulation process in the wound area which causes closure of the skin so that visually a reduction in the diameter of the wound can be seen. The comparison and observation of the administration of taro leaf stalk extract ointment can be seen in Figure 2. there is a clear reduction in the size of the diameter wound started on days 1-5, 6-12, and 18.

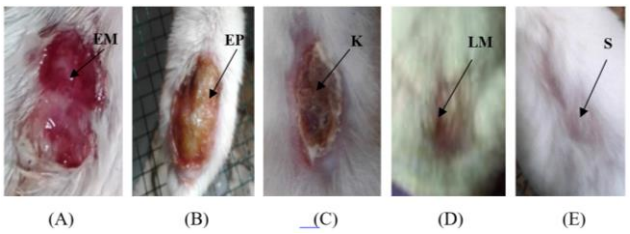


Figure 2. Comparison of the Development of Visual Burns Diameter Reduction in Mice on Days 1-5, 6-12 and 18 after Administration of 8% Taro Leaf Stem Extract Ointment.
Description: **(A)** and (B) Days 1 to 5 are marked with Erythema Blisters (EM), and Erythema Swelling (EP), (C) Days 6 to day 12 are marked with Scabs (K), (D), and (E) The 18th day was marked by Closing Wounds (LM) and Healing (S)

Day 1 to day 5 is the inflammatory phase or the initial stage of wound healing where the inflammatory phase that occurs the fastest for all treatment groups is the 8% ointment group which occurs from day 1 to day 5. the other group where the inflammatory phase occurred up to day 5.5 and day 6. The inflammatory phase can take place quickly due to the presence of flavonoid compounds in the form of the Quercetin group which can reduce the inflammatory period when an injury occurs, according to Sutrisno et al., (2016) stating that anti-inflammatory compound Quercetin can reduce inflammatory symptoms such as pain, redness, and swelling. The anti-

inflammatory activity of Quercetin compounds works by inhibiting the cyclo-oxygenase (COX) enzyme which induces the formation of prostaglandins as inflammatory mediators. Observation parameters in this inflammatory phase are by looking at the swelling, blistering, and erythema.

The 6th day to the 12th day is the proliferative phase in which the fastest proliferation phase for all treatment groups is the 8% ointment group which occurs from day 6 to day 12 when compared to other groups in the proliferative phase. occurred up to day 12.5 and day 13. Parameters observed in this proliferative phase are characterized by the formation of granulation tissue in the wound, fibroblasts in the form of a crust or scab layer. Scabs that form on the surface of the skin form homeostasis and prevent contamination of wounds by microorganisms.

The 18th day is the remodeling phase which is the last and longest phase in the wound healing process where the fastest maturation phase for all treatment groups is the 8% ointment group whose wounds have healed on the 16th day compared to the other groups who had the wound had healed on day 16.5 to day 18. The parameter observed in this phase was to see that the burn wound in the mice had closed and healed, which was indicated by the growth of hair around the wound.

Burn Healing Percentage

Table 4. Burn Healing Percentage.

Group	Healing Percentage (Mean ± SD)			
	Day 1st	Day 6th	Day 12th	Day 18th
KN (-)	0	11.56±1.19	42.5±1.19	88.12±1.61[a]
KP (+)	0	13.12±0.72	49.3±1.19	96.87±1.25[bc]
K1	0	12.18±1.19	43.75±1.76	95.31±1.57[b]
K2	0	13.75±1.02	46.25±4.62	95.62±1.61[b]
K3	0	15.93±1.87	51.87±2.77	98.12±0.72[c]

Information:
KP = Bioplacenton 10%
KN = Ointment Base
K1 = Taro Leaf Stalk Extract Ointment 4%
K2 = Taro Leaf Stalk Extract Ointment 6%
K3 = Taro Leaf Stalk Extract Ointment 8%

Based on the table above, shows that the 8% ointment group had a high mean percentage of burn healing of 98.12%, while the lowest mean percentage of burn healing was the negative control group of 88.12%. The results of this study are higher than those of Mawarsari's (2015) study which used taro tubers as a burning medicine by 73.79%. Healing burns due to 8% taro leaf stalk extract ointment contains secondary metabolites in the form of flavonoids and saponins that can accelerate the healing process of burns. According to (Wijaya et al., 2014), taro leaf stalks contain secondary metabolites of flavonoids, alkaloids, saponins, tannins, steroids, and terpenoids.

Taro leaf stalk extract ointment 8% contains secondary metabolites in the form of flavonoids and saponins which are high when compared to 4% and 6% ointments. According to Ramayani et al., (2020) that total The flavonoid content contained in 100 mg of taro leaf stalk extract was 0.92 mg QE/gram, this means that 8% ointment containing 2 grams of taro leaf stalk extract had flavonoid levels of 18.4 mg QE/gram, while based on research by Lindawati and Solikhah (2018) in 250 mg of taro leaf stalk extract, the total flavonoid content was 10.2223 mg QE/gram, this means that 8% ointment containing 2 grams of taro leaf stalk extract had 81.778 mg QE/gram of flavonoid content.

Based on the results of the One Way ANOVA test (α = 0.05) (Appendix 9) show a significance value of $p < 0.05$, which is equal to $p = 0.000$, which means that there are significant differences in each treatment group. Based on the results of the LSD test (Appendix 12) it can be concluded that the negative control group had a significant difference with the positive control and the ointment treatment group of 4%, 6%, and 8% with a value of ($p < 0.05$) i.e $p = 0.000$, while the positive control group was not significantly different from the 4%, 6% and 8% taro leaf stalk extract ointment treatment groups with values ($p > 0.05$)

The main flavonoid compounds quercetin and quercitrin have anti-inflammatory effects by inhibiting signals in microglia cells resulting in impaired inducible nitric oxide synthase (iNOS) and decreased nitric oxide (NO) levels. This results in analgesic and neuroprotective effects so that

pain in the skin affected by burn trauma is reduced (Kumar et al., 2012). Quercetin and quercitrin can also stimulate the induction of vascular endothelial cell growth factor (VEGF) in the angiogenesis process which is very important in the burn wound healing process because it has a function to facilitate growth factors such as PDGF, EGF, TGF-ß, and FGF that play a role in the healing process.

Prasetyo et al., (2010) reported that saponins can boost the immune system, optimize blood sugar levels and reduce blood clotting. Saponin compounds can also help stimulate the formation of new epithelial cells and support the re-epithelialization process, because the faster the re-epithelialization process, the faster the wound healing process. Saponin compounds also have the ability as an antiseptic that functions to kill or prevent the growth of microorganisms in infected wounds.

Conclusions

Based on the results of the study, it can be concluded as follows:

1. The effectiveness of taro leaf stalk extract ointment on the healing of burns which includes the length of time for wound healing and wound diameter shows that 8% taro leaf stalk extract ointment has the best and fastest healing power with an average burn healing time of 16 days and a burn diameter of 0.37. mm, followed by 6% ointment with an average healing time of 17 days and the diameter of the burn being 0.75 mm, 4% ointment with an average healing time of 17.25 days, and the diameter of the burn being 0.93 mm.
2. The highest percentage of burn healing was taro leaf stalk extract ointment with a healing percentage of 98.12%, followed by 6% ointment at 95.62% and 4% ointment at 95.31%.

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