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Extract of 75% and 95% *Chromolaena odorata* Effective to Reduce Bleeding Time of Acute Wound: Traditional Wound Care Approach

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ABSTRACT

Chromolaena odorata is a plant containing tannins, phenols, flavonoids, saponins, and steroids. They were traditionally used as a remedy for bleeding cessation. This research to knows the difference in the effectiveness of *Chromolaena odorata* extract 75% and 95% to bleeding time of acute wounds. Research used an experimental approach with posttest only control group. The research was conducted at the Laboratory of the Faculty of Medicine, Unversitas Muhammadiyah Surakarta. Samples were 48 *Rattus norvegicus*, consisting of 16 samples/group. A random sampling technique was used to select the sample. The instruments were an observation sheet and stopwatch. Data were analyzed using the Mann Whitney test. The mean of the bleeding time in the control group, extract of 75% *Chromolaenao odorata* group, and extract of 95% *Chromolaenao odorata* were 1.17 seconds, 0.23 seconds, and 0.20 seconds. Among the three groups, extract 75% and 95% groups effectively reduce the bleeding time (p=0.000). There was a significant difference using an extract of 75% and 95% *Chromolaenao odorata* to bleeding time (p= 0.000). Extract 75% and 95% *Chromolaenao odorata* effectively reduce bleeding time in an acute wound. Extract of 95% *Chromolaenao odorata* was the most effective to reduce bleeding time in a new wound.

Keywords: Bleeding time, Chromolaena odorata, Wound, Wound care

A. Introduction

The wound is lost or damaged in part of the body tissue. Wounds are also defined as physical damage due to loose or broken skin, which causes an imbalance in healthy skin's function and anatomy.[1] Wounds can be repaired based on their duration and depth into acute and chronic wounds. Acute wounds usually heal within 3 weeks, whereas chronic wounds are usually more than 3 months. Besides, wounds that can be repaired as wounds that can repair themselves can be repaired, and the process is timely (usually acute) and wounds that cannot (usually chronic wounds).[2] The American wound association reports wounds in the world based on the etiology of the disease, with the most number of surgical wounds with 110.30 million cases and the second due to injuries of 20.40 million cases.[3]

According to the Indonesian Ministry of Health (2008), the prevalence of open wound injuries in Indonesia is 25.4%. Based on the age group, the prevalence of open wounds that were most common was in the age group of 25 to 34 years (32.0%). The Basic Health Research results concluded that in 2013 the prevalence of injury in Indonesia increased from 7.5% in 2007 to 8.2%. The most common causes of injury were falls (40.9%) and motorcycle accidents (40.6%). The number of motorbikes in Indonesia is significant, and there is an increase every year. In 2015 the number of motorbikes was > 98 million, and in 2018 it became > 137 million.[4] A result of falls and motorcycle accidents can cause open wounds. Healing in acute wounds, especially in acute superficial wounds, is often underestimated and ignored. This is because the normal wound will heal itself without problems. However, small wounds or blisters also need proper care to prevent complications, especially infections.[5]

Open wounds cause damage to the skin and tissues, causing bleeding. Bleeding cannot be considered trivial and must be treated immediately.[6] Bleeding from the injured area is

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expected during and shortly after trauma. Hemostasis occurs within a few minutes unless the injury affects a large blood vessel or a person's blood clotting function is reduced.[7] The body typically protects itself from excessive and deadly blood loss through various complex and interrelated mechanisms.[8] Bleeding time is the time interval from the first blood drop until the blood stops dripping, bleeding time is one of the measurement parameters for blood clotting to determine the vasoconstriction process.[9-11]

Wound management can be done in a modern or traditional way. The use of traditional medicine for wound management has been developed from generation to generation in various societies before modern medicine. Traditional medicine is a health practice, approach, knowledge, and belief combining plants, veterinary medicines and minerals, spiritual therapy, techniques, and manual training, applied singly or treat, diagnose and prevent disease or maintain well-being.[12] In some Asian and African countries, around 80% of the population depend on traditional medicine for their primary health care needs. China uses herbal medicines, including herbs, herbal ingredients, herbal preparations, and finished herbal products that contain active ingredients, plant parts, or other plant ingredients, or combinations.[13] In traditional African approaches to wound care, various practices include herbal medicines, forecasts, and other physical interventions.[14]

Indonesia is an archipelago consisting of thousands of islands with various ethnicities, cultures, and customs. Some people live in rural areas and are far from health facilities. The community is also actively using traditional medicine by utilizing herbal plants in the surrounding environment. The community uses plants in the event of injury and bleeding. Bleeding time is shortened by using herbal plants on wounds, one of which is by using plant *Chromolaena odorata*. This plant is easy to grow in all regions of Indonesia or other countries, so it is easy to find. *Chromolaena odorata* is a type of plant from the *Asteraceae* family. The leaves contain several significant compounds, such as tannins, phenols, flavonoids, saponins, and steroids. The content can accelerate wound healing by inhibiting and killing bacterial growth and shortening the bleeding time by shortening the blood clotting time.[15]

Since Indonesian people had been using plants as an alternative treatment a long time ago, people use plants as daily treatment because they are easy to get and cheap, and are not many and have almost no side effects that can be dangerous if not used excessively. In Indonesia, many *Chromolaena odorata* are found and have not been used optimally. Therefore researchers are interested in examining the effects of *Chromolaena odorata* on the bleeding time of new wounds that community nurses can utilize as one of their nursing care.

B. Methods

1. Study Design

This type of research is an experiment with a posttest only control group design. Data were collected at the Faculty of Medicine Laboratory, Universitas Muhammadiyah Surakarta, on June 8th, 2019.

2. Samples

The research sample was Wistar strain white rats (*Rattus norvegicus*) calculated using the Federer formula obtained 48 tails. The sample consisted of 3 control groups, 75% tackle group and 95% tackle group. Each group with a sample of 16 animals. Samples were selected using random sampling according to inclusion and exclusion criteria. Inclusion criteria: male, age 2-3 months, body temperature 36.5-37.50 °C, healthy, weight 150-200

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grams. Exclusion criteria were mice that died or were sick during the study. Before the data collection process, the sample was treated for a week in a cage with an adjusted environment to the specified criteria. Samples were given food and drink three times. After data collection, the wound in the sample is treated and treated. Then researchers submit samples that have been used to the laboratory manager to be used as material for scientific progress. Submission of research samples based on an agreement on the transfer of experimental animals.

3. Instruments

Research tools are scales, rulers, stopwatches, and scalpels. The research materials are *Chromolaena odorata* leaf extracts, wound plaster, mask, hand soon, food and drink rats, standard operational procedures, and observation sheets. The manufacture of 75% *Chromolaena odorata* using leaves are cleaned then weighed 3.5 kg, then carried out by drying in the sun for 1 week. After drying, the leaves are weighed again with a dry weight of 1 kg. Then, the leaves were extracted using 95% ethanol as much as 100 ml. The making of extract *Chromolaena odorata* 95% by way of leaves was cleaned then weighed 4.45 kg, which was then carried out by drying in the sun for 1 week. After drying, the leaves were weighed again with a dry weight of 1.27 kg. Extract Then, the leaves were extracted using 95% ethanol as much as 100 ml. The extract was made by competent laboratory personnel. *Chromolaena odorata* leaves that have been extracted in liquid form will then be dropped on the wound area (incision).

4. Data Collection

The sample was incised with a scalpel as long as 1 cm, and the wound depth was 0.2 cm at the tail, and the bleeding time was measured. The bleeding time is when the blood is first incised until the blood stops dripping. In the control group only measured the time of bleeding, no treatment was given. While the experimental group, after the first drops of blood in the incision area, then leaf extract was dropped. One group was dropped with 75% *Chromolaena odorata* extracts and the other group with 95% *Chromolaena odorata* extracts. Bleeding time is calculated, starting from the dropping of the extract until the blood stops dripping. Bleeding time is measured with a stopwatch. After the study of white Wistar rats treated wounds until healed, then transferred ownership to the laboratory.

5. Data Analysis and Ethical Consideration

The data normality test used the Shapiro Wilk test with abnormal results, so the statistical test uses the Mann U Whitney test. The ethical approval was obtained from the Health Ethics Committee of Faculty Medicine of Universitas Muhammadiyah Surakarta with an approval number of 697/A.2/KEPK-FKUMS/V/2019. The study permission was also obtained from the Dean of Faculty Medicine of Universitas Muhammadiyah Surakarta. Experimental animal care is following ARRIVE guidelines and is carried out following the UK Animal Act (Scientific Procedure), 1986, and National Health Institute guidelines for the care and use of laboratory animals (NIH Publications No. 8023, revised 1978).

C. Results

Table 1 Distribution of Sample Based on Temperature and Weight

Variable	Control Group	Extract of 75% *Chromolaena odorata* Group	Extract of 95% *Chromolaena odorata* Group

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	f	%	f	%	f	%
Temperature (^{0}C)						
36.5-36.9	10	62.5	10	62.5	10	62.5
37-37.5	6	37.5	6	37.5	6	37.5
Total	**16**	**100.0**	**16**	**100.0**	**16**	**100.0**
Weight (gram)						
150-175	2	12.5	12	75	12	75
176-200	14	87.5	4	25	4	25
Total	**16**	**100.0**	**16**	**100.0**	**16**	**100.0**

Table 1 is known in all groups; the majority of samples have a temperature of 36.5-36.9 0C. In the 75% and 95% tackle groups, the majority of the sample body weight was 150-175 grams, while the majority of the control group was 176-200 grams.

Table 2. Bleeding Time of Sample

Variable	Bleeding Time (seconds)		
	Control Group	Extract of 75% *Chromolaena odorata* Group	Extract of 95% *Chromolaena odorata* Group
Min	16.2	3.60	0.00
Max	138	56.40	25.80
Mean	71.7375	14.1375	13.8375
Median	59.40	12.9	13.2
SD	33.35768	12.61422	6.758

SD=Standard Deviation

Table 2 shows the shortest and maximum bleeding time in the 95% *Chromolaena odorata* group extract and the longest in the control group. The average bleeding time was the shortest in the extract of 95% *Chromolaena odorata* group and the longest in the control group.

Table 3. Relationship of Body Weight and Sample Temperature with Bleeding Time

Variable	Bleeding Time (seconds)		
	Control Group	Extract of 75% *Chromolaena odorata* Group	Extract of 95% *Chromolaena odorata* Group
Weight (gram)			
Mean	189.06	165.19	165.38

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SD	12.272	19.163	19.047
r *(CC)*	0.269	0.280	0.066
p *Value**	0.314	0.309	0.808
Temperature (°C)			
Mean	36.678	36.9188	36.9125
SD	0.3346	0.31031	0.33242
r *(CC)*	0.395	0.309	0.317
p *Value**	0.130	0.243	0.231

* Spearman Rank
CC=Coeficient Correlation
SD=Standard Deviation

Table 3 is known in *the* control group, extract of 75% *Chromolaena odorata* group, and extract of 95% *Chromolaena odorata* group did not find a significant relationship between body weight and temperature with bleeding time (p> 0.05).

Table 4. Effect of Extract 75% and 95% *Chromolaena odorata* on Bleeding Time

Groups	Bleeding Time (seconds)					p-*value**
	Min	Max	SD	Mean	Difference Mean	
Control	16.20	138.00	33.35768	71.74	57.60	0,000
Extract 75%	3.60	56.40	12.61422	14.14		
Control	16.20	138.00	33.35768	71.74	57.94	0,000
Extract 95%	0.00	25.80	12.61422	13.80		
Extract 75%	3.60	56.40	12.61422	14.14	0.34	0,000
Extract 95%	0.00	25.80	13.81022	13.80		

**Man U Whitney*)

Table 4 found that extract 75% and 95% *Chromolaena odorata* was effective in reducing bleeding time (p 0,000 <0.05). Between extract of 75% *Chromolaena odorata* group and extract of 95% *Chromolaena odorata* group, there was a difference in reducing bleeding time.

D. Discussion

Bleeding is the discharge of blood from blood vessels in varying amounts, ranging from a little to a large amount and at risk of causing.[16] External bleeding is bleeding that comes from an open wound to be seen from a physical examination.[17] The cause of bleeding that is often found is external trauma, hemostasis abnormalities, and lack of blood clotting factors.[18] In this study, bleeding was made by giving an incision as long as 1 cm and a wound depth of 0.2 cm in the tail in all mice. When bleeding occurs, the body will naturally respond with a hemostatic mechanism to stop the bleeding. A system of stopping the bleeding that is functioning correctly is essential for the life of the organism because if hemostasis is disrupted, even a small wound can cause life-threatening bleeding, on the contrary, the

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bloodline to freeze will facilitate the formation of thrombus and increase the risk of thrombosis and embolism.[19]

The time of bleeding is proportional to the amount of blood that comes out. The longer the bleeding time, the more amount of blood will come out. Bleeding time is the time interval from the first blood drop until the blood stops dripping. Bleeding time is one of the parameters of blood clotting measurement to determine the vasoconstriction process. Hemostasis is a very controlled and balanced process and is limited only in the place of damage to the walls of blood vessels and should not be systemically expanded.[10] At the time of trauma, platelets, blood clotting factors in the plasma, and blood vessel walls interact to close leakage in blood vessels. Damaged blood vessels will constrict, release endothelin, and platelets aggregate at the wound site and attract other platelets to seal the leak with a platelet blockage. The time needed to close the wound is called bleeding time, which ranges from 2-4 minutes. Furthermore, the coagulation system will produce cross-linked fibrin that forms fibrin clots or thrombus, which strengthens the wound closure process. The process of recanalization of blood vessels can be done through fibrinolysis.[19]

According to Sonjaya (2008) and Syoghy (2010), several factors affect bleeding time, such as the size of the wound, temperature, health status, age, body size and activity, hemoglobin levels in plasma, and globulin levels in the blood.[20] The results of the study revealed that most of the samples had a body temperature of 36.5-36.9 ° C and had a bodyweight of 176-200 grams. The temperature and weight are standard conditions of experimental animals. The bivariate test showed no relationship between body temperature and body weight with bleeding time in all groups ($p > 0.05$). In this study, no relationship was found because researchers used samples of mice with average temperature and weight categories. The reason researchers use samples with average temperature and weight is so that the research results are not biased. Bleeding time was measured without any influence from factors other than *Chromolaena odorata* leaf extract. The results of this study support the study of Zheng et al. (2014), there is no relationship between body temperature with the severity of intracranial hemorrhage ($p > 0.05$) and Kander & Schott (2019), mild hypothermia does not cause an increased risk of bleeding. The results do not support the study of Etulain et al. (2012), mentioning an increase in body temperature decreases platelet function so that it affects bleeding time ($p < 0.05$) and Poucke et la (2014), hypothermia effects on platelet function and hemostasis.[21-23]

First aid in external bleeding is absolutely necessary to reduce the risk of blood from the body. Bleeding from the injured area is normal during and shortly after trauma. Hemostasis occurs within a few minutes unless the injury affects a large blood vessel, or a person's blood clotting function is reduced.[7] According to Sucipto (2009), the way to deal with bleeding is to suppress the source of bleeding, use pressure pads, and use ice water or ice cubes wrapped in cloth and then affixed to the wound to stop the bleeding by vasoconstriction in the wound. In developing countries, 25% of treatment is based on the use of medicinal plants, which are widely used in rural communities.[24] Community attention has been increasing in finding plant extracts to increase wound healing regeneration, although plant extracts for wound treatment are generally only a custom practiced by traditional communities.[13] Herbal plants to deal with bleeding in wounds such as using *Chromolaena odorata* leaves.

The results showed that 75% and 95% *Chromolaena odorata* leaf extracts effectively reduced bleeding time. In between, 95% of the *Chromolaena odorata* leaf extract was more

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effective in reducing bleeding time. The average difference in bleeding time after giving *Chromolaena odorata* extract 95% 0.34 seconds is shorter than the 75% *Chromolaena odorata* extract group. *Chromolaena odorata* is a type of plant in the Asteraceae family. *Chromolaena odorata* leaves are often considered pests because they grow very fast and are very widespread; these plants can be found in almost all regions in Indonesia and other parts of the world. In some regions in Indonesia, people use this plant as a wound medicine and food supplement for decades. Traditionally, *Chromolaena odorata* leaves are used as medicine in wound healing, mouthwash to treat sore throat, cough medicine, malaria medication, antimicrobial, headache, antidiarrheal, astringent, antispasmodic, antihypertensive, anti-inflammatory and diuretic. This tackle plant is known to function as an antiviral.[25] Essential oils from *Chromolaena odorata* leaves contain α pinene, cadinene, camphor, limonene, β-caryophyllene, and cardinal isomers.[26] *Chromolaena odorata* leaves contain several main compounds, such as tannins, phenols, flavonoids, saponins, and steroids.

Flavonoids have been known to function as antioxidants in tumor growth. Flavonoids have also been shown to improve immune responses, although much controversy has been found. This is because the mechanism in terms of its activities is not yet appropriate.[27] The effects of *Chromolaenao odorata* leaf extract can inhibit bacterial growth, including *Pseudomonas aeroginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Neisseria*. According to Robinson (1995) cit Yenti, (2011), flavonoids can inhibit bacterial growth by damaging the permeability of bacterial cell walls, microsomes and lysosomes as a result of interactions between flavonoids with bacterial DNA and also being able to release energy transduction to the bacterial cytoplasmic membrane and inhibit motility bacteria. Other ingredients that have antimicrobial effects are saponins. According to Harbone (1987), cit Yenti, (2011), saponin has the ability as a cleaner and which functions to kill or prevent the growth of microorganisms that generally arise in the wound so that the wound does not experience a severe infection. The content of flavonoids and saponins in *Chromolaena odorata* causes antibiotics' function and prevents infection in wounds.[15]

Another ingredient in *Chromolaena odorata* is tannin. Tannin functions as an astringent that can cause shrinkage of skin pores, harden the skin, stop exudates and mild bleeding, so that it can cover the wound and prevent bleeding that usually arises in the wound. According to Simes (1959), cit Yenti (2011), tannin can change animal skin into leather because of its ability to cross-connect proteins. Tannin reacts with proteins to form stable copolymers, which are insoluble in water. In plants, tannins' location is separated from proteins and cytoplasmic enzymes, but if the tissue is damaged, there will be a tanning reaction. The presence of tannin makes the bleeding time in the sample shorter. Another ingredient that affects bleeding time is bioflavonoids.[15] According to Amri (2009), in his research on routine bioflavonoid activity testing on blood clotting time and platelet cell count, the research found that routine bioflavonoid administration can shorten the bleeding time, shorten blood clotting time and increase the number of female white mice thrombocytes at each dose very significant ($p < 0.01$). The dosage of 100 mg/kg body weight has had the maximum effect in shortening bleeding and clotting time and increasing the number of thrombocytes. The contents of tannin and bioflavonoids cause bleeding in the wound incision samples to quickly stop.[28]

In Vietnam, freshly squeezed *Chromolaena odorata* leaves or boiled water is used for the treatment of leech bites; healing wound tissue, burns, skin infections, dental, alveolitis. Traditionally people use *Chromolaena odorata* leaves as eupolin ointment (topical agent).

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Chromolaena odorata leaf extract can stimulate granulation tissue formation and wound reepithelialization. East Timorese people also use the juice of *Chromolaena odorata* leaves to be used for new wound medicine.[29] In Aceh, residents use *Chromolaena odorata* leaves as medicine for gangrene. Local residents think that *Chromolaena odorata* leaves can heal gangrene wounds. *Chromolaena odorata* leaves have antioxidant effects, can stop bleeding and reduce inflammation, inhibit bacterial growth, stimulate tissue formation, and re-epithelialization of the wound so that it is suitable for healing gangrene wounds.[30,25]

Yenti has conducted previous studies, et al. (2011), who examined the formulation of ethanol extract of *Chromolaena odorata* leaves cream for wound healing, where the wound made was cut in mice with the results of wound healing effect test of ethanol extract of *Chromolaena odorata* leaves 10% showed the results wound healing is faster when compared to the cream base and its comparison which contains 10% povidone-iodine.[15] Yuliani (2012) also tested *Chromolaena odorata* leaf ethanol extract's effect on incision wound healing in Sprague-Dawley rats. The results of both studies stated that the ethanol extract of *Chromolaena odorata* leaves could be used for wound healing.[29]

E. Conclusion

The herbal plant *Chromolaena odorata*, which has been extracted with a concentration of 75% and 95% concentration, effectively reduces bleeding time in acute wounds in white Wistar rats (*Rattus norvegicus*). *Chromolaena odorata*, with a concentration of 95%, reduces bleeding time faster than 75%. Furthermore, based on the results, research in humans with minor injuries can be developed as a basis for applying nursing practice in the community.

F. Acknowledgments

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G. Conflict of Interest

There was no conflict of interest in this study.

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