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POTENTIAL TEST OF TURMERIC ETHANOL EXTRACT CREAM FOR WOUND HEALING IN WISTAR RATS

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ABSTRACT

The shape of the wound is different depending on the cause; some are open and closed, and the healing consists of several phases, namely the inflammatory phase, proliferative phase, and maturation phase. Several sources state that turmeric rhizome extract is effective in wound healing. This study aimed to test the potential of turmeric rhizome extract to be effective in wound healing. This type of research is experimental with a Pre-test and Post-test group-control design approach, conducted from November to December 2020. The samples used were turmeric rhizomes (Curcuma Longa) and male white rats. Determination of sample size according to Frederer's formula, so the number of pieces was 25 rats, the division of 4 treatment groups and one control group. The data will be analyzed for normality and continued with the ANOVA test. The results of turmeric extract contain chemical compounds of alkaloids, flavonoids, saponins, and tannins. The results of the Fcount value of 8.442 ≥ Ftable of 2.67, with a p-value of 0.004 ≤ 0.05, state that turmeric extract administration significantly affects wound healing in rats. The optimum concentration of turmeric ethanol extract (Curcuma Longa) that can heal cut wounds in white rats is 6%. The highest percentage of healing on day k-14 was in positive control (Bioplacenton®), which was 95%, followed by 6% v/v extract. The cream preparation of turmeric ethanol extract (Curcuma Longa) has an ability that is close to Bioplacenton® in healing cut wounds in rats.

KEYWORDS: ***Turmeric Rhizome, Cream, Wound Healing***

INTRODUCTION

Wounds take different forms depending on the cause; some are open, and some are closed. One example of an open wound is an incision with a linear tear in the skin and underlying tissue. Wounds are a typical cause of injury experienced by every human being. A wound is losing or damaging some body tissue (1) due to a factor that disrupts the body's protective system. Some factors that cause wounds include bites, accidents, sharp objects, bullets, and metal objects (2). The wound healing phase is divided into several stages: inflammatory, proliferative, and maturation. The inflammatory phase is characterized by hemostasis, chemotaxis, and increased vascular permeability that limit further damage, seal the wound, remove cellular and bacterial debris, and promote cellular migration. The duration of the inflammatory stage usually lasts a few days (3). The proliferative phase is characterized by granulation tissue formation, re-epithelialization, and neovascularization. This phase may last several weeks. The maturation and remodeling phase is where the wound reaches maximum strength at maturity (4), (5), (6). Wound healing is the body's attempt to restore its structural integrity and normal function following tissue disruption (7). The wound healing process can be divided into three main phases, namely, the inflammatory phase, the proliferation phase, and the remodeling phase (8).

Turmeric (Curcuma longa Linn or Curcuma domestica Val) belongs to the Zingiberaceae family. The public has long known it as a plant with many benefits, such as anti-inflammatory, anticancer, antioxidant, antiulcer, and antibacterial (9). According to research by Wientarsih et al. (2012), it is known that turmeric rhizome extract is effective in wound healing (10). Supported by research by Yunianto et al. (2017), from the results of a study on the activity test of ointments with turmeric active ingredients in vitro and in vivo, turmeric is an antimicrobial that can kill and inhibit the growth of several types of fungi, bacteria, and viruses (11). This study aims to test the potential of turmeric rhizome extract to be effective in wound healing.

RESEARCH METHODOLOGY

This type of research is experimental with a Pre-test and Post-test group control design approach, conducted in March 2023. The samples used were turmeric rhizomes (Curcuma Longa) and male white rats. Determination of sample size according to Frederer's formula, so the number of pieces was 25 rats, the division of 4 treatment groups and one control group. The materials used are alcohol, aluminum foil, distilled water, turmeric (Curcuma Longa), 96% ethanol, rat test animals (Mus musculus), sterile gauze, Whatman filter paper, methylparaben, petroleum ether, plaster, propylene glycol, gloves, triethanolamine. The tools used included glassware (pyrex®), an autoclave, a maceration vessel, a blender (Maspion®), a porcelain cup, a caliper (Tricle brand®), an oven, tweezers, rotavapor (Heidolf®), iron spoon, analytical balance (Precisa®), and water bath.

The turmeric (Curcuma Longa) that has been identified is washed thoroughly with running water, then drained and

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spread on morning paper until the water is absorbed, after which the turmeric (Curcuma Longa) sample is weighed. Then, the material was dried, pulverized into powder, and formed simplisia (12). A total of 25 rats were divided into five groups; each group consisted of a group. I was given standard feed and a cream preparation of turmeric ethanol extract (Curcuma Longa) 2% as much as 1g applied once every 24 hours. Group II was given standard feed and a cream preparation of turmeric ethanol extract (Curcuma Longa) 4% as much as 1 g applied once every 24 hours. Group III was given standard feed and a cream preparation of turmeric ethanol extract (Curcuma Longa) 6% as much as 1g applied once every 24 hours. Group IV was given standard feed and 8% turmeric ethanol extract cream (Curcuma Longa) as much as 1g used once every 24 hours. Group V positive control, given standard feed and used 1 g of Bioplacenton® once every 24 hours. Inclusion criteria included white rats, male sex, 6 - 8 weeks of age, body weight 150 - 200 g, and healthy if the rats were given an incision wound on the back area of 2 cm extended. Exclusion criteria include sick rats during the adaptation period, unhappy during treatment, and death during treatment. Data processing techniques were carried out from observations regarding changes that occurred in the wound and changes in the size of the damage in the area that had been treated. Then, I analyzed the normality of the data and continued with the ANOVA test.

RESULTS AND DISCUSSION

Table 1. Phytochemical Screening of Turmeric (Curcuma Longa)

Test	Results	Description
Alkaloid	Red brown precipitate	(+)
	White precipitate	(+)
	Brown precipitate	(+)
Flavonoid	Red color in amyl alcohol layer	(+)
Saponin	Permanent foam	(+)
Tanin	Blackish green color	(+)

Table 1 shows that turmeric extract (Curcuma Longa) contains alkaloid, flavonoid, saponin, and tannin chemical compounds (13). Tannin compounds can act as astringents in wounds, while saponins work to increase the speed of epithelialization. Flavonoid compounds also play a role in damage healing by stopping bleeding, namely through the mechanism of vasoconstriction in blood vessels, accessible radical antidotes, inhibitors of enzyme hydrolysis and oxidation, and anti-inflammatory (14).

Table 2. Data on the percentage inhibition of turmeric extract (Curcuma Longa) against DPPH

Extract Concentration (ppm)	Absorbance Extract	Absorbance Control	Inhibition (%)
3	0.236	0,545	56.51
5	0.228	0,545	57.68
7	0.219	0,545	57.74
9	0.178	0,545	63.44

Based on Table 2, it can be seen that the absorbance of DPPH by turmeric extract (Curcuma Longa) decreases as the extract's concentration increases. The inhibition value of the section also increases with the increase in extract concentration, with the most significant inhibition value being 63.44% at a concentration of 9 ppm. The results of research by Suhendra, 2017, show turmeric extract has a yield of 7.82%, a total amount of phenol of 2.82%, the ability of DPPH antiradical activity of 1.14%, and high activity in inhibiting the fat oxidation process (15).

Table 3.Changes in wound length with various extract concentrations

Days	Change in Wound Length (cm)				
	Concentration 2%	Concentration 4%	Concentration 6%	Concentration 8%	Bioplacenton
1	3	3	3	3	3
3	1.4	1.4	1.4	1.4	1.4
5	1.6	1.4	1.4	1.4	1.3
7	1.3	1.2	1.2	1.2	0.7
9	1.2	0.8	0.8	1	0.7
11	1	0.5	0.5	0.4	0.6
14	0.7	0.7	0.6	0.4	0.2

Based on Table 3, it can be seen that Bioplacenton®, as the positive control, experienced faster wound healing. On day 3, the wound length was already reduced, and on day 14, the incision wound treated with Bioplacenton® had the highest percentage of recovery. This is because the composition of Bioplacenton® has active ingredients of placenta extract and

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neomycin sulfate, which are effective in triggering new tissue formation and preventing infection in the wound area (16). Turmeric (Curcuma longa) can heal wounds, although the healing speed is not as fast as Bioplacenton® when seen from the reduction in wound length from day to day. This wound-healing ability may be influenced by the compounds in the extract, such as flavonoids, alkaloids, saponins, and tannins.

Bioplacenton had the highest percentage of wound healing at 95%, with the remaining wound length on day 14 being 0.2 cm out of 3 cm. Followed by a concentration of 6% v/v turmeric extract (Curcuma Longa), then with a concentration of 4% v/v turmeric extract, and so on. According to Indah's research (2019), turmeric rhizome extract ointment at a dose of 8% can be used as a cut wound medicine but is less effective when compared to povidone-iodine (17). The inflammatory phase lasts from the onset of the wound until approximately day 3 (18). The first thing that happens after an injury is platelet activation. Blood vessels damaged during an injury will cause bleeding, and the body will stop it with vasoconstriction, constriction of the ends of the damaged blood vessels, and hemostasis reactions (19).

The following healing phase is the destructive phase, which is the clearance of dead tissue and bacteria by polymorphs and macrophages. This phase occurs around day 2 to day five after the wound occurs (20). These cells cannot only destroy bacteria and remove devitalized tissue and excessive fibrin but can stimulate the formation of fibroblasts that synthesize collagen protein structures and produce a factor that can stimulate angiogenesis. Healing stops when macrophages deactivate, but the healing process continues despite reducing large amounts of polymorphs (20).

The next phase of wound healing is the proliferation phase, also known as the fibroplasia phase, because in this phase, the proliferation of fibroblast cells is very prominent (19,20). The wound is filled with inflammatory cells, fibroblasts, and collagen during the proliferation phase. In this phase, the formation of new blood vessels (angiogenesis) also occurs, forming a reddish-colored tissue with a smooth, bumpy surface called granulation tissue (18). The wound edge epithelium consisting of basal cells detaches from its base and moves to fill the wound surface, while its place is filled by new cells formed from the mitotic process. The process of fibroplasia and granulation tissue formation stops when all epithelia touch each other and cover the wound surface, after which the maturation process begins in the maturation or remodeling phase (5).

The final phase of wound healing is the maturation phase. Epithelialization, contraction, and reorganization of connective tissue occur in this phase. The maturation phase takes place after the proliferation phase ends, around day 14, and can be up to 365 days after the wound occurs and is declared over when all signs of inflammation have disappeared (21). In this phase, the body tries restoring everything that became abnormal during the wound-healing process. Edema and inflammatory cells are absorbed, young cells mature, new capillaries close and are reabsorbed, excess collagen is absorbed, and the rest shrinks according to the amount of strain (10). This process produces pale, thin, pliable, easily movable scar tissue from its base. There is maximum shrinkage of the wound, and at the end of this phase, the wound bed can withstand up to 80% of the strain of normal skin.

The normality test results in Table 4 using the Kolmogorov-Smirnov method show an Absolute value of 0.090. The Kolmogorov table value for a sample size of 140 is 0.115, then 0.90<0.115, or the calculated Kolmogorov value is less than the Kolmogorov table value. This means that the wound healing data for the extract is usually distributed. This is also evidenced by the results of the probability test on SPSS, namely, see the Asymp. Sig. (2 tailed) value is 0.207, where > 0.05 means the data is usually distributed. For the favorable control treatment (Bioplacenton®), the calculated Kolmogorov value is 0.108 with N = 25. Table data with N = 25 is 0.224, then 0.109 < 0.224. Data Asymp. Sig. (2 tailed) data shows a value of 0.800, which means that the data for wound healing using Bioplacenton® is usually distributed, which means that the overall data is usually spread.

Table 4. Test Results of the Effect of Extract Administration on Wound Healing

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Turmeric Extract	Between Groups	7.822	3	2.577	8.442	.004
	Within Groups	37.328	136	.382		
	Total	46.178	139			

Table 4. shows the F-count value of 8.442. To find the value in the F-Value Table for df = 3/136 with a probability (α) of 0.05, the F-table value is 2.67. So, the importance of F-count > F-table means that overall, the administration of turmeric extract (Curcuma Longa) has a natural effect on wound healing. To emphasize this hypothesis test, it can be seen in the Sig. Calculated value of 0.004 while the Sig (α) value is 0.05, which means the Sig. Calculated value < Sig (α). This means that the administration of turmeric extract (Curcuma Longa) has a natural effect on wound healing in rats.

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Table 5. Test Results of the Effect of Bioplacenton® (positive control) on Wound Length.

ANOVA

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	11.927	6	1.987	33.422	.002
Within Groups	1.704	28	.061		
Total	13.631	34			

Based on table 5. It can be seen that the Fcount value is 33.422 while the F-table value is 2.45, which means F-count> F-table. When viewed at the significance value, the calculated significance value is 0.002, smaller than the alpha value of 0.05 or p < 0.05. From this data, it can be concluded that there is a significant effect of the administration of Bioplacenton® on wound healing. The wound-healing process requires proper management and treatment so that the wound area does not become infected, eventually leading to chronic wounds (22). Wound healing is a complex biological process that results in the restoration of tissue integrity. Physiologically, the wound healing process can be divided into four stages: hemostasis, inflammation, proliferation, and tissue remodeling. Many factors slow wound healing, including poor nutrition, hypoxia, immunosuppression, chronic disease, and post-surgical conditions (23); (24).

CONCLUSION

Based on the results of research and data analysis on the effectiveness of the administration of turmeric ethanol extract (Curcuma Longa) and Bioplacenton® on wound healing in white rats, it can be concluded that turmeric ethanol extract (Curcuma Longa) has several bioactive compounds such as alkaloids, flavonoids, saponins, and tannins that play a role in wound healing. The optimum concentration of turmeric ethanol extract (Curcuma Longa) that can heal cut wounds in white rats is 6%. The highest percentage of healing on day k-14 was in the positive control (Bioplacenton®) which was 95% and followed by 6% v/v extract. The cream preparation of turmeric ethanol extract (Curcuma Longa) has an ability that is close to Bioplacenton® in healing cut wounds in rats.

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