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

Song Yuanqing[1], Suhartina[2]
[1]Master of Clinical Medicine, Department of Clinical Medicine, Faculty of Medicine, Dentistry, Health Sciences, University Prima Indonesia
[2]Department of Clinical Medicine, Faculty of Medicine, Dentistry, Health Sciences, University Prima Indonesia
Email: songyu-yiang@gmail.com

Abstract: *Wound healing is the body's attempt to restore structural integrity and normal function after injury through complex inflammation, proliferation, and remodeling. This understanding suggests that wound healing involves coordinated processes to achieve optimal recovery. Numerous sources indicate the efficacy of turmeric rhizome extract in facilitating wound healing. This study seeks to assess the potential effectiveness of turmeric rhizome extract in promoting wound healing. The research adopts an experimental approach with a Pre-test and Post-test group-control design conducted in January 2024. Turmeric rhizomes (Curcuma Longa) and male white rats serve as the samples, with a sample size determined by Frederer's formula, resulting in 25 rats divided into four treatment groups and one control group. Data will undergo normality analysis, followed by an ANOVA test. The study reveals turmeric extract contains alkaloids, flavonoids, saponins, and tannins. The F-count value of 6.425 ≥ F-table of 3.03, with a p-value of 0.022 ≤ 0.05, indicates a significant impact of turmeric extract administration on rat wound healing. The optimal concentration for turmeric ethanol extract (Curcuma Longa) in healing cut wounds in white rats is 4%. On day k-14, the highest healing percentage was observed in the positive control (Bioplacenton®) at 98%, closely followed by the 4% v/v extract. The cream formulation of turmeric ethanol extract (Curcuma Longa) demonstrates a healing capability comparable to Bioplacenton® in cut wound recovery in rats*

Key Words: *Wound Healing; Turmeric Rhizome Extract; Experimental Study; Rat Wound Healing; Turmeric Ethanol Cream.*

1. INTRODUCTION:

The shape of the wound varies depending on the cause; it can be open or closed. An example of an open wound is an incision with a linear tear in the skin and underlying tissue. Wounds, as a case of joint injury, are experienced by every human being and cause loss or damage to part of body tissue (Suarni and Prameswarie, 2015) due to a factor that interferes with the body's protective system. Some factors that cause injuries such as bites, accidents, sharp objects, bullet shots, and metal objects (Afandi, 2017). Wound healing has several phases, including the inflammatory, proliferative, and maturation phases. The inflammatory phase is characterized by hemostasis, chemotaxis, and increased vascular permeability to prevent further damage. This stage includes wound closure, eliminating cellular debris and bacteria, and encouraging cellular migration. The duration of the inflammatory phase generally lasts for several days (Wissen et al., 2020). The formation of granulation, reepithelialization, and neovascularization tissues characterizes the proliferative phase. This phase can last several weeks. The maturation and remodeling phase is where the wound reaches maximum strength at maturity (Kartika et al., 2015); (Hernawati, 2015); (Hardhani, Lastianny, and Herawati, 2014). Wound healing is the body's attempt to restore its structural integrity and normal function after a tissue disruption (Johnston, 2017). The wound-healing process can be divided into three phases: inflammatory, proliferation, and remodeling (Novyana and Susanti, 2016).

Turmeric (Curcuma longa Linn or Curcuma domestica Val) belongs to the Zingiberaceae family. The public has long recognized it as a plant with various benefits, such as anti-inflammatory, anticancer, antioxidant, anti-ulcer, and antibacterial properties (Purwaningsih, 2016). According to research by Wientarsih et al. (2012), turmeric rhizome extract is effective in wound healing (Wientarsih, Winarsih, and Sutardi, 2012). Support from research Yunianto et al. (2017) showed that in the test of ointment activity with turmeric active ingredients, turmeric has antimicrobial properties that are effective in killing and inhibiting the growth of several types of fungi, bacteria, and viruses, both in vitro and in vivo (Yunianto, Lestari and Winarso, 2017). This study aimed to test the potential of turmeric rhizome extract to be effective in wound healing.

2. METHOD:

This type of research is experimental, using a pre-test and post-test group-only control design approach, and it was carried out in January 2024. The research sample included turmeric rhizomes (Curcuma Longa) and male white rats. The number of pieces was determined based on Frederer's formula, so 25 rats were divided into four treatment groups and one control group. The materials used included alcohol, aluminum foil, aqua dest, turmeric (Curcuma Longa), 96% ethanol, test rats (Mus musculus), sterile gauze, Whatman filter paper, methylparaben, petroleum ether, plaster, propylene glycol, gloves, and triethanolamine. The tools used involved glassware (pyrex®), an autoclave, a maceration vessel, a blender (Maspion®), a porcelain cup, caliper (Tricle brand®), oven, tweezers, rotavapor (Heidolf®), iron spoon, analytical balance (Precisa®), and water bath.

After being identified, Turmeric (Curcuma longa) rhizomes were washed thoroughly with running water, drained, and spread on morning paper to remove excess water. After that, turmeric samples were weighed, dried, and pulverized into powder, forming simplisia (Kosasih et al., 2019). Next, 25 rats were divided into five groups, with each group given a different treatment, including the positive control group, which was applied with Bioplacenton®. The inclusion criteria involved male white rats aged 6-8 weeks, with a body weight of 150-200 g, and a case of.

3. RESULTS AND DISCUSSION:

a. Phytochemical Screening

Table 1. Phytochemical Screening of Turmeric (Curcuma Longa)

Test	Results	Description
Alkaloids	Red-brown precipitate	(+)
	White precipitate	(+)
	Brown precipitate	(+)
	Red color in the alcohol layer	(+)
Flavonoids	Permanent foam	(+)
Saponins	Blackish green color	(+)

Table 1 shows that turmeric (Curcuma Longa) extract contains chemical compounds such as alkaloids, flavonoids, saponins, and tannins (Baud, Sangi, and Koleangan, 2014). Tannin compounds act as astringents in wounds, while saponins increase the speed of epithelialization. Flavonoids also have a role in wound healing by stopping bleeding through vasoconstriction mechanisms in blood vessels, acting as a free radical antidote, inhibiting hydrolysis and oxidation of enzymes, and being anti-inflammatory (Soni and Singhai, 2012).

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

Extract Concentration (ppm)	Absorbance Extract	Control Absorbance	Inhibition (%)
1	0.336	0,664	57.51
2	0.338	0,664	57.78
3	0.319	0,664	57.74
4	0.178	0,664	73.12

Based on the table above, it can be seen that the absorbance of DPPH by turmeric extract (Curcuma Longa) decreased along with the increase in extract concentration. The inhibition value of the section also increased in line with the increase in extract concentration, reaching the highest inhibition value of 73.12% at a concentration of 9 ppm. The results of Suhendra's research (2017) showed that turmeric extract has a yield of 7.82%, total phenol of 2.82%, DPPH antiradical activity ability of 1.14%, and shows high activity in inhibiting the fat oxidation process (Suhendra, 2017).

Table 3. Changes in wound length with various extract concentrations

Day to -	Change in Wound Length (cm)				
	Concentration 1%	Concentration 2%	Concentration 3%	Concentration 4%	Bioplacenton
1	3	3	3	3	3
3	2.2	2.2	2.2	2.2	1.9
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	0.8	0.8	0.4	0.3	0.1

Based on Table 3, it can be observed that Bioplacenton®, as the positive control, showed faster wound healing. By day 3, the wound length had already been reduced, and by day 14, the incision wounds treated with Bioplacenton® reached the most significant percentage of healing. This speed of healing is due to the composition of Bioplacenton®, which contains the active ingredients placenta extract and neomycin sulfate, which are known to stimulate the formation of new tissue and prevent infection in the wound area (Fitria, Arifin, and Kurniasih, 2017).

Although turmeric (Curcuma Longa) can also heal wounds, its healing speed is not as fast as Bioplacenton®, as seen from the reduction in wound length from day to day. The healing potential of turmeric may be influenced by the content of compounds in its extract, such as flavonoids, alkaloids, saponins, and tannins. Bioplacenton showed the highest percentage of wound healing, which was 98%, with the remaining wound length on day 14 only about 0.1 cm from the initial size of 3 cm. This was followed by a 4% v/v concentration of turmeric (Curcuma Longa) extract, and so on, with a 3% v/v concentration of turmeric extract, and so on.

According to research conducted by Indah (2019), turmeric rhizome extract ointment (Curcuma domestica Val.) at a dose of 8% can be used as a treatment for cuts. Still, its effectiveness is less when compared to povidone-iodine (Indah and Br, 2019). The inflammatory phase starts from the wound's occurrence until around day 3, as Purnama, Sriwidodo, and Ratnawulan (2017) described. The initial stage after wounding is platelet activation. Damage to blood vessels, when a wound occurs, can cause bleeding, and the body will stop it through vasoconstriction, contraction of the ends of damaged blood vessels, and involving hemostasis reactions (Pebri, Rinidar, and Amiruddin, 2017).

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 (Sentat and Permatasari, 2015). These cells cannot only destroy bacteria and remove devitalized tissue and excessive fibrin but can also stimulate the formation of fibroblasts. These fibroblasts synthesize collagen protein structures and produce factors that promote angiogenesis, forming new blood vessels. Although the healing process continues after the reduction of large amounts of polymorphs and deactivation of macrophages, healing stops when the entire epithelium touches and closes the wound surface, entering the maturation or remodeling phase (Sentat and Permatasari, 2015).

The next phase in wound healing is the proliferation phase, also known as the fibroplasia phase, where fibroblast cell proliferation becomes very prominent (Sentat and Permatasari, 2015; Pebri, Rinidar, and Amiruddin, 2017). In this phase, the wound is filled with inflammatory cells, fibroblasts, and collagen. New blood vessels (angiogenesis) and reddish granulation tissue are formed with a smooth, bumpy surface. Basal cells of the wound edge epithelium detach from their base and migrate to fill the wound surface, while new cells are formed through mitosis to fill the gap left behind—the process of fibroplasia (Hernawati, 2015).

The final phase of wound healing is the maturation phase, in which epithelialization, contraction, and reorganization of connective tissue occur. The maturation phase takes place after the proliferation phase ends, around day 14, and can be up to 365 days after the wound appears and is declared over when all signs of inflammation have disappeared (Synthesis and Pada, 2020). In this phase, the body tries to restore everything that has become abnormal during the wound-healing process to normal. 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

(Wientarsih, Winarsih, and Sutardi, 2012). During this process, pale, thin, pliable scar tissue is produced and quickly moved from its base. There is maximum shrinkage of the wound, and at the end of this phase, the wound bed can withstand strains of up to 80% of average skin ability.

The normality test results in Table 4 use the Kolmogorov-Smirnov method, which shows 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 treatment of positive control (Bioplacenton®).

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	4.225	3	3.474	6.425	.022
	Within Groups	23.112	22	.556		
	Total	27.337	25			

The table above shows the F-count value of 6.425. To find the value in the F-value Table for degrees of freedom (df) = 3/25 with a probability (α) of 0.05, the F-table value is 3.03. Therefore, the value of F-calculated > F-table indicates that turmeric extract really influences wound healing (Curcuma Longa). To strengthen this hypothesis test, it can be seen that the calculated Significance (Sig.) value is 0.022, while the value of Sig. (α) is 0.05. This means that the calculated Sig. Value < Sig. (α), indicating a significant effect of turmeric (Curcuma Longa) extract on wound healing in rats (Nuryadi et al. 2017).

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	9.445	3	5.325	22.328	.003
Within Groups	2.504	22	.554		
Total	11.945	25			

Table 5 shows that the F-count value is 22.328, while the F-table value is 3.03, which indicates that F-count > F-table. The significance analysis shows the calculated significance value of 0.003, smaller than the alpha (α) value of 0.05 or p < 0.05. From this data, it can be concluded that there is a significant effect of Bioplacenton® administration on wound healing. Bioplacenton® is a trademark of a product commonly used to promote wound healing. The product is usually in the form of a cream or ointment that contains active ingredients such as placenta extract and neomycin sulfate. Placenta extract has regenerative properties and triggers the formation of new tissue, while neomycin sulfate is an antibiotic that can help prevent infection in the wound area. Applying Bioplacenton® to the incision wound accelerates healing by stimulating tissue regeneration and stopping disease. The neomycin sulfate in the formulation may also provide additional protection from bacteria that may inhibit the healing process. It is important to note that the effectiveness of Bioplacenton® may vary depending on the type of wound, individual condition, and other factors. Before using this product, it is best to consult a healthcare professional to ensure suitability and obtain proper guidance.

The wound-healing process requires proper management and treatment to prevent infection and the occurrence of chronic wounds. Practical management steps involve maintaining cleanliness and wound care, monitoring infection symptoms, and applying appropriate healing methods based on the type of wound. Proper treatment includes using ointments or creams containing active healing ingredients, such as antibiotics if necessary, and a holistic approach to ensure the body's condition supports the healing process. It is essential to seek professional health advice to plan management tailored to the characteristics of the wound and individual requirements (Aminuddin et al., 2020). Wound healing is a complex biological process that restores body tissue integrity. This process involves several stages, including hemostasis to stop bleeding, the inflammatory phase to clean the wound area from debris and bacteria, the proliferative phase to form granulation tissue and new blood vessels, and the remodeling phase to strengthen and perfect tissue structure. Cellular interactions, molecular techniques, and growth factors carefully regulate wound healing. Factors such as nutrition, overall health, and individual conditions can also influence the success and speed of wound healing.

Physiologically, the wound-healing process can be divided into four main stages. The first stage is hemostasis, where bleeding is stopped through blood clot formation. The second phase is inflammation, involving the body's immune response to clean the wound area from debris and pathogenic microorganisms. Subsequently, the proliferation stage occurs, where new cells develop and form granulation tissue to fill the wound area. The final stage is tissue remodeling, where tissue structure is perfected and strengthened as the healing process continues. These stages are tightly and coordinately regulated to achieve optimal recovery from the wound. Factors such as poor nutrition, hypoxia, immunosuppression, chronic diseases, and post-surgery conditions slow down the wound healing process. Therefore, a good understanding of the physiological processes of wound healing is crucial for surgeons to reduce patient morbidity resulting from delayed wound healing (Phillips, 2000); (Young and McNaught, 2011).

4. CONCLUSION :

Based on the results of research and data analysis regarding the effectiveness of turmeric ethanol extract (Curcuma Longa) and Bioplacenton® on wound healing in white rats, it can be concluded that turmeric ethanol extract (Curcuma Longa) contains some bioactive compounds such as alkaloids, flavonoids, saponins, and tannins which have an essential role in the wound healing process. The optimal concentration of turmeric ethanol extract (Curcuma longa) for healing incision wounds in white rats is 4%. The highest percentage of cure on day 14 occurred in the positive control group (Bioplacenton®) at 98%, followed by the group with 4% v/v extract. Turmeric ethanol extract cream preparation (Curcuma longa) showed an ability similar to Bioplacenton® in healing incision wounds in rats.

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