

Effectiveness Of Ethanol Extract Of Turmeric (*Curcuma Domestica Valet*) Gel Against Grade Iia Burn In White Rats (*Rattus Norvegicus*)

Risyad Rizki Maulidi¹, Ermi Girsang^{2*}, Ali Napiyah Nasution³, Sahna Ferdinand Ginting⁴

^{1,2,3,4} Program Study Master Of Biomedical Science Faculty Of Medicine
University Prima Indonesia Medan, North Sumatera, Indonesia

*Corresponding Author:

Email : ermigirsang@unprimdn.ac.id

Abstract

*This study aims to determine the acceleration of burn wound healing in rats given ethanol extract of turmeric rhizome (*Curcuma Domestica Valet*) gel and to see the granulation of the skin histopathology of rats. This research method is experimental with a post-test-only design. The research location is in the UNPRI Bio-Molecular Laboratory with 24 rat samples. Treated with Turmeric Rhizome Extract Gel with Concentrations of 25%, 50%, 75%, and 100% and Silver Sulvadizine as Positive Control and Gel as Negative Control. The results showed that the effectiveness of the best Turmeric Rhizome Extract Gel for wound healing was a concentration of 100% on the 21st day of 15 mm. the worst diameter was the negative control on the 21st day of 20 mm. This happens in the healing of burns because of the content of tannins and flavonoids. Measurement of the granulation tissue diameter on the histopathological picture with the results of a concentration of 100% with a thickness of 863 m. Hypothesis test H_a is accepted There is Effectiveness of Ethanol Extract of Turmeric Rhizome Extract (*Curcuma Domestica VALET*) in Healing Grade IIA Burns. Suggestion It is necessary to do further research related to the factors that cause weak anti-inflammatory and antibiotic Kunit rhizome Extract Gel against second-degree burns.*

Keywords: Gel, Turmeric Rhizome Ethanol Extract, Burns Degree IIA.

I. INTRODUCTION

The skin has a complex structure of epithelial tissue, is elastic, and sensitive, and has a variety of types and colors depending on climate, race, gender, and age (Haerani et al., 2018). The skin is made up of millions of skin cells that can die and are then replaced by new, growing, living skin cells. The skin consists of three main layers, namely the epidermis (thin outer layer), dermis (middle layer), and subcutaneous (innermost layer) (Haerani et al., 2018). Drugs diffuse into the skin through direct contact with the skin to the epidermis and dermis as drug target sites. The route of penetration is divided into two, namely the transepidermal and transapendageal penetration routes. The transepidermal skin penetration route is further divided into two, namely intercellular and transcellular. The transcellular route is a direct route by which the drug will penetrate the skin by passing through the fat layer in the stratum corneum. The transapendageal route transports drugs through sweat glands and hairs on the skin (Qisti, Nurahmanto, and Rosyidi, 2018). A wound is a condition where the continuity of tissue, structure, and normal skin anatomical function is damaged due to pathological processes originating from the internal or external environment and affecting certain organs. This case, treatment and management of wounds are factors that determine the outcome of the wound healing process (Fauziah and Soniya, 2020). Burns cause not only damage to the skin, but also affect all body systems.

Skin with burns will experience damage to the epidermis, dermis, or subcutaneously, depending on the causative factor and the length of time the skin is in contact with the heat source. Gel preparations provide a cooling effect because they contain a lot of water so that the substance penetrates the tissue better. The gel is not sticky and easy to wash, so it can accelerate the healing of burns (Rinaldi, Fauziah, and Musfira, 2019). Turmeric rhizome medicinal plant (*Curcuma Domestica Valet*) is currently able to maintain health naturally. (Cobra, Amini and Putri, 2019). Silver sulfadiazine is the gold standard of topical therapy for burns. Silver sulfadiazine drug is often used in the form of 1% cream. This cream is very useful because it is bacteriostatic, has penetration power which is quite effective against all germs, does not cause resistance, and is safe to use. Based on this description, in this study silver sulfadiazine was used as a positive control (Nugraha and Muhartono, 2013). Based on the description above, the researcher wanted to test the

effectiveness of the turmeric rhizome extract gel (*Curcuma domestica VALET*) against second-degree burns in white rats (*Rattus norvegicus*) by assessing the diameter of the post-treated repair and the histopathology of the skin on the rats.

II. LITERATURE REVIEW

2.1. Turmeric Rhizome (*Curcuma Domestica VALET*)

Turmeric consists of roots, rhizomes, stems, leaves, flower stalks, and flower buds. The type of turmeric root is fibrous (radix adventitia) and looks like a thread connected to the turmeric rhizome. The length of the root is approximately 22.50 cm, the thickness of the young rhizome is 1.61 cm and the thickness of the old rhizome is 4 cm. The depth of the rhizome from the surface to the ground is about 16 cm. Turmeric is an annual plant that grows in clumps and there are 7-10 turmeric rhizomes in 1 turmeric clump (Rukmana, 1995; Larasati, Dwi Jayati, and Widiya, 2018). The essential oil and yellow dye (*curcuminoids*) present in turmeric are the main components contained that are useful as medicine. There are three components found in turmeric rhizome: curcumin, flavonoids, desmethoxycurcumin, and bis-desmethoxycurcumin. Turmeric rhizome contains essential oil levels of about 3% and curcuminoid content of 10%.

Turmeric (*Curcuma domestica Valet*) contains various compounds such as alkaloids, flavonoids, curcumin, essential oils, saponins, tannins, and terpenoids. (Muadifah, Eka Putri and Latifah, 2019; Silfi et al., 2019). Turmeric rhizome has several beneficial components, namely the substance curcumin is effective as a chemopreventive agent and for cancer, it functions as chemotherapy. This has been tested in both in vitro and in vivo studies. It was found that curcumin activity can regulate inflammatory cytokines, protein kinases, enzymes, transcription factors, and growth factors (Mutiah, 2015). The content of tannins functions as an astringent, stops bleeding, accelerates wound healing and inflammation of mucous membranes, and regenerates new tissue. Flavonoids contain antioxidants that function as antimicrobial and anti-inflammatory in burns. Essential oils contain phenol derivatives, namely the hydroxyl and carbonyl functional groups used as antibacterial. This phenol derivative can interact with the structure of the bacterial cell wall (Rinaldi, Fauziah, and Musfira, 2019).

2.2. Burns

Burns is the response of the skin and subcutaneous tissue to temperature/thermal trauma such as fire, hot water, electricity, or flammable substances such as strong acids and strong bases. Partial-thickness burns are burns that do not damage the skin epithelium or only partially damage the epithelium. Full-thickness burns destroy all sources of skin epithelial regrowth (Mz, 2017). The degree of burns is classified into 3, namely: a) first-degree burns caused by sunburn; b) second-degree burns caused by hot liquids or explosions; and c) third-degree burns caused by hot objects, electric shocks, hot liquids, and chemicals.

2.3. Gel

According to the Indonesian Pharmacopeia IV edition, gels are sometimes called jellies, are semisolid systems consisting of suspensions made of small inorganic particles or large organic molecules, penetrated by a liquid (Depkes RI, 1995). Types of gel include (Shu, 2013):

1. Hydrogel Hydrogel system is a hydrophilic gel containing 85-95% water or an alcohol-water mixture and a gelling agent.
2. Lipogel Lipogel or oleogel is produced by adding a suitable thickening agent and is soluble in oil or fat liquid. Colloidal silica can be used to form a special type of lipogel with a silicone base.

2.4. Extract

According to the Ministry of Health of the Republic of Indonesia in 2014, the thick preparation produced uses the right solvent by extracting the active substance from vegetable and animal simplicia using the right solvent, then almost all of the solvent is evaporated and the remaining powder or mass is treated in such a way that it meets the standard that has been set. set is called extract (Anonymous, 2014).

2.5. Skin

Skin is a special organ in humans. Unlike other organs, the skin, which is located on the outermost side of the human body, makes it easier to observe, both in normal and sick conditions. Humans are

consciously continuously observing this organ, whether owned by other organs (eg. when they meet eyes) or themselves (sometimes to the point of becoming a kind of obsession). The skin has 4 layers, namely the epidermis (dynamic skin layer), dermis (bottom tissue of the epidermis which also provides resistance to the skin), and subcutis (consisting of fatty tissue that can maintain body temperature and is an energy reserve).

III. METHODS

The design of this study was to use an experimental method with a post-test-only design. In this research design, the intervention that has been carried out is then measured (observed) or post-test on the results. Treatment as the independent variable and the results as the dependent variable. Where this research includes sample collection and processing, extract making, phytochemical testing, preparation of gel preparations, testing of gel preparations for burns, measuring burn diameter, and microscopic histopathological testing by assessing the granulation found. The location of this research was carried out in the Bio-Molecular Medicine laboratory at Prima Indonesia University and the Haji Hospital Medan Laboratory and the time of the study was from February to March. The population used in this study was white rats (*Ratus Novergicus*). Samples of experimental animals that had the inclusion criteria were: male, aged 2 to 3 months, weighed 200-300gr, and were healthy. Calculation of the number of samples using the federe formula:

$$(t-1)(n-1) > 15$$

$$= (6-1)(n-1) > 15$$

$$= 5(n-1) > 15$$

$$= 5n-5 > 15$$

$$= 5n > 20$$

$$N > 4 = 4 \text{ group subject}$$

Where:

T: number of groups (gerk 25% + gerk50% + gerk75% + gerk100% + control{+} + control{-}) = 6 groups

N: number of subjects per group

Sampling using a purposive sampling technique. The extract used was turmeric rhizome extract (*Curcuma domestica VALET*). The samples tested were obtained at the market center of MMTC Medan Jl. William Iskandar Muda.

3.1. Tools and Materials

The tools used are 60 mesh sieve, caliper, analytical balance, measuring cup, flannel cloth/filter paper, cotton, hair clipper, beaker glass, hotplate magnetic stirrer, Bunsen burner, oven, markers, labels, rotary evaporator, micropipette, animal facilities, microscope object-glass, and plastic wrap. The ingredients used were 5kg Turmeric Rhizome Powder (*Curcuma Domestica VALET*), white male rat (*Rattus Novergicus*), 70% alcohol, Na-CMC, glycerin, Propylene glycol, and Aquadest, and silver sulfadiazine.

3.2. Extraction

The extraction was carried out starting with processing the sample through the turmeric rhizome to become a powder, then calculating the liquid extract by mixing the turmeric rhizome powder and alcohol, and then making the turmeric rhizome extract until it became thick.

3.3. Phytochemical Screening

Phytochemical screening was carried out through a test tube reaction, using a sample in the form of a test solution. Preparation of the test solution was carried out by dissolving 300 mg of thick extract into 30 ml of 0% ethanol solvent. Screening carried out is a) identification of alkaloid compounds; b) identification of flavonoid compounds; c) identification of saponin group compounds; d) identification of tannin class compounds; and e) identification of steroid/terpenoid group compounds.

3.4. Gel Making

This research will make a burn gel preparation with 4 concentration variations, 25%, 50%, 75%, and 100%. The standard formulation of carboxymethyl cellulose (CMC) gel base can be seen in Table 1 below.

Table 1. CMC Gel Base Standard Formulation

Component	%b/ b
GMC	5%
Glycerin	10%
Propylene glycol	5%
Aquabidest	100

Based on the standard gel in table 1, a 50g gel formulation with four variations of concentration will be made as follows:

Table 2. Gel Concentration Formulation

	Concentratio			
	n			
Ingredients	25%	50%	75%	100%
Extract	12,5 g	25 g	37,5 g	50 g
CMC	2,5 g	2,5 g	2,5 g	2,5 g
Glycerin	0,25 g	0,25 g	0,25 g	0,25 g
Propylene glycol	0,41 g	0,41 g	0,41 g	0,41 g
Aquades ad	50 g	50 g	50 g	50 g

The method of manufacture is that all the materials used are weighed first according to the formulation. CMC was dissolved in a beaker filled with some water which had been heated at 50°C. Added 25% extract and stirred using a magnetic stirrer until homogeneous. Glycerin, propylene glycol, and water were added with continuous stirring until a gel was formed. The manufacture of gels with concentrations of 50%, 75%, and 100% is carried out in the same way. After that, it was stored at room temperature for 1 night (Sangadji, Wullur, and Bodhi, 2018).

3.5. Work procedures

1. Prepare the necessary tools and materials, then shave the back area the day before making the wound about 3 cm.
2. Anesthetize using a combination of anesthetic ketamine and xylazine so that the ratio of 2:1 is 0.03 mL.
3. Clean the back of the rat that has been shaved using 70% alcohol.
4. Take a cylinder with a size of 0.8-1 cm and heat it for 10 seconds until it turns red and then stick it on the back (Wardani, 2020).

3.6. Analisis Data

The data from the antibacterial activity test were then analyzed statistically with SPSS software using the One Way Anova Test with Tukey's Post Hoc Test.

H0: There is no Effectiveness of Ethanol Extract of Turmeric Rhizome Extract (*Curcuma Domestica VALET*) in healing second-degree burns.

Ha: There is an Effectiveness of Ethanol Extract of Turmeric Rhizome Extract (*Curcuma Domestica VALET*) in healing second-degree burns.

IV. ANALYZE AND RESULT

After conducting research for approximately 1 month, it was found that, giving turmeric rhizome extract gel to burns on the skin of white rats (*Rattus Novergicus*) that there was effective in healing burns starting with wound healing and histopathological examination of the skin tissue.

4.1. Phytochemical Test Results

The active chemical content in turmeric (*Curcuma Domestica VALET*) that has been tested is in the form of flavonoids, alkaloids, saponins, and tannins.

4.2. Diameter of the Burn that has been given Turmeric Rhizome Extract Gel (*Curcuma Domestica VALET*)

The speed of healing produced by the Turmeric Rimang Extract Gel for second-degree burns can be seen from the change in the diameter of the burn. Measuring the diameter of the burn using a ruler by adding up the measurement results from the four latitudes, namely the vertical, horizontal, diagonal 1, and diagonal

2 which is then divided by four, this is done for each treatment so that the average diameter can be as shown in the table below. this. In this study, 1% silver sulfadiazine was used as a control (+), and CMC gel as a control (-).

Table 1. Burn Results With Turmeric Rhizome Extract Gel

No.	Treatment Day	Concentration					
		25%	50%	75%	100%	K+	K-
1.	1st day	27 mm	27 mm	27 mm	27 mm	27 mm	27 mm
2.	3rd day	27 mm	27 mm	26 mm	26 mm	26 mm	27 mm
3.	7th day	26 mm	25 mm	25 mm	25 mm	25 mm	27 mm
4.	12th day	23 mm	20 mm	20 mm	19 mm	19 mm	24 mm
5.	15th day	23 mm	19 mm	18 mm	18 mm	18 mm	23 mm
6.	21st day	18 mm	16 mm	16 mm	15 mm	16 mm	20 mm

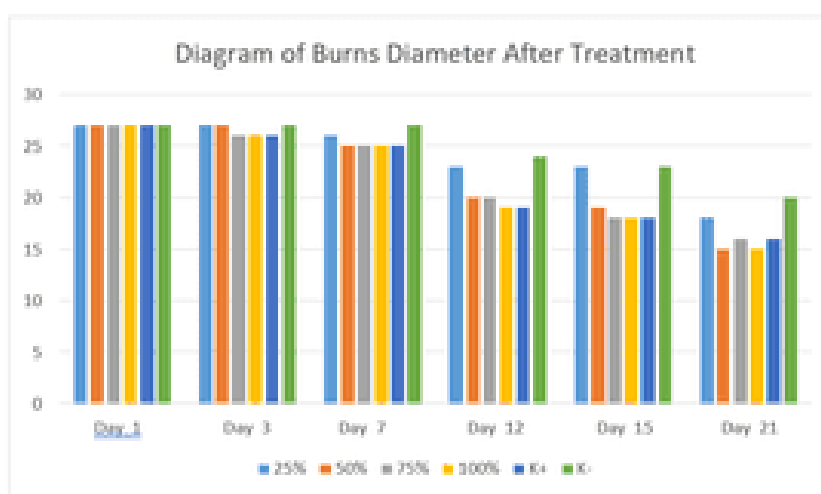


Fig1.Diagram of Burns Diameter After Treatment With Turmeric Rhizome Extract Gel (*Curcuma Domestica VALET*)

Based on the results of the study shown in table 1 and figure 1, it was concluded that the best effectiveness for healing second-degree burns was Turmeric Rhizome Extract Gel with a concentration of 100% where the diameter on the 21st day after treatment was 15 mm. This happens to heal burns because of the anti-inflammatory and antibiotic content in these ingredients. while the worst diameter was those who were given negative control treatment using gel-based ingredients only on the 21st day with a diameter of 20 mm, this was caused by the absence of Anti-inflammatory and Antibiotic content in the material so that healing took longer and infection in the wound area had been induced. With a hot iron on the skin of male white rats (*Rattus norvegicus*). While the positive control treatment using 1% silver sulfadiazine was also good for healing burns where it was found to have a diameter of 16 mm which was the same as the treatment of Turmeric Rhizome Extract Gel with a concentration of 50% in diameter, which was 16 mm.



Fig 2.Initial burns before being treated



Fig 3. Final burn after being treated for 21 days

4.3. Burns Granulation Tissue Thickness that has been given Turmeric Rhizome Extract Gel (*Curcuma Domestica VALET*)

One of the other parameters to assess the speed of healing of a burn wound is the histopathological appearance of the thickness of granulation tissue formed during the healing process. In this study, the average thickness of granulation tissue formed during the healing process of grade IIA burns that had been induced with Turmeric Rhizome Extract Gel can be seen in the table and figure below.

Table 2. Histopathological Examination Results from Rat Skin

No.	Concentratio	I			II			III			Average
1	K+	877	861	885	857	869	863	861	807	803	853
2	K-	934	756	743	798	764	724	673	643	597	738
3	25%	414	397	436	344	362	311	588	530	527	434
4	50%	419	454	460	370	384	389	407	400	402	409
5	75%	675	669	534	487	498	501	599	592	573	569
6	100%	820	760	882	788	812	800	1030	958	967	868

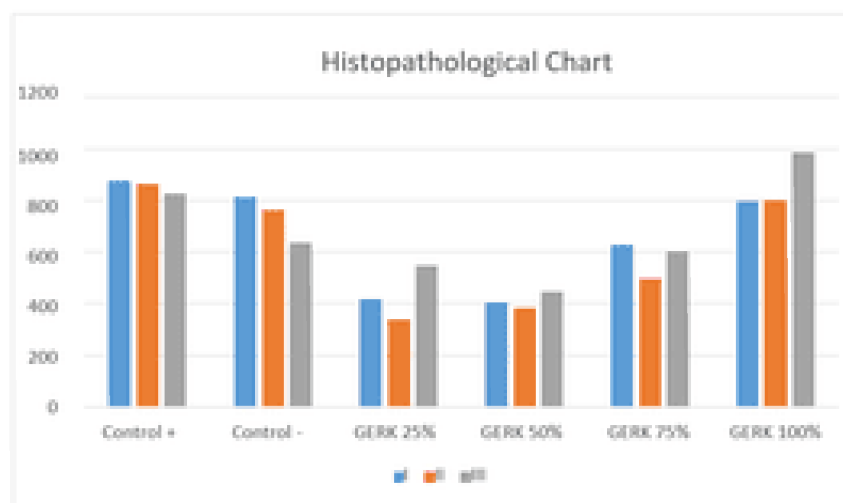


Fig 4. Graph of Histopathological Examination Results

Based on table 2 and figure 4, it was found that the results were the formation of granulation on the histopathological picture with treatment using Turmeric Rhizome Extract Gel or using 1% Silver Sulfadiazine where the granulation formed was caused by the skin's response to increased healing with the more granulation the better in the healing process.

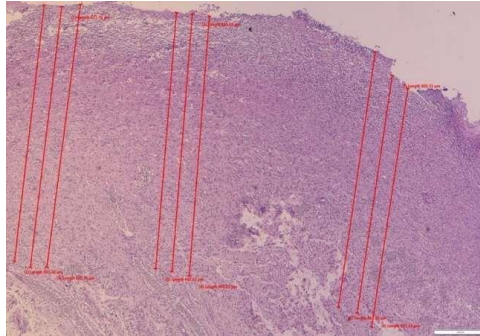


Fig 5. Skin Histopathology Treatment Using Positive Control

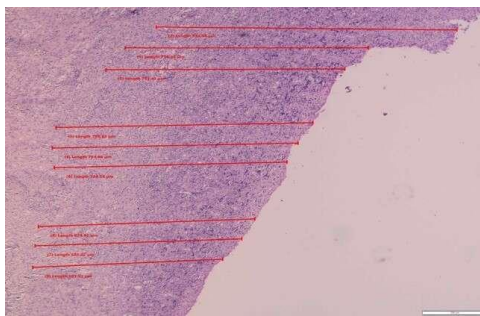


Fig 6. Skin Histopathology Treatment Using Negative Control

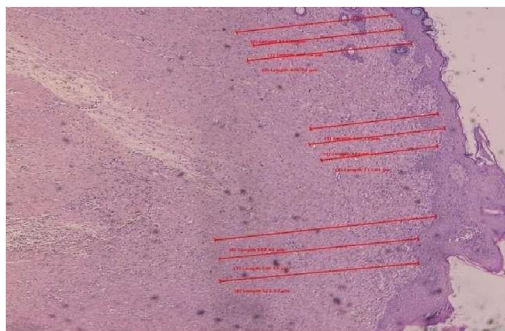


Fig 7. Histopathology of the skin with the treatment of Turmeric Rhizome Extract with a Concentration of 25%

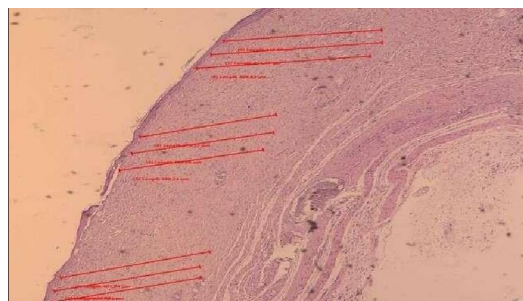


Fig 8. Histopathology of the skin with the treatment of turmeric rhizome extract gel with a concentration of 50%

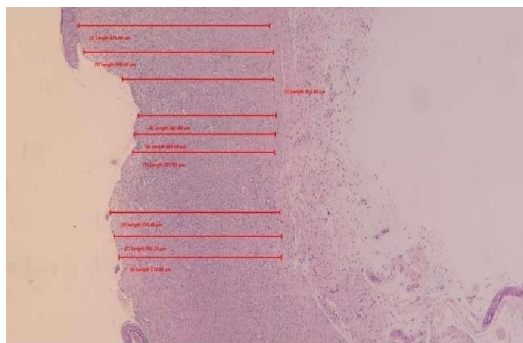


Fig 9. Histopathology of the skin with the treatment of Turmeric Rhizome Extract Gel with 75% Concentration

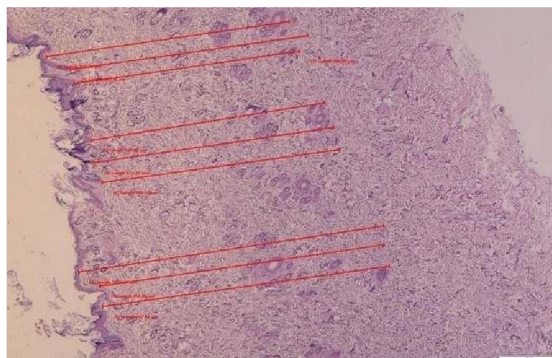


Fig 10. Histopathology of the skin with the treatment of Turmeric Rhizome Extract Gel with 100% Concentration

In the histopathological description above, it was found that the most granulation images were on the skin that was treated using Turmeric Rhizome Extract Gel Concentration of 100% with a thickness of 863 m this is shown in Figure 10 while the worst granulation thickness description was those treated using Turmeric Rhizome Extract Gel with The concentration of 50% thickness is 405 m, this is shown in Figure 8. This is due to the chemicals contained in the turmeric rhizome, namely tannins and flavonoids as polyphenolic substances that can help the wound healing process, where these two substances play a role in the fibrogenesis stage which causes cells - Fibroblast cells proliferate so that the thicker the granulation tissue, the better the wound healing process.

4.4. Results of Data Analysis with SPSS

The data from the antibacterial activity test were then analyzed statistically with SPSS software using the One Way Anova Test with Tukey's Post Hoc Test. Before testing using the One Way Anova test, the normality test was carried out first and the results were >0.05 where the data were normally distributed. Furthermore, the homogeneity test was carried out and the results were >0.05 and it can be concluded that the data were homogeneous. After carrying out the normality and homogeneity test, it is continued with the One Way Anova test, and the results are shown in Table 3 below.

Table 3. One Way Anova Test with SPSS Version 24

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	48.889	5	9.778	.522	.004
Within Groups	562.333	30	18.744		
Total	611.222	35			

Table 3 shows the results of Sig <0.05 , namely 0.004 where HA can be accepted and HO can be rejected, therefore there is an Effectiveness of Turmeric Rhizome Ethanol Extract Gel (*Curcuma Domestica VALET*) for Healing Grade IIA Burns.

V. CONCLUSION

1. In the Turmeric Rhizome Extract Gel (*Curcuma Domestica VALET*) there are phytochemical compounds with evidence on examination of Tannins there is a blackish-green color change, Tannins (+), examination of Saponins with foam results means Saponins (+). Flavanoid examination with the results of a blue-purple-black color change, then Flavanoid (+).
2. The best concentration of Turmeric Rhizome Extract Gel is 100% concentration, this can be proven by the small wound diameter of 15 mm.
3. Assessment of the diameter of the burn on day 21 with the administration of Turmeric Rhizome Extract was at a concentration of 25%, the results were 18 mm, 50% and 75% concentration were found to be 16 m. while the positive control was found to be 16 mm and the negative control 20 mm.
4. In the histopathological description of the administration of the Turmeric Rhizome Extract Gel treatment the effect on the wound healing process can be proven in histopathological examination it was found that there was a thickness of granulation formed in the healing process. 100% concentration is the best concentration in the formation of granulation thickness, which is 868 μm

REFERENCES.

- [1] Anonim. (2014). Farmakope Indonesia. V. Jakarta: Kementerian Kesehatan RI.
- [2] Cobra, L. S., Amini, H. W. and Putri, A. E. (2019). Skirining Fitokimia Ekstrak Sokhletasi Rimpang Kunyit (*Curcuma longa*) dengan Pelarut Etanol 96 %. *Jurnal Ilmiah Kesehatan Karya Putra Bangsa*, 1(1), pp. 12–17.
- [3] Depkes RI (1995). Farmakope Indonesia edisi IV. Jakarta: Departemen Kesehatan Republik Indonesia.
- [4] Fauziah, M. and Soniya, F. (2020). Potensi Tanaman Zigzag sebagai Penyembuh Luka. *Jurnal Penelitian Perawat Profesional*, 2(1), pp. 39–44.
- [5] Haerani, A. et al. (2018). Antioksidan Untuk Kulit. Farmaka Universitas Padjadjaran, Bandung, 16(2), pp. 135–151.
- [6] Muadifah, A., Eka Putri, A. and Latifah, N. (2019). Aktivitas Gel Ekstrak Rimpang Kunyit (*Curcuma Domestica Val*) Terhadap Bakteri *Staphylococcus aureus*. *Jurnal SainHealth*, 3(1), pp. 45–54.
- [7] Mutiah, R. (2015). Evidence Based Kurkumin Dari Tanaman Kunyit (*Curcuma longa*) Sebagai Terapi Kanker. 1(1), pp. 28–41.
- [8] Mz, A. (2017). Pengaruh Madu terhadap Luka Bakar. Medical Professional. *Journal Of Lampung*, 7(5), pp. 71–74.
- [9] Nugraha, A. and Muhartono (2013). Perbandingan Tingkat Kesembuhan Luka Bakar Derajat II antara Pemberian Mahasiswa Fakultas Kedokteran Universitas Lampung , 2) Staf Pengajar Fakultas Level Comparison of Recovery Second Degree Burns Between Giving Honey Nectar Coffee with Silver Sulfadiaz. *MAJORITY (Medical Journal of Lampung Universit)*, pp. 24–32.
- [10] Qisti, B. W. K., Nurahmanto, D. and Rosyidi, V. A. (2018) ‘Optimasi Propilen Glikol dan Etanol sebagai Peningkat Penetrasi Ibuprofen dalam Sediaan Gel dengan Metode Simplex Lattice Design (Propylene Glycol and Ethanol Optimization as Ibuprofen Penetration Enhancer in Gel Dosage using Simplex Lattice Design Metho’, *Pustaka Kesehatan*, 6(1), p. 11. doi: 10.19184/pk.v6i1.6611.
- [11] Rinaldi, R., Fauziah, F. and Musfira, Y. (2019). Studi Formulasi dan Efektivitas Gel Ekstrak Etanol Daun Sirih (*Piper betle L.*) terhadap Penyembuhan Luka Bakar pada Kelinci (*Oryctolagus cuniculus*)’, *Jurnal Dunia Farmasi*, 4(1), pp. 23–33.
- [12] Rukmana, R. (1995). Kunyit. Yogyakarta: Kansius.
- [13] Sangadji, S., Wullur, A. C. and Bodhi, W. (2018). Formulasi Dan Uji Gel Ekstrak Etanol Herba Suruhan (*Peperomia Pellucida [L.] Kunth*) Terhadap Luka Bakar Pada Kelinci (*Oryctolagus cuniculus*). *Pharmacon*, 7(1), pp. 10–21.