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Research Article

Formulation and Test of Burns Healing Effects of Preparations Cream Extract Leaf Nangka Kuning (*Vincetoxicum villosum* (Blume) Kuntze)

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Abstract:
V. villosum (Blume) Kuntze shows inhibition of the growth of Pseudomonas aeruginosa which is usually the cause of infection in burn wounds. The aim of this research was to formulate *V. villosum* (Blume) Kuntze leaf extract into a cream preparation and determine the time needed for *V. villosum* (Blume) Kuntze leaf extract cream to heal burn wounds in rabbits. This research was a type of experimental research. The research was conducted at the University of Bengkulu Laboratory in September 2022-August 2023. The equipment used was the Ohaus Starter 3100 brand pH meter and the NDJ-8S viscometer. The materials used are *V. villosum* (Blume) Kuntze leaf extract, mice, ethanol solvent. Oil-in-water (O/W) phase cream formulation with 3 variations of stearic acid and triethonolamine emulsifiers (15:4), (16:3) and (17:2). Then the three formulas were evaluated for their preparations which included organoleptic tests, homogeneity tests, pH tests, adhesion tests, spreadability tests, viscosity tests and descriptive stability tests. The activity test against burn wound infections used rabbits consisting of groups K1 (without treatment), K2 (given 0.2% hyaluronic acid cream), P1 (given 2% *V. villosum* (Blume) Kuntze leaf extract), and P2 (given 2% *V. villosum* (Blume) Kuntze leaf extract cream). Groups K2, P1 and P2 showed perfect wound healing on day 12. Meanwhile group K1 experienced incomplete wound healing until day 14. Based on the results of the study it can be concluded that the cream formulations I, II and III were declared stable at a temperature of 25º and the extract cream Kuntze *V. villosum* (Blume) Kuntze leaves showed complete wound healing in 12 days. The results of the Kruskal Wallis test obtained p value = 0.670 > 0.05, which means there is no difference in the length of the healing process for all treatments.
Keywords: *Vincetoxicum villosum* (Blume) Kuntze, Burn Wound Infection, Oil-in-Water Cream, Stearic Acid & Triethonolamine

1. INTRODUCTION

Indonesia, with a tropical climate, is a country rich various plants, however is also a country with a fairly high ranking in the ranking of diseases caused by pathogenic bacteria. One of the diseases that often arises is skin and soft tissue infections. Infection can be caused by various microorganisms, such as bacteria, by entering the body's tissues and multiplying in the tissues. For example, *Propionibacterium acnes* and *Pseudomonas aeruginosa* which is a bacteria that causes skin infections in humans (Oktaviani et al., 2023). *Pseudomonas aeruginosa* itself is often found in burn wound infections (El Hamzaoui et al., 2020; Ervianingsih et al., 2020; Kunwar et al., 2021).

In general, burn wounds will become contaminated immediately after injury. If burns are not treated properly, infection can occur (Farhan & Jeffery, 2021; Kelly et al., 2022). The principle of treating burns is to cool the burned area or reduce inflammation, prevent infection and give epithelial remnants the opportunity to proliferate and close the wound (Haris et al., 2022). Therefore, preparations can be chosen that soothe the inflamed part, reduce flavor itching and pain like cream. Then, to prevent infection, creams can be formulated with active preparations that have inhibitory activity against bacteria that cause burn wound infections (Cooley et al., 2023; Javanmardi et al., 2021; Stan et al., 2021).

According to previous research results, *V. villosum* (Blume) Kuntze showed that there is an inhibitory effect on the growth of *Pseudomonas aeruginosa* bacteria (Oktoviani et al., 2023, 2021). To take advantage of these activities, then preparation is needed pharmacy that lasts a long time and is safe to use on the skin. Then extraction using several solvents shows the leaf extract *V. villosum* (Blume) Kuntze has a higher yield in ethanol solvent and has good solubility in oil, making it suitable for making O/W cream (Oktoviani et al., 2022). O/W cream is

usually used to moisturize the skin and reduce skin lesions (Nuralifah et al., 2019).

The researchers were interested in testing the activity of nangka kuning leaf extract cream *V. villosum* (Blume) Kuntze. With the use of *V. villosum* (Blume) Kuntze as a wound medicine, this can be an alternative treatment for the community. The cream was chosen because this preparation has the advantages of being easy to apply to the skin, easy to wash off after application, the cream can be used on skin with wet wounds, and is evenly distributed.

2. MATERIAL AND METHOD

This research is a type of experimental research. The research was conducted at the Bengkulu University Laboratory in September 2022-August 2023. The equipment used was the Ohaus Starter 3100 brand pH meter and the NDJ-8S viscometer. The materials used are *V. villosum* (Blume) Kuntze) leaf extract, mice, ethanol solvent.

2.1 Cream formulation

V. Villosum (Blume) Kuntze leaf extract with variations of stearic acid and triethanolamine as an emulsifier with several modifications as can be seen in table 1. The oil phase ingredients are heated to a temperature of 70^0C-80^0C. After everything has melted, the water phase is added little by little into a hot mortar containing the oil phase, crushed until homogeneous and a cream base is formed. Then put *the V. Villosum* (Blume) Kuntze leaf extract in a mortar.

Table 1. Cream formulation O/W *V. villosum* (Blume) Kuntze leaf extract

Material name	F1	F2	F3	Function	Phase
V. villosum (Blume) Kuntze leaf extract	0.3 g	0.3g	0.3g	Active substance	Oil
Sesame oil	4.5g	4.5g	4.5g	Extract Solvent	Oil
Stearic Acid	15%	16%	17 %	Emulgator	Oil
TEA	4 %	3%	2 %	Humectant	Water
Paraffin	5.0 %	5.0 %	5.0 %	Emollient	Oil
Adeps Lanae	3.0 %	3.0 %	3.0 %	Oil Base	Oil
Na Benzoate	0.2 %	0.2 %	0.2 %	Preservative	Water
Aquadest	Ad 100 %	Ad 100 %	Ad 100 %	Water Base	Water

2.2 Evaluation of the Cream

Evaluation of preparations includes Organoleptic tests are carried out with the help of the senses of sight and smell to see the color and smell of the cream preparation. Then, to test homogeneity, 1 gram of cream was smeared on the glass object. Then overlap it with another glass object and provide light.

The adhesion test was carried out using a cream adhesion test tool. Two transparent glasses, a stopwatch, gram weights and this is done by placing enough cream on top of another transparent glass on top of the cream, then pressing it with a weight of 250 grams for 5 minutes, the weight is lifted and the two transparent object glasses are removed and the time is recorded until both of the object's windows fell off.

Ohaus Starter 3100 brand pH meter. The instrument is calibrated first using a buffer solution of pH 4, pH 7 and pH 10. The pH check is carried out by dipping the electrode into 1 gram of cream diluted with distilled water to 10 ml. Measuring the pH of the preparation by inserting an electrode into the cream preparation and looking at the number printed on the tool. Then, to test the spreadability, 0.5 grams of cream was placed in the middle of the petri dish in an inverted position, left for 1 minute and given a load of 50, 100, 150 and 200 grams every 1 minute.

Test Nangka Kuning leaf extract cream using the method cycling test where the preparation is kept at a temperature of 4º for 24 hours, then the preparation is tested for its physical properties, then transferred to an oven at a temperature of 40º for 24 hours (counts as one cycle) and the physical properties are tested again, the test is carried out for 4 cycles then observed whether there is separation or not phase in preparation.

The viscosity test was carried out using an NDJ-8S viscometer and using *spindle* 4. Use is carried out by inserting the preparation into a container in the form of a glass cylinder tube (glass beaker) and the appropriate *spindle* no. 4, is inserted the limit line up to the viscometer needle then set a speed of 6.0 rpm. This measurement was carried out in three repetitions.

2.3 Making Wounds on Test Animals

The wound healing effect was carried out on rabbits. Rabbits were divided into 4 groups, namely: 4 groups K1, K2, P1 and P2 which were respectively the negative group (without treatment), the positive

control group (given 0.2% hyaluronic acid cream), the 1st treatment group (given 2% *V. villosum* (Blume) Kuntze leaf extract), treatment group 2 (given 2% *V. villosum* (Blume) Kuntze leaf extract cream).

The first step is to shave the rabbit's fur or shed it, then the rabbit's back is measured to a diameter of 1.5 cm and outlined with a marker. Then a shallow second degree burn was made by inducing the skin on the rabbit's back using a hot metal plate that had been heated using a heat inducer for 10 seconds, then placing the metal on the rabbit's back for 3-5 seconds until bullae were visible.

The cream or extract is applied to the wound twice a day, for 14 days. The wound is covered with gauze and plaster, then the wound diameter is observed and measured to the nearest 0 cm or new tissue has formed covering the wound. During the research period the rabbits were fed in cages 2 times a day with pelleted food.

3. RESULT AND DISCUSSION

Evaluation carried out on the rounded formula including organoleptic tests, homogeneity tests, pH tests, adhesion tests, spreadability tests, stability tests and viscosity tests. Organoleptis test results for formulas I, II and III has a light green color. The preparation obtained is in semi- solid form and has a distinctive extract smell so that organoleptically, the preparation is good. Then from observations of the homogeneity test formulas I, II and III, it is known that the color is even and there are no fine grains in the preparation. This shows that the base can support the leaf extract *V. villosum* (Blume) Kuntze because the base and extract can form a homogeneous cream.

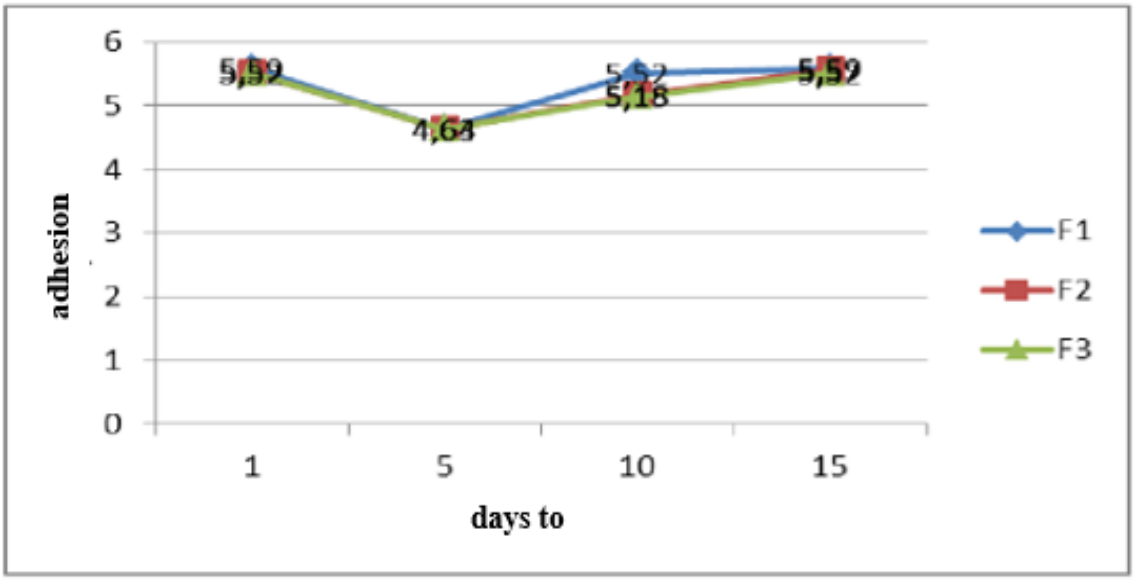

Figure 1. Adhesion Test Results

Results evaluation adhesion test for formulas I, II and III meets the specified requirements, namely above 4 seconds (Figure 1). Stearic acid has the effect of increasing concentration and making the cream stiffer thereby increasing the adhesion of the cream (Jayanti & Puspitasari, 2021), while TEA can dilute the concentration of the cream so that the use of a combination of these ingredients creates a base with good adhesion (Endriyatno & Puspitasari, 2023). The higher the concentration of TEA and the lower the concentration of stearic acid, the stickiness of the cream will be getting lower.

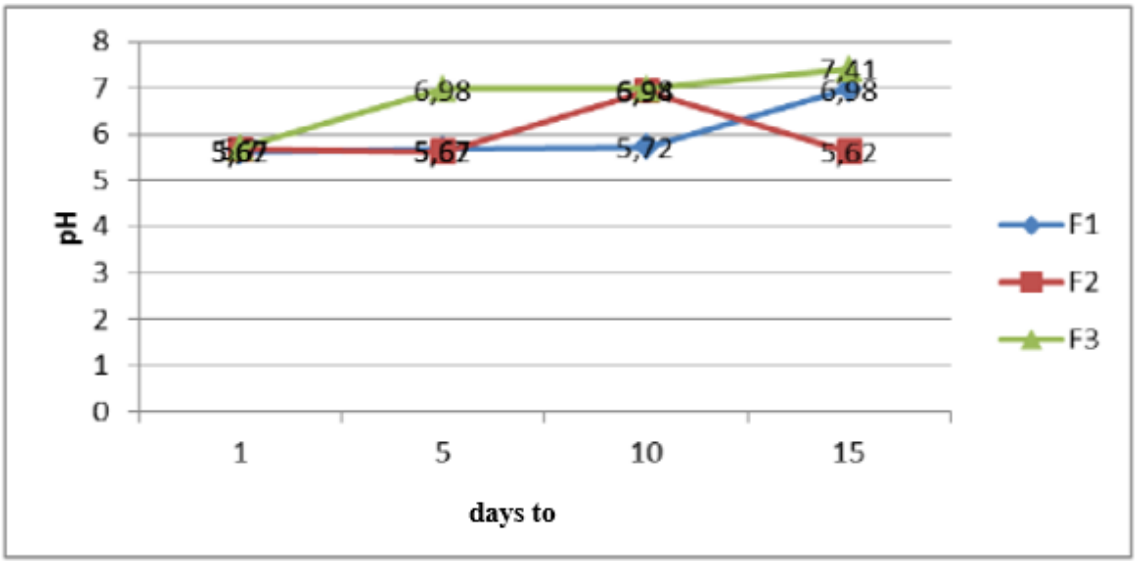

Figure 2. pH Test Results

pH measurements for formulas I, II and III show numbers that fluctuate during storage but are still within the pH acidity range that is good for the skin . The pH value of leather products in accordance with SNI 16-4399-1999 from 4.5-8 (Sari et al., 2021). In formulas I, II and III, TEA can contribute to increasing the pH because it is alkaline and stearic acid has an acidic pH so it plays a role in lowering the pH (Saryanti et al., 2019). The pH test shows that all formulas meet the pH requirements (Figure 2) .

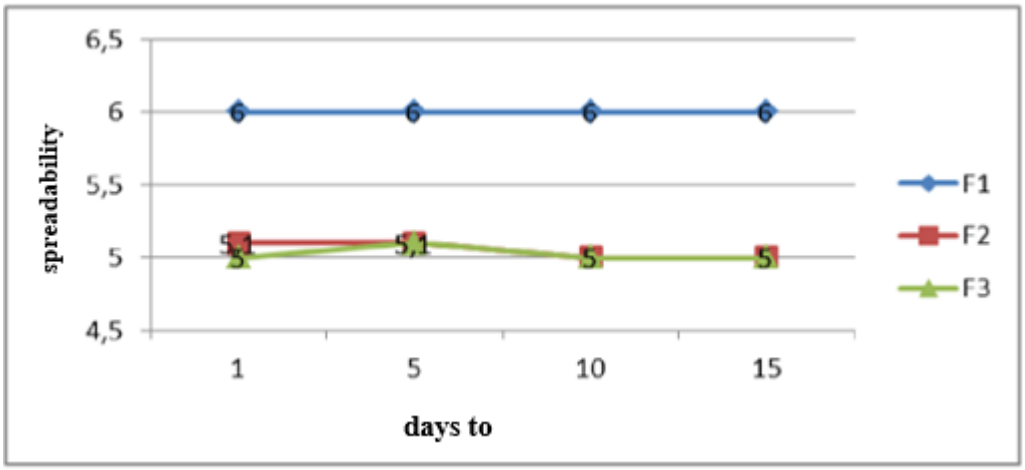

Figure 3. Spreadability Test Results

Evaluation of the spreadability of the cream aims to see the spreadability of the cream when applied to the skin. Spreadability measurements are carried out by placing a load which is likened to a pressing cream when applied to the skin. According to the Pharmacopoeia 4th Edition (1995), the spreadability of semi-solid preparations which are very comfortable to use is between 5-7cm. The test results show that formulas I, II and III meet the requirements of good spreadability .

Test stability with cycling test at a cold temperature of 4ºC is stored in the refrigerator, and at a hot temperature of 40ºC is stored in the oven for 24 hours. Evaluation is carried out by comparing the condition of the three preparation formulas before and after testing. Ogranoleptis test before cycling test and after cycling test (4 cycles did not change color and smell. Homogeneity test Cycling test cream structure shows a homogeneous composition. The cream also does not separate between the water phase and the oil phase, so it meets the stability test.

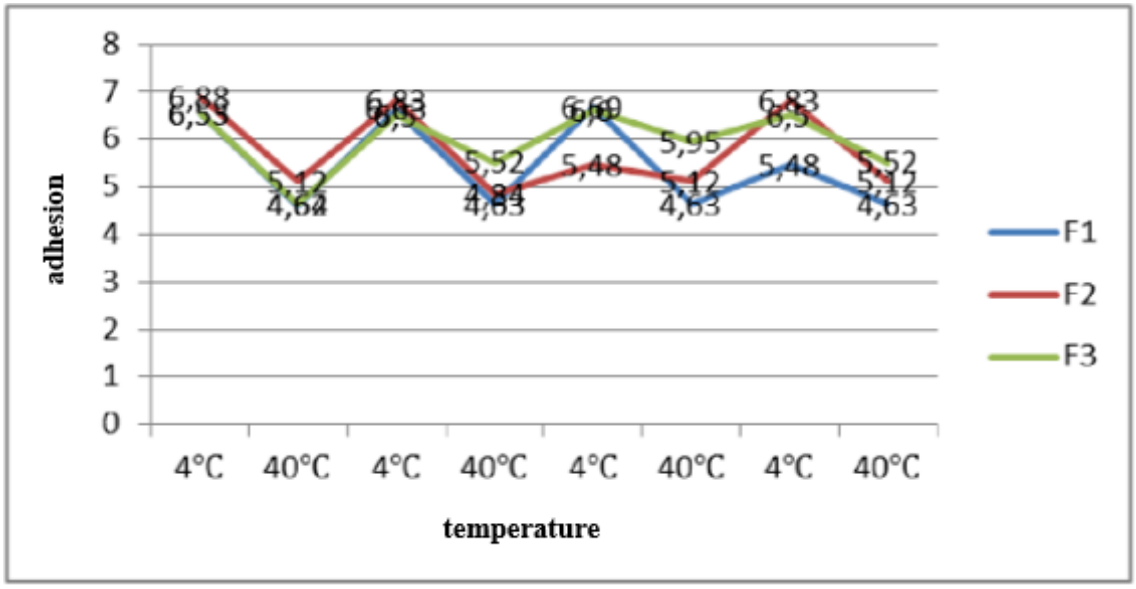

Figure 4. Adhesion Test Results at 4º C and 40º C Temperatures

The adhesion strength test of the 4 cycle experienced increases and decreases in value because it was influenced by temperature during storage and still met the spreadability standards for storage stability (Figure 4). Then to test the pH cycling testduring the process cycling test with 4 cycles experienced an increase and decrease in the pH of the cream, due to the influence of temperature. However, this still meets the pH standards for topical preparations (Figure 5).

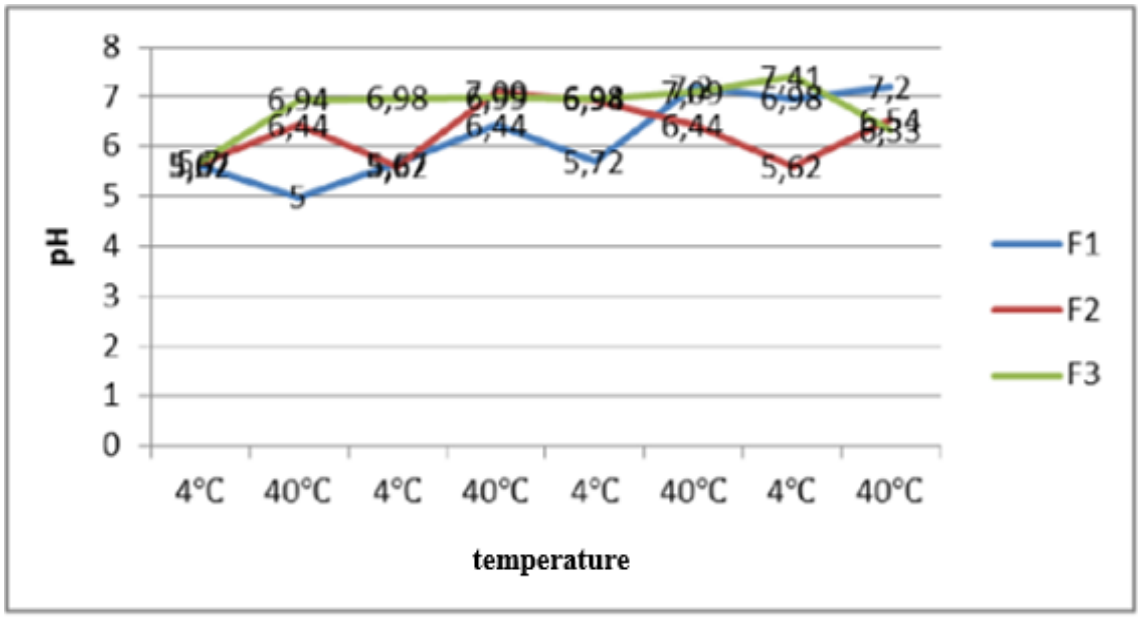

Figure 5. pH test results at temperatures of 4º C and 40º C

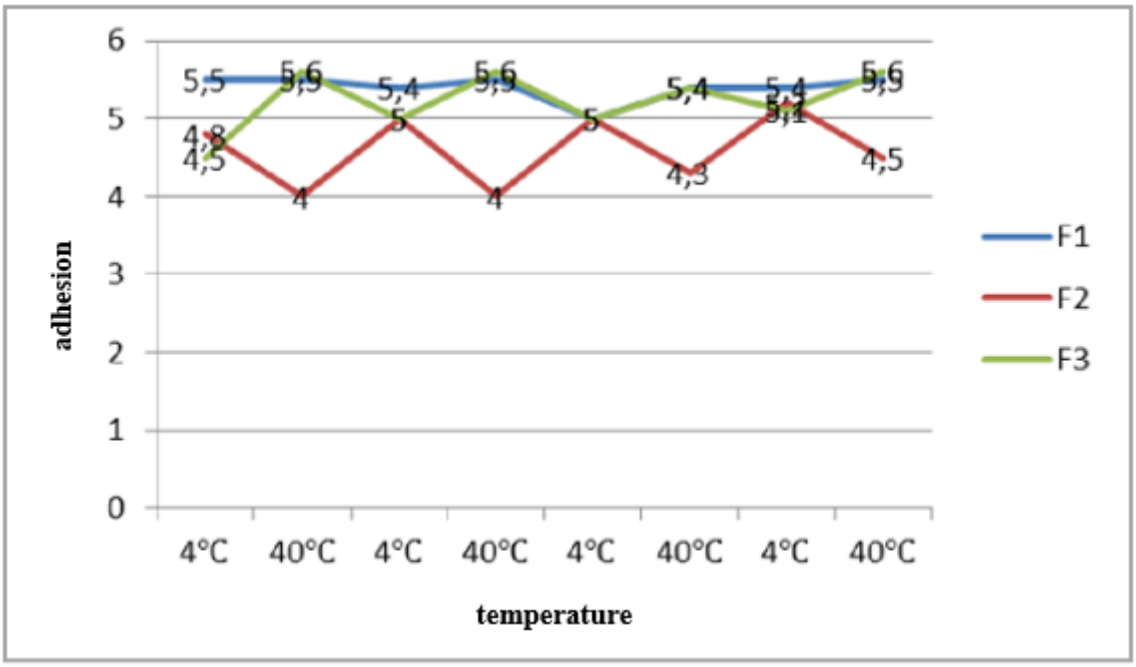

Figure 6. Spreadability Test Results at Temperatures of 4º C and 40º C

Spreadability test cycling test 4 cycles, the spreadability test results experience increases and decreases in value because it is influenced by temperature, there will be changes in the viscosity of the cream which can change the spreadability of the cream, but these results still meet the spreadability standards (Figure 6). The 4 cycles viscosity cycling test results from the viscosity test here experienced ups and downs but still met the iscosity standards for cream preparations. However, at a temperature 40ºC, the viscosity changes slightly (Figure 7).

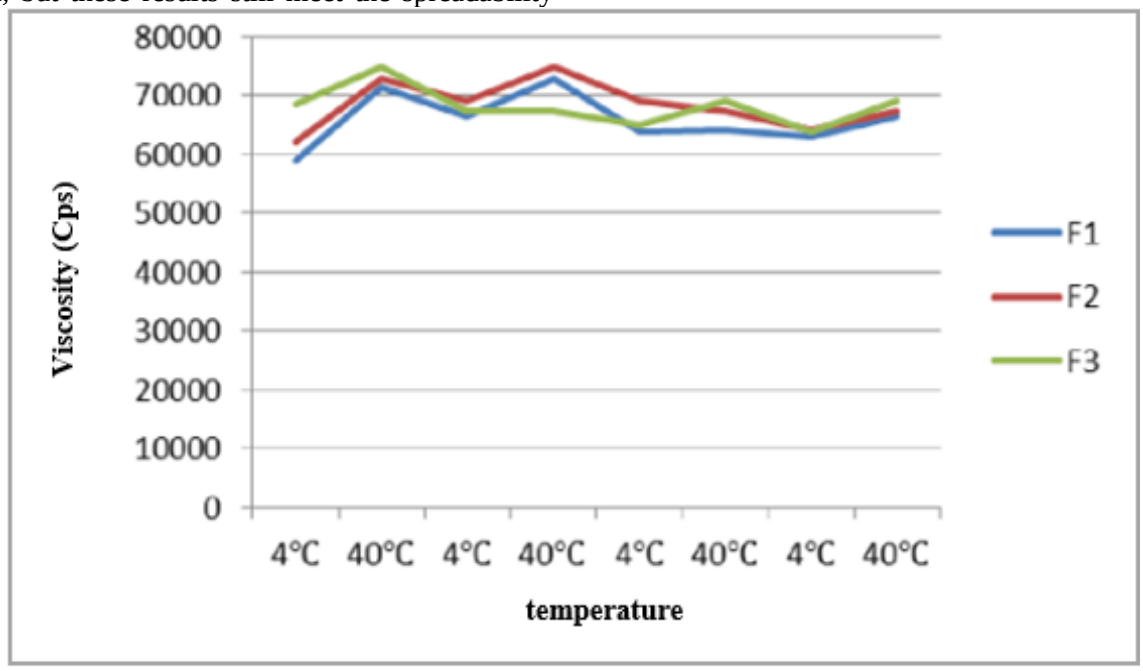

Figure 7. Viscosity Test Results at Temperatures 4º C and 40º C

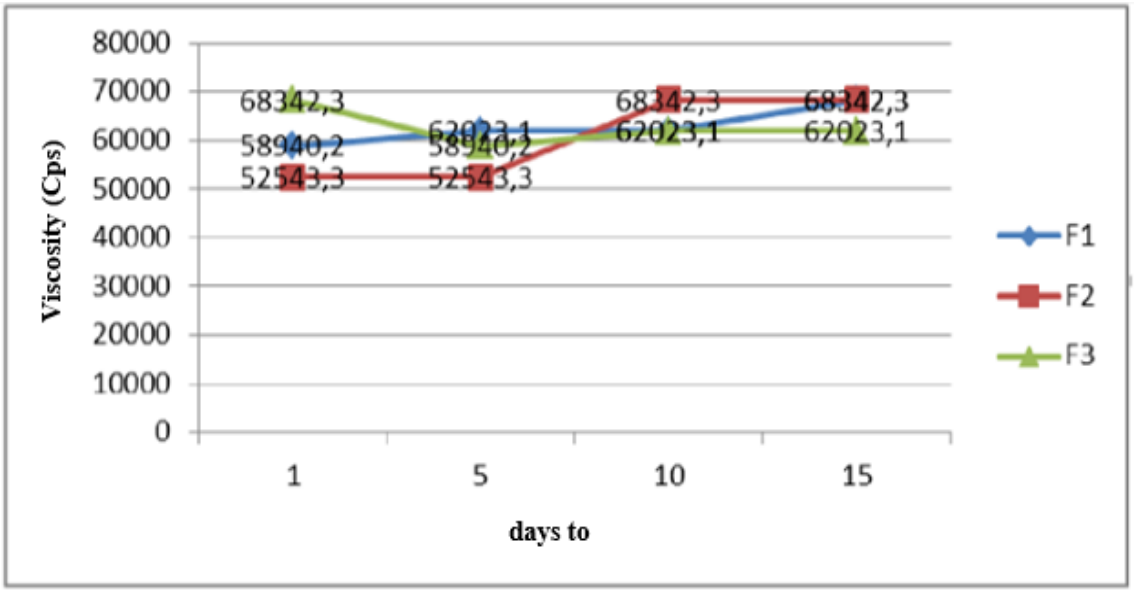

Figure 8. Viscosity Test Results

Viscosity testing aims to determine the effect of concentration of the emulsifier used in making cream preparations. The viscosity of a good cream ranges from 30,000-70,000cps. Based on the data produced, formulas I, II and III meet the requirements for good cream viscosity (Figure 8). Acid can increase the viscosity of cream. The increase in viscosity is due to the role of stearate stiffening agent. In addition, TEA acts as an aqueous phase emulsifier, which when mixed with stearic acid forms an anionic emulsifier and can increase the size of fine and rigid molecules.

Based on the evaluation results concluded that formulas I, II and III of *V. villosum* (Blume) Kuntze extract cream is stable at 25º ℃ and breaks down at 40ºC. Then, the effect of healing burns was proven to be faster in rabbits given *V. villosum* (Blume) Kuntze leaf extract cream when compared to rabbits given *V. villosum* (Blume) Kuntze leaf extract. This can be caused by the presence of a base in the *V. villosum* (Blume) Kuntze leaf extract cream which makes nutritious substances more easily absorbed and has a wound healing effect. However, further research is still needed to state that *V. villosum* (Blume) Kuntze leaf extract cream provides wound healing differs significantly from wound healing provided by *V. villosum* (Blume) Kuntze leaf extract. For further research, it is recommended to increase the number of rabbits in each group so that there is sufficient data to carry out statistical tests.

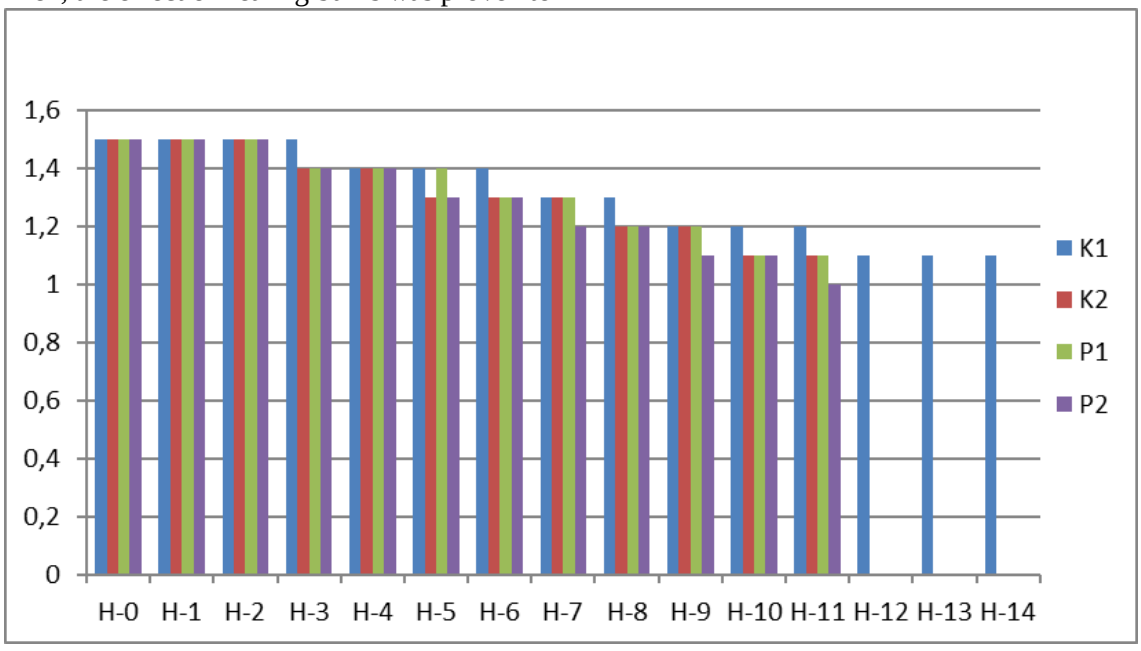

Figure 9 . Graph of the Average Results of Measuring the Diameter of Rabbit Burn Wounds for 14 Days

Type: K1: Control 1
K2: Control 2
P1: Treatment 1
P2: Treatment 2
H0-H14: Day 1-Day 14

Quite surprising results were seen in faster healing of burn wounds in rabbits given *V. villosum* (Blume) Kuntze leaf extract cream when compared to rabbits given 2% hyaluronate acid cream from a circulating preparation. Hyaluronic acid works by stimulating growth factors, resulting in collagen production in fibroblasts and connective tissue in the wound healing process (Taskan et al., 2021; Yang et al., 2021; Zhai et al., 2020). Meanwhile, the *V. villosum* (Blume) Kuntze leaf extract cream preparation 2%, has inhibitory power against *Pseudomonas aeruginosa* bacteria (Oktoviani et al., 2023, 2021) so that it can overcome the incidence of infection and can speed up the healing of burn wounds. This difference in mechanism of action shows differences in the healing time of burn wounds in rabbits. Rabbits given hyaluronic acid cream showed a burn wound diameter of 1.1 cm on the 11th day. Meanwhile, rabbits were given *V. villosum* (Blume) Kuntze leaf extract cream showed a burn wound diameter of 1.0 cm on the same day (Figure 9).

Apart from the mechanism of action, differences in burn wound healing time can be caused by differences in concentration. The concentration of hyaluronic acid cream was ten times smaller than the concentration of *V. villosum* (Blume) Kuntze leaf extract cream. Based on research, the diameter of burn wounds in rabbits given hyaluronic acid cream was greater than in rabbits given *V. villosum* (Blume) Kuntze leaf extract cream.

The results of the normality test for rabbit burn diameter data using the Shapiro-Wilk test obtained a p value (sig.) for each treatment. The p value turned out to be <0.05, which means the data was not normally distributed, so the non-parametric Kruskal Wallis test was used. The results of the Kruskal Wallis test obtained a p value = 0.670 > 0.05, so it was not significant, which means there was no difference in the length of the healing process for all treatments.

4. CONCLUSION

Based on the results of the research that has been carried out, it can be concluded that *V. villosum* (Blume) Kuntze leaf extract cream Formulas I, II and III with variations of stearic acid and TEA as emulsifiers were stated to have good results and were stable at a temperature of 25º and unstable at a temperature of 40º. Effects *V. villosum* (Blume) Kuntze of leaf extract cream for healing burns looks perfect within 12 days.

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