

# Optimization formula and evaluation of polyherbal cream for antimicrobial and wound healing activity

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Received: 08 September 2024; Accepted: 25 October 2024; Published online: 31 October 2024

**Abstract.** The aim of the research is to develop a preparation formula and evaluate the antibacterial and wound healing capabilities of the product polyherbal cream. The optimal ratio of ingredients polyherbal cream formulation was found by testing the antibacterial properties based on the evaluation of the diameter of the antibacterial zone of different bacterial strains and evaluating the acute toxicity and wound healing ability of polyherbal cream in a mouse model. The research has produced the optimal formulation of polyherbal cream, which includes tamanu oil, tea tree essential oil, and cajeput essential oil at concentrations of 28%, 1%, and 9%, respectively, along with excipients such as hydroxyethyl acrylate (1 g), PEG-600 stearate (3.95 g), and cetyl alcohol (5.45 g) in a 100 g preparation. Polyherbal cream determined the acute skin toxicity dose on mice greater than 2000 mg/kg and evaluated the wound healing ability of the preparation. A formula for the preparation of polyherbal cream has been developed and tested for its antibacterial and wound healing effects, contributing to orienting further research on the beneficial pharmacological effects of products made from tamanu (*Calophyllum inophyllum*), cajeput (*Melaleuca quinquenervia*), and tea tree (*Melaleuca alternifolia*) in Vietnam.

**Keywords:** Tamanu oil, Tamanu cream formulation, antibacterial, wound healing, and acute toxicity.

**Cite this as:** Bui D.-T., Bui M.-T. & Nguyen N.-V.T. (2024). Optimization formula and evaluation of polyherbal cream for antimicrobial and wound healing activity. J. Multidiscip. Sci. 6(2), 35-44.

## 1. Introduction

Human skin forms a protective barrier against the external environment and is our first line of defense against solar and pathogenic insults. The skin also protects our internal tissues and organs, acts as a sensory interface, and prevents dehydration (Hill, 2019; Harris-Tryon & Grice, 2022). Skin injuries destroy the barrier, thereby increasing the penetration of bacteria, fungi, and viruses. Skin is often damaged for many reasons, but it is often due to wounds or physical trauma. The process of skin damage is very complicated, but the process of restoring the skin's barrier function is even more sophisticated. After injury, skin integrity must be promptly restored in order to maintain its functions (Flanagan, 2013; Ansel et al., 2016; Cañedo-Dorantes & Cañedo-Ayala, 2019). Because of that, skin care products are widely developed, not without mentioning cream—a type of topical cosmetic that is very popular because of its ease of application on the skin. More specifically, the use of plants as a source of active principles for cosmetics has significantly increased in the last few years. Safety, compatibility with all types of skin, fewer side effects, and availability are among the advantages of herbal cosmetics above synthetic ingredients (Mansoor et al., 2023).

*Calophyllum inophyllum* L. is a plant that grows a lot in Vietnam, especially in western provinces such as Ben Tre and Ca Mau. People have used tamanu oil from tamanu seeds to treat various skin-related ailments (Pribowo et al., 2021). Tamanu oil is known for its anti-inflammatory, antifungal, antibacterial, and insecticidal pharmacological activities. In particular, tamanu oil is excellent for restoring skin after injury (Léguillier et al., 2015; Hua et al., 2022; Ferdosh, 2024; Krishnappa et al., 2024).

Additionally, cajeput essential oil (*Melaleuca quinquenervia*) and tea tree essential oil (*Melaleuca alternifolia*) can help with swelling, pain, inflammation, and fever. They can also kill insects (Carson et al., 2006; Acha et al., 2019; Porusia & Septiyana, 2021).

However, because the properties, application potential, and medical value of *Calophyllum inophyllum* L. have not been fully exploited, this research was conducted to create a product from tamanu oil that is preferred by users for everyday life. In order for tamanu oil-based products to gain popularity, it is crucial to not only promote but also maintain their pharmacological properties. Tamanu oil-based products remain scarce, particularly those that combine with other medicinal herbs. Therefore, this study aimed to formulate a Tamanu cream product using tamanu oil and cajeput essential oils, and assess its antibacterial and wound healing potential, drawing from the latest research on tamanu oil use.

## 2. Materials and Methods

### 2.1. Plant materials

Tamanu oil (*Calophyllum inophyllum* L.), cajeput essential oil (*Melaleuca quinquenervia*), and tea tree essential oil (*Melaleuca alternifolia*) were collected by Dong Thap Muoi Pharmaceutical Research and Development Joint Stock Company.

### 2.2. Chemicals, solvents, standard solutions and bacteria strains

Chemicals, solvents, and standard solutions: Water, *Calophyllum inophyllum* Oil, Glycerine, Cetyl Alcohol, Hydroxyethyl Acrylate, PEG 600 Stearate, *Melaleuca alternifolia* Oil, and 1,2-Hexanediol.

Test bacteria strains: *Staphylococcus aureus* ATCC® 29213, *Pseudomonas aeruginosa* ATCC® 27853, and *Escherichia coli* ATCC® 25922 were provided by Saigon Pharmaceutical Science Technology Center, Sapharcen.

### 2.3. Develop a recipe for preparing tamanu cream

#### 2.3.1. Appropriate ratio of tea tree essential oil and tamanu oil in tamanu cream product

The antibacterial ability of tea tree essential oil combined with tamanu oil was determined by the agar diffusion method. The test bacterial strains *Staphylococcus aureus* ATCC® 29213 and *Pseudomonas aeruginosa* ATCC® 27853 on Mueller-Hinton agar (MHA) medium were diluted in 0.9% NaCl to reach a density of  $1-1.2 \times 10^8$  CFU/mL spread each prepared bacterial strain on MHA medium. Place 6 mm-diameter paper discs on the agar plate. Tea tree essential oils 0.5, 1, and 1.5% were combined with 24, 26, 28% tamanu oil diluted in DMSO solvent and 0.01% Tween 80 and dropped directly onto the paper disc at a volume of 30  $\mu$ L/disc. The agar box was incubated at 37 °C for 24 hours. The essential oil combined with tamanu oil had antibacterial ability when there was an antibacterial ring around the hole (CLSI, 2023).

	<b>Chemicals and solvents</b>	<b>Weight (kg)</b>
1	Water	Add to enough
2	Glycerine	6
3	Hydroxyethyl acrylate	2
4	PEG - 600 stearate	5
5	Cetyl alcohol	5
6	<i>Calophyllum inophyllum</i> oil	Investigate the ratio
7	<i>Melaleuca alternifolia</i> essential oil	Investigate the ratio
8	1.2 - Hexanediol	1
	<b>Total</b>	<b>100</b>

#### 2.3.2. Appropriate ratio of tea tree, cajeput essential oil, and tamanu oil in the tamanu cream product

After investigating the ratio of tamanu oil and tea tree essential oil in the cream preparation, the research conducted a survey of the ratio of cajeput essential oil in tamanu cream. The concentrations of cajeput essential oil in the tested formula were: 3%, 6%, 9%, and 12%, respectively. The antibacterial rate of *Staphylococcus* and *Pseudomonas* strains was evaluated as above when changing the concentration of cajeput essential oil.

### 2.3.3. Acute toxicity and antibacterial and wound healing properties of tea tree and cajeput essential oils

Qualitative antibacterial activity of tea tree and cajeput essential oils and determination of Minimum Inhibitory Concentration (MIC) of test substances (%). The test was performed with the test strains *S. aureus* ATCC® 29213 and *E. coli* ATCC® 25922 on MHA agar diluted in 0.9% NaCl to a density of at least 108 CFU/mL. Add 100 µL of each bacterial suspension to a tube containing 10 mL of hand sanitizer. Incubate the sample tubes containing bacteria and hand sanitizer at room temperature for 30 seconds. Determine the number of bacteria remaining in the test sample by the MHA medium live count method. Repeat three times for each test strain. Do the same with the negative control, replacing 10 mL of hand sanitizer with 10 mL of 0.9% NaCl (Kampf et al., 2013).

### 2.4. Optimize the ingredients of the tamanu cream formulation

Formulation was optimized by considering the three important excipients. Three quantitative variable levels were developed for this purpose: 3–7 g cetyl alcohol (a), 0.5–1.5 g hydroxyethyl acrylate (b), and 2–5 g PEG 600 stearate (c). Box-Behnken design (BBD) was then conducted with these values in mind. The design matrix that was employed, along with 15 formulas generated from the variables that were evaluated and their respective levels in the optimization process, and derive the regression equation of the regression equation of the response. The experimental model was designed using Design Expert 12.0.0 (Stat Ease) software according to the Box-Behnken response surface model, with the objective function in this test being the cream's thinness between 6.5 and 7.5 cm, the highest bacterial inhibition ability, and the highest wound healing rate. This optimal prediction formula was evaluated by repeating it three times to obtain results with quite high accuracy. Thus, the model is highly compatible with the experiment.

### 2.5. Acute toxicity and wound healing ability of tamanu cream and tamanu oil combined with cajeput oil on mice model

#### 2.5.1. Determining the acute toxicity of tamanu cream-cajeput oil on white mice model

Follow Organisation for Economic Co-operation and Development (OECD) Guideline 402: "Acute Dermal Toxicity: Fixed Dose Procedure" (OECD, 2002). The first test dose was 200 mg/kg of mouse body weight, then the dose was changed according to the response of the test animals according to the instructions in Appendix 2, and the impact of tamanu cream was evaluated according to the Globally Harmonised System (GHS) toxicity classification level.

Preparation of experimental animals: White, male mice were acclimatized to laboratory conditions for 7 days before starting the study. Mice were randomly selected and marked. Tested on 2 mice with tamanu cream according to Appendix 2 in OECD Guideline 402: "Acute Dermal Toxicity: Fixed Dose Procedure." Two test mice weighing 25 g were tested with a dose of 200 mg/kg body weight. Evaluation of changes in skin, hair, and eyes of test mice.

After 72 hours, if the test mice returned to normal, following OECD guidelines, the test dose was increased to 1000 and 2000 mg/kg body weight of mice, and 1 control group replaced the tamanu oil and essential oil in the tamanu cream with glycerin. Each group tested on 6 mice and monitored for 14 days.

#### 2.5.2. Evaluation of the wound healing ability of tamanu cream

Creating skin wounds and testing gel application. The test mice were divided into 3 groups, each group of 6 mice:

- a) Physiological group: causing skin loss wounds with a diameter of 12 mm on the back, applying glycerin.
- b) Placebo cream test group: causing skin loss wounds with a diameter of 12 mm on the back, applying placebo gel.
- c) Tamanu cream test group: causing skin loss wounds with a diameter of 12 mm on the back, applying tamanu cream.

Observe the mouse wounds and measure the wound area on days 2, 6, and 10 of the experiment to calculate the % wound closure over time.

$$\% \text{ Wound closure} = (\text{Wound area day 0} - \text{Wound area day n}) / \text{Wound area day 0} \times 100$$

### 2.6. Statistical analysis

All of the collected data were entered and analyzed using Microsoft Excel 2016.

### 3. Results and Discussion

#### 3.1. Develop a recipe for preparing tamanu cream

##### 3.1.1. Appropriate ratio of tea tree essential oil and tamanu oil in tamanu cream product

Tea tree essential oil and tamanu essential oil have three survey ratios. Combining the three ratios together results in nine survey formulas. Evaluate the antibacterial rate of 9 formulas as follows:

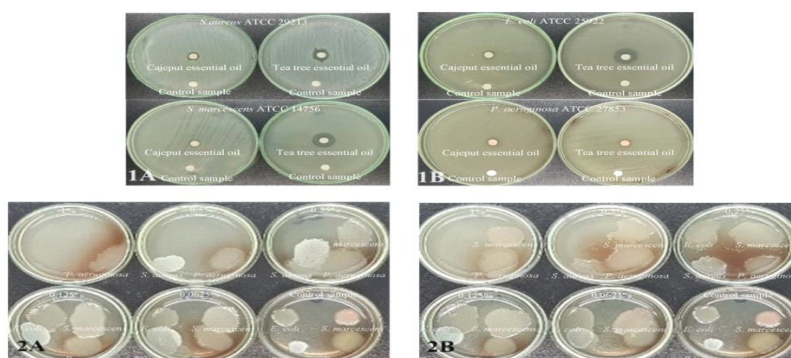
Tea tree essential oil and tamanu oil (w/w %)	Antimicrobial zone diameter of <i>Staphylococcus</i> (mm)	Antimicrobial zone diameter of <i>Pseudomonas</i> (mm)
0.5 - 24	8.7	-
0.5 - 26	8.8	-
0.5 - 28	9.0	-
1 - 24	9.3	7.8
1 - 26	9.4	7.9
1 - 28	9.6	8.5
1.5 - 24	9.5	8.1
1.5 - 26	9.6	8.3
1.5 - 28	9.8	8.4

Survey results show that increasing the concentration of tea tree essential oil in the formula helps improve the antibacterial ability of tamanu cream. Increasing the concentration of tamanu oil also helps improve the antibacterial ability of tamanu cream. The results showed that tamanu oil concentrations of 26–28% and tea tree essential oils of 1% and 1.5% had the best antibacterial properties. Because the price of tea tree essential oil is higher than tamanu oil, when comparing the antibacterial effectiveness, the research team chose a ratio of 1% and 28% of tea tree essential oil and tamanu oil for the next test.

##### 3.1.2. Appropriate ratio of tea tree, cajeput essential oil, and tamanu oil in the tamanu cream product

The antibacterial ability of tamanu cream at the concentration of cajeput essential oil in the survey formula is 3%, 6%, 9%, and 12%, respectively.

Cajeput essential oil (w/w %)	Antimicrobial zone diameter of <i>Staphylococcus</i> (mm)	Antimicrobial zone diameter of <i>Pseudomonas</i> (mm)
3%	9.7	8.6
6%	9.8	8.7
9%	10.5	8.9
12%	10.5	8.9



**Figure 1 (A, B).** Qualitative results of the antibacterial ability of tea tree and cajeput essential oils; and **2 (A, B).** MIC results of the two essential oils tested

### 3.1.3. Acute toxicity and antibacterial and wound healing properties of tea tree and cajeput essential oils

Based on Figure 1, it shows that tea tree essential oil has excellent antibacterial ability, with an antibacterial zone diameter of 10.94 mm for *S. aureus* and 14.73 mm for *E. coli*. Tea tree essential oil is not resistant to *P. aeruginosa*. Cajeput essential oil has average antibacterial ability, with an antibacterial zone diameter of 7.74 mm for *S. aureus*, 8.5 mm for *E. coli*, and 7.0 mm for *S. marcescens*. Cajeput essential oil does not show resistance to *P. aeruginosa*.

Based on Figure 2, the MIC value of tea tree essential oil with *S. aureus* is 1%, with *E. coli* is 0.25%, and with *S. marcescens* is 0.5%. In general, the MIC of tea tree essential oil with the tested strains is quite low, proving that the essential oil has excellent antibacterial activity. The MIC value of cajeput essential oil with *S. aureus* is 1%, with *E. coli* is 0.5%, and with *S. marcescens* is > 1.5%. In general, the MIC of cajeput essential oil is higher than that of tea tree essential oil.

### 3.2. Optimize the ingredients of the tamanu cream formulation

The statistical summary of the model suggested by the software is presented in Table 4.

	Cetyl alcohol (g)	Hydroxyethyl acrylate (g)	PEG 600 Stearate (g)	Y <sub>1</sub> Cream's thickness	Y <sub>2</sub> <i>S. aureus</i> eradication rate	Y <sub>3</sub> Wound closure rate (%)
1	3	0.5	3.5	11.8	53.78	46.76
2	7	0.5	3.5	8	45.67	42.02
3	3	1.5	3.5	6.6	52.73	45.82
4	7	1.5	3.5	4.7	78.91	58.22
5	3	1	2	7.1	55.21	48.04
6	7	1	2	5.9	59.07	51.49
7	3	1	5	7.6	62.4	54.46
8	7	1	5	5.3	76.61	67.16
9	5	0.5	2	11	52.93	45.99
10	5	1.5	2	5.7	63.27	55.24
11	5	0.5	5	8.1	59.53	53.21
12	5	1.5	5	5.4	81.38	72.32
13	5	1	3.5	7	86.21	77.24
14	5	1	3.5	6.7	87.08	78.12
15	5	1	3.5	7	85.12	76.34

Two factors that have a statistically significant effect on the thinness of the sample are: cetyl alcohol and hydroxyethyl acrylate ( $p < 0.05$ ), while PEG 600 stearate has no statistically significant difference on the thinness of the cream (Figure 1A). With two excipients, cetyl alcohol and hydroxyethyl acrylate, increasing the concentration of excipients reduces the thinness of the cream to about 4–5 cm. Changing the concentration of hydroxyethyl acrylate affects the thinning more than cetyl alcohol.

The response's regression equation can be found below:

$$\text{Thinness (cm)} = 15.15 + 0.89b - 0.575a - 4.125b - 0.275c$$

Note. a, b, c being the variables representing the factors cetyl alcohol, hydroxyethyl acrylate and PEG 600 stearate respectively.

The bacterial inhibition ability of the test samples was influenced by all 3 excipients in the first and second order (Figure 1B), with  $p \leq 0.004$ . This proves that changing the excipients affects the dispersion and the impact of cajuput essential oil in the test sample on bacteria. The graph shows that at varying concentrations of cetyl alcohol and hydroxyethyl acrylate, the spreadability of the sample changes and leads to a decrease in the diffusion ability of the essential oil, thus changing the percentage of bacterial inhibition. The ability to inhibit bacteria is highest when the concentration of the two excipients is near the center point. It shows that increasing the concentration of PEG 600 stearate and hydroxyethyl acrylate also increases the ability of the test sample to inhibit bacteria.

The regression equation of the response is as follows:

$$\text{Inhibition (\%)} = -75.13 + 27.32a + 69.44b + 21.34c + 8.57ab + 0.86ac + 3.84bc - 3.66a^2 - 54.82b^2 - 3.62c^2$$

Note. a, b, c being the variables representing the factors cetyl alcohol, hydroxyethyl acrylate and PEG 600 stearate respectively.

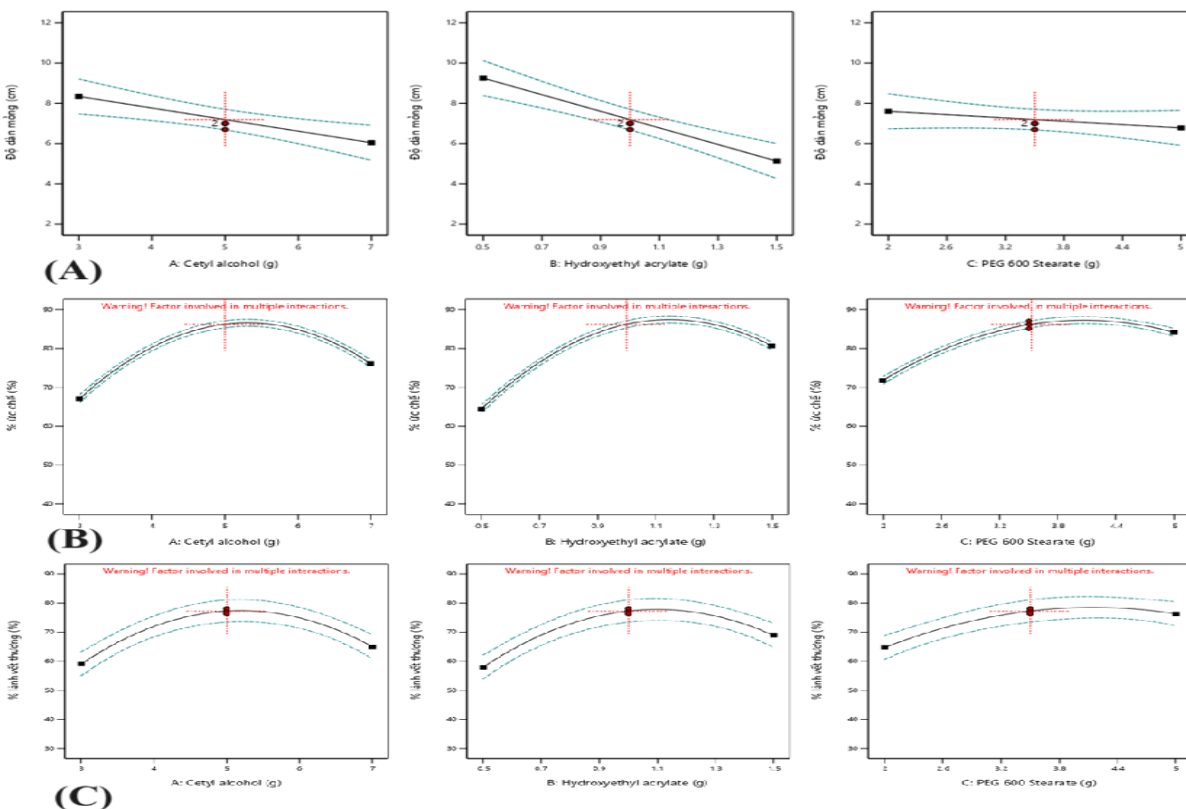
The wound healing rate of the test samples is influenced by all 3 excipients according to the first-order effect and a second-order effect, in which the two main influencing excipients according to the 1st order are hydroxyethyl acrylate and PEG 600 Stearate, while cyl alcohol affects the main effect according to order 2 (Figure 3C). With two excipients, hydroxyethyl acrylate and PEG 600 stearate, it has both a first-order effect and a second-order effect on the wound healing rate, meaning that increasing the concentration of the excipient has a positive effect on the wound healing rate, but if it is too high, it will make it difficult for essential oils and tamanu oil to disperse, leading to a decrease in wound healing rate.

The regression equation of the response is as follows:

$$\text{Wound healing (\%)} = -95.22 + 32.54a + 88.48b + 17.66c + 4.29ab - 3.80a^2 - 55.25b^2 - 2.99c^2$$

Note. a, b, c being the variables representing the factors cetyl alcohol, hydroxyethyl acrylate and PEG 600 stearate respectively.

The target function in this test is the thickness of the wound in the range of 6.5–7.5 cm, the highest ability to inhibit bacteria, the highest wound healing rate, and the concentration of excipients in the test portion. Predict the score of the software as follows: The concentration of cetyl alcohol is 5.47 g/100 g cream, hydroxyethyl acrylate is 0.98 g/100 g cream, and PEG 600 stearate is 3.94 g/100 g cream. With these optimal values, the thinness is 6.86 cm, the ability to inhibit bacteria is 87.32%, and the wound healing rate is 78.13%. This optimal prediction formula was evaluated by repeating it three times to obtain results with quite high accuracy. Thus, the model is highly compatible with the experiment.



**Figure 3.** Graph illustrating the influence of experimental factors on: (A) thinness ability; (B) bacterial inhibition; (C) wound healing rate



**Table 5.** Report the results of design experiments.

	Cream's thickness (cm)			Ability to inhibit bacteria (%)			Wound healing rate (%)		
	First times	Second times	Third times	First times	Second times	Third times	First times	Second times	Third times
<b>Experiment</b>	6.7	6.8	6.7	88.2	87.8	87.6	77.1	78.2	78.3
<b>Forecast</b>	6.86	6.86	6.86	87.32	87.32	87.32	78.13	78.13	78.13

After optimizing the concentration of the 3 excipients used, the recipe for tamanu cream is as follows:

**Table 6.** Table of preparation formula of Tamanu cream

	Ingredient	Weight (g/100 g)
1	Water	45
2	Glycerine	6
3	Hydroxyethyl acrylate	1
4	PEG - 600 stearate	3.95
5	Cetyl alcohol	5.45
6	Tamanu oil	28
7	Tea tree essential oil	1
8	Cajeput essential oil	9
9	1.2 - Hexanediol	0.6

Research on tamanu cream with ingredients such as tamanu oil, tea tree oil, and cajuput oil has highlighted the antibacterial and wound healing properties with high efficiency but has not yet demonstrated the full benefits of tamanu oil in the formula. There are many studies published worldwide on tamanu oil-related products with different effects.

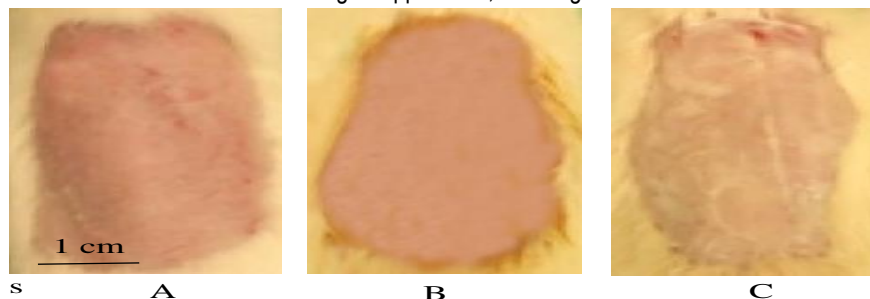
One of them is the research of Ilmaknun and Endriyatno (2024), a sunscreen product made from tamanu oil with different concentrations of stearic acid and triethanolamine. Tamanu oil has been identified for its sunscreen activity, reducing the intensity of ultraviolet (UV) radiation on the skin by absorbing UV rays. The tamanu oil cream was prepared using the melting and emulsification processes. Based on the physical test requirements and the highest SPF value, the best formula was determined to be Formula 2 with stearic acid and triethanolamine concentrations of 18%:2% (Ilmaknun & Endriyatno, 2024).

Besides, research on tamanu oil in cream form has the great advantage of being easy and frequent to use; the disadvantage is that it is not diverse, so research on other forms appears a lot. Typically the soap form in Pakdeechot and Kaewsichan (2020), research on a mixture of tamanu and coconut oil to make soap separates oil from raw tamanu kernels (*Calophyllum inophyllum* L.) with milk from fresh coconut (*Cocos nucifera* L.) to obtain a blend tamanu and coconut oil mix (TCO) of these substances. Soaps made from coconut oil (CO) were assessed, and a target TCO was investigated. The soap properties tested satisfied the Thai Community Product Standard of soap (TCPS 94-2546) and the Thai Industrial Standard TIS 29-2545 (Pakdeechot and Kaewsichan, 2020).

### 3.3. Acute toxicity and wound healing ability of tamanu cream on mice model

#### 3.3.1. Determining the acute toxicity of tamanu cream on white mice model

Tested on 2 mice with tamanu cream according to Appendix 2, OECD guidelines.



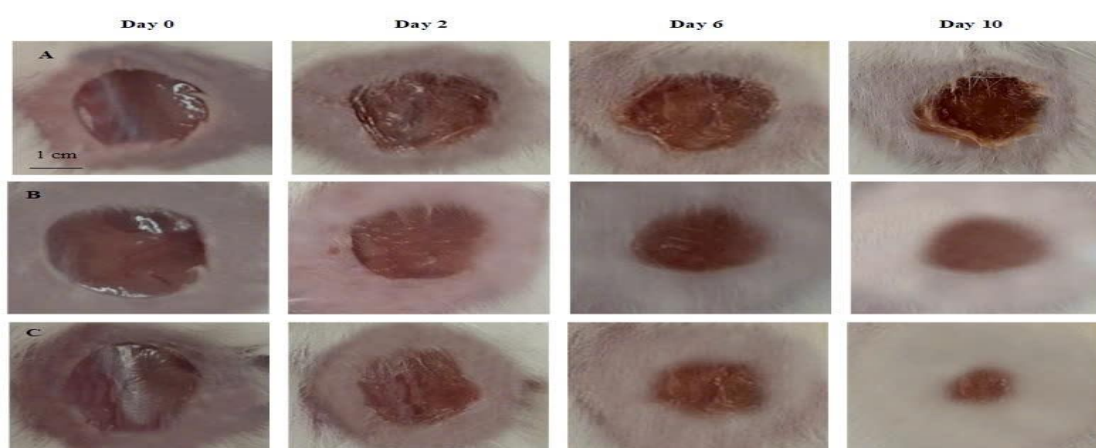
**Figure 4.** Acute toxicity test of tamanu cream on mice model after 24 hours. **A:** Control batch; **B:** Test batch 1000 mg/kg body weight; and **C:** Test batch 2000 mg/kg body weight

The test results showed that in both test batches, mice showed no abnormal signs on the skin, such as redness, dry skin, or rough skin, after 30 minutes as well as the first 24 hours. The mouse skin area was similar to the control batch. After 72 hours, mice in the test batches did not show any abnormal signs on the skin, fur, or eyes compared to the control batch. After 14 days of testing, mice gained weight normally, and there was no difference compared to the control batch; the activities and behaviors of the test mice were normal. After 7 days and 14 days of testing, the mice gained weight normally, and there was no difference compared to the control group; the activities and behaviors of the test mice were normal. Therefore, the acute skin toxicity dose of the tamanu cream is greater than 2000 mg/kg.

### 3.3.2. Evaluation of the wound healing ability of tamanu cream

The results showed that in the physiological groups and the experimental groups using placebo cream as well as the group of mice applying tamanu cream, the mice gained weight normally, and there was no statistically significant difference between the experimental groups.

Especially, the mice in the experimental group applying tamanu cream had a faster wound healing rate than the physiological group and the group using placebo cream. The wound closure rate on the 6<sup>th</sup> and 10<sup>th</sup> days was statistically significantly different from the physiological group, with the wound closure percentage 3.9 times faster than the physiological group and 1.5 times faster than the group using placebo cream.



**Figure 5.** Mice in experimental groups causing skin loss wounds on day 0 to day 10.

A: Physiological group; B: Experimental group using placebo cream;  
C: Experimental group using tamanu cream

Experimental group	% Wound closure		
	Day 2	Day 6	Day 10
Physiological group	7.03±1.43 <sup>a</sup>	9.40±2.80 <sup>c</sup>	20.08±1.91 <sup>c</sup>
Experimental group using placebo cream	10.62±3.23 <sup>a</sup>	28.61±2.93 <sup>b</sup>	51.91±2.05 <sup>b</sup>
Experimental group using tamanu cream	10.83±4.14 <sup>a</sup>	47.76±2.04 <sup>a</sup>	78.35±2.45 <sup>a</sup>

a. Statistically significant difference with the physiological group on day 6 and day 10 ( $p < 0.01$ )

b. Statistically significant difference with the placebo cream group on day 6 and day 10 ( $p < 0.01$ )

Thus, the results show that the use of tamanu cream has the effect of healing skin loss wounds faster due to the cell proliferation-stimulating effect of tamanu oil and the antibacterial ability of tea tree and cajeput essential oils.

Wound healing is an important physiological process important to preserve the integrity of the skin after trauma (Sorg et al., 2017). In this study, the beneficial effects of tamanu essential oil on the healing of cutaneous wounds were investigated in a rat model. The wound closure rate on the 6<sup>th</sup> and 10<sup>th</sup> days was 3.9 times faster than the physiological group and 1.5 times faster than the group using placebo cream.



Erdogan et al. (2021) investigated the wound-healing effect of tamanu oil on cutaneous wounds induced by rats. They came to the conclusion that tamanu oil sped up the formation of macrophages, granulation tissues, and fibrosis in rat wounds, which made the wounds less likely to contract. The results showed that wound contraction was significantly lower in the tamanu group compared with the other groups. Macrophages and mature granulation tissues were found in much higher amounts in the centella and tamanu groups compared to the control group. Fibrosis and collagen density were higher in the tamanu group than the other groups on day 7 (Erdogan et al., 2021).

Moreover, Krishnappa et al. (2024) investigated the formulation of tamanu oil bigels as an anti-scarring agent. They concluded that the study substantiates the wound-healing and scar reduction potential of tamanu oil bigels. The findings demonstrated that within 15 days of wound induction, the wounds healed and sealed completely, showing no signs of scarring (Krishnappa et al., 2024).

#### 4. Conclusions

Tamanu cream product was developed and optimized by combining tamanu oil, tea tree, and cajeput essential oils. This research team discovered that the most effective antibacterial properties were exhibited by tamanu oil concentrations of 26–28%, tea tree essential oils of 1% and 1.5%, and cajeput essential oil concentrations of 9% and 12%. The tamanu ointment formula contained 28%, 1%, and 9% of these oils, respectively. The antibacterial and wound healing properties of these essential oils were determined to be superior to those of tea tree and cajeput oils, as well as their acute toxicity. That acute skin toxicity dose for rodents was determined to be greater than 2000 mg/kg, and the concentration of excipients was optimized. This antibacterial and wound healing property of the tamanu cream was evaluated, thereby facilitating additional research on the advantageous pharmacological effects of products derived from the tamanu tree, particularly tamanu oil.

**Conflicts of interest.** The authors mentioned that none of them have a conflict of interest when it comes to this article.

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#### References

- Acha, E., Ahounou, Aikpe J.F., Adovelande, J., Assogba, M.F., Agossou, G. & Sezan, A. (2019). Anti-inflammatory properties of *Melaleuca quinquenervia* (Cav.) ST Blake Myrtaceae (Niaouli) leaves' essential oil. *International Journal of Current Research in Chemistry and Pharmaceutical Sciences*, 6(1), 30-40.
- Ansel, J.L., Lupo, E., Mijouin, L., Guillot, S., Butaud, J.F., Ho, R., ... & Pichon, C. (2016). Biological activity of polynesian *Calophyllum inophyllum* oil extract on human skin cells. *Planta medica*, 82(11/12), 961-966.
- Cañedo-Dorantes, L. & Cañedo-Ayala, M. (2019). Skin acute wound healing: a comprehensive review. *International Journal of Inflammation*, 2019(1), 3706315.
- Carson, C.F., Hammer, K.A. & Riley, T.V. (2006). *Melaleuca alternifolia* (tea tree) oil: A review of antimicrobial and other medicinal properties. *Clinical Microbiology Reviews*, 19(1), 50-62.
- Clinical and Laboratory Standards Institute (CLSI, 2023). *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 33rd Edition, M100-ed33.
- Erdogan, S.S., Gur, T.F., Terzi, N.K. & Dogan, B. (2021). Evaluation of the cutaneous wound healing potential of tamanu oil in wounds induced in rats. *Journal of Wound Care*, 30(Sup9a), Vi-Vx.
- Ferdosh, S. (2024). The Extraction of Bioactive Agents from *Calophyllum inophyllum* L., and Their Pharmacological Properties. *Scientia Pharmaceutica*, 92(1), 6.
- Flanagan, M. (2013). *Wound healing and skin integrity: principles and practice*. John Wiley & Sons.
- Harris-Tryon, T.A. & Grice, E.A. (2022). Microbiota and maintenance of skin barrier function. *Science*, 376(6596), 940-945.
- Hill, M.A. (2019). Skin and Integument. *In: Brüne, M. & Schiefenhövel, W. (eds), Oxford Handbook of Evolutionary Medicine*, Oxford University Press. P.300-356.

- Hua, O.H., Tran, Q.T.T., Trinh, D.T.T., Nguyen, V.D., Duong, D.P.N. & Nguyen, T.T. (2022). A review of traditional uses, phytochemistry and pharmacological properties of some Vietnamese wound-healing medicinal plants. *Natural Product Communications*, 17(4), 1934578X221088379.
- Ilmaknun, L. & Endriyatno, N.C. (2024). Formulasi dan penentuan nilai spf krim minyak tamanu (*Calophyllum inophyllum* L.) dengan variasi konsentrasi asam stearat dan trietanolamin. *Forte Journal*, 4(1), 122-133.
- Kampf, G., Ruselack, S., Eggerstedt, S., Nowak, N. & Bashir, M. (2013). Less and less-influence of volume on hand coverage and bactericidal efficacy in hand disinfection. *BMC Infectious Diseases*, 13, 1-7.
- Krishnappa, M., Abraham, S., Furtado, S.C., Krishnamurthy, S., Rifaya, A., Asiri, Y.I., ... & Pavadai, P. (2024). An integrated computational and experimental approach to formulate tamanu oil bigels as anti-scarring agent. *Pharmaceuticals*, 17(1), 102.
- Léguillier, T., Lecsö-Bornet, M., Lémus, C., Rousseau-Ralliard, D., Lebouvier, N., Hnawia, E., ... & Rat, P. (2015). The wound healing and antibacterial activity of five ethnomedical *Calophyllum inophyllum* oils: an alternative therapeutic strategy to treat infected wounds. *PLoS one*, 10(9), e0138602.
- Mansoor, K., Aburjai, T., Al-Mamoori, F. & Schmidt, M. (2023). Plants with cosmetic uses. *Phytotherapy Research*, 37(12), 5755-5768.
- Organisation for Economic Co-operation and Development (OECD, 2002). Test No. 420: Acute oral toxicity-fixed dose procedure. OECD Publishing.
- Pakdeechot, S. & Kaewsichan, L. (2020). Tamanu and coconut oil blends for soap making from extraction of tamanu kernel with coconut milk. *Engineering & Applied Science Research*, 47(4).
- Porusia, M. & Septiyana, D. (2021). Larvicidal activity of *Melaleuca leucadendra* leaves extract against *Aedes aegypti*. *Caspian Journal of Environmental Sciences*, 19(2), 277-285.
- Pribowo, A., Girish, J., Gustiananda, M., Nandhira, R.G. & Hartrianti, P. (2021). Potential of tamanu (*Calophyllum inophyllum*) oil for *Atopic dermatitis* Treatment. *Evidence-Based Complementary and Alternative Medicine*, 2021(1), 6332867.
- Sorg, H., Tilkorn, D.J., Hager, S., Hauser, J. & Mirastschijski, U. (2017). Skin wound healing: An update on the current knowledge and concepts. *European Surgical Research*, 58(1-2), 81-94.



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