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Formulation of Serum Using a Combination of Tamanu Oil and Tea Tree Oil as Antiacne

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ABSTRACT

Acne is a chronic inflammation of the skin caused by bacteria. Tamanu oil contains neoflavonoids and tea tree oil contains terpenes-4-ol, both of which have good antibacterial agents. The combination of Tamanu oil and tea tree oil will produce a preparation synergistic in inhibiting bacterial growth. This study was to determine the best formula for serum preparations with good characteristics and stability against bacteria without irritating the skin. Serum formulation in three different concentrations of Tamanu oil is 0.5%, 0.75%, and 1%, each combined with 2% tea tree oil. Then the characteristics test (organoleptic, homogeneity, viscosity, dispersibility, and pH), stability test (organoleptic, homogenous, and pH) using cyclic temperature stress testing, and antibacterial test against *Staphylococcus aureus* and *Propionibacterium acnes* using well-diffusion method and irritation test using Hen's egg test chorioallantoic membrane (HET-CAM) were carried out. The results showed that the overall viscosity, spreadability, and pH matched the specification, were stable, and had no irritation effect. Serum formulation containing Tamanu oil 1% and tea tree oil 2% is the best antibacterial activity which zones inhibition of 12.5 mm on *Propionibacterium acnes* and 11.6 mm on *Staphylococcus aureus*.

Keywords: Antiacne; Serum; Tamanu oil; Tea tree oil

INTRODUCTION

Acne (*Acne vulgaris*) is a pilosebaceous disorder. Bacterial activity and the connection between the two affect the formation of pimples. Bacteria that play a role in acne include *Propionibacterium acnes* and *Staphylococcus aureus*.[1] However, cases of resistance to the use of antibiotics such as erythromycin and clindamycin for topical treatment are increasing, is cause the use of herbal ingredients as an alternative to treat infections is of concern.[2,3]

Tea tree oil is an essential oil obtained from *Melaleuca alternifolia* leaves containing more than 80-90% monoterpenes, namely terpinene-4-ol, ϒ-cymene, α-terpinene, limonene 1,8-cineol, α-terpineol, terpinolene, 1, 8-cineol, sabinene, and α-pinene. These monoterpenes have broad-spectrum anti-microbial properties for the treatment of acne and are commonly used in a variety of topical preparations. Tea tree oil 2% lotion is effective at treating acne and is better than 5% zinc sulfate.[4]

Antimicrobial properties, against *Staphylococcus aureus* as much as 20 µL, the calophyllodine content has an inhibition zone of 16mm, inophyllum C is 10mm, and inophyllum E is 13 mm.[5] Another study found the antibacterial activity of Tamanu oil originating from various regions against *Staphylococcus aureus* with a Minimum Inhibitory Concentration (MIC) value of 0.01 to 0.1%, while for *Propionibacterium acnes* bacteria it had a MIC value of 0.01 to 0.025%.[6] It also contains omega-6 fatty acids such as linoleic acid, ϒ-linoleic acid,

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and arachidonic acid which have analgesic and anti-inflammatory activity.[7]

The combination of tea tree oil together with tamanu oil is expected to provide a synergistic effect as an antibacterial to treat acne cases. To facilitate their application, these two ingredients are formulated in the form of serum preparations. The serum is a cosmetic product that has a high concentration of active ingredients in its formulation to reach deeper layers of the skin and has a non-sticky texture that is suitable for the skin. The serum form was chosen because the serum is easily absorbed into the skin and has a high-water content so that it can hydrate the stratum corneum, besides that, it also does not make it look greasy so it is suitable for the treatment of acne-prone skin.[8]

The purpose of this study was to examine the characterization and stability of serum containing the active ingredients tea tree oil and tamanu oil, to prove its antibacterial activity against *Propionibacterium acnes* and *Staphylococcus aureus* and to test the irritating effect of the serum preparations made.

METHODS

The research design is laboratory experimental. The activity carried out was the manufacture of serum with the active ingredients tamanu oil (0.5%, 0.75%, and 1%) and 2% tea tree oil. The serum characteristics were tested which included organoleptic, homogeneity, viscosity, spreadability, and pH. After that, a stability test of the freeze–thaw cycling method was carried out with the test parameters being organoleptic, homogeneity, and pH. Antibacterial activity against *Staphylococcus aureus* and *Propionibacterium acnes* using the good diffusion method. Irritating effect using the Hen's egg test chorioallantoic membrane (HET-CAM) method.

Tools and materials

Tools

Analytical balance (Ohaus PA224), pH meter (Mettler Toledo), universal oven (Memmert UN 75), Brookfield-LVT viscometer, laminar airflow (Esco).

Material of serum

Tamanu oil (Happy green), Tea tree oil (Nusaroma), propylparaben (Golden Era), methylparaben (Golden Era), Carbomer 940 (Ashland), Tween 80 (Industrial Chimica Panzeri S.r.l.), Span 20 (Sigma-Aldrich), propylene glycol (DoW), butyl hydroxytoluene (Sigma-Aldrich), distilled water (Smart-lab).

Material of antibacterial test

Propionibacterium acnes, Staphylococcus aureus, Mueller Hinton Agar, Clindamycin gel 1%.

Material of irritation test

Hen's egg, Sodium laureth sulfate, NaCl 0,9%.

Production of serums

Carbomer 940 was developed in water and then added with Triethanolamine (TEA) until a serum base was formed. Prepared the oil phase (BHT, nipasol, tamanu oil, tea tree oil, and Span 20) and the water phase (Tween 80, propylene glycol and nipagin). The oil phase and the water phase are mixed until an emulsion is formed. The emulsion is then mixed with the serum base until it is homogeneous to obtain tamanu oil serum and tea tree oil. The serum for each formula was replicated 3 times. The composition of the Tea tree oil-Tamanu Oil serum can be seen in Table 1.

Evaluation

Serum characterization tests included organoleptic, homogeneity, viscosity, spreadability, and pH.

Organoleptic

The serum was observed for shape, color, texture, and aroma.

Homogeneity test

Observations were performed by smearing 1 g of the preparation on the object glass, after which covered with another glass object, and observing whether or not there were coarse grains visual whether or not there were lumps and coarse grains in the serum preparation.[8]

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Spreadability

A total of 1 g of a sample was placed in the middle of a glass plate with a size of 20cmx20cm and had scale paper placed underneath. The Sample has been given a piece of glass measuring 20x20 cm weighing approx 125 g. Left for 1 minute and then measured diameter was sample formed.[9]

pH

Before use, the pH meter was calibrated with a standard buffer solution. Put the test sample in a beaker, then the electrode is dipped in the sample, and observed the pH score on the screen.[10]

Stability Test

The method used for the stability test is freeze-thaw cycling with a temperature of 4°C and 40°C, each of which was stored for 24 hours for six cycles.[11] Parameters observed included organoleptic, homogeneity, and pH.

Antibacterial activity

In vitro antibacterial activity tests using the well method.[12] As a positive control, 1% clindamycin gel preparation was used, as a negative control is aqua dest

Irritation test

The irritation test used the HET-CAM (Hen's egg test chorioallantoic membrane) method using Leghorn chicken eggs fertilized and had been incubated/incubated for 9-10 days. The positive control used sodium lauryl sulfate (SLS), and the negative control used distilled water. Visual observations are exsanguination, coagulation, and lysis done out for 300 seconds/5 minutes. The Score is calculated by the formula below.[13]

$$T = \frac{300 - H}{300} \times 5 + \frac{301 - L}{300} \times 7 + \frac{301 - C}{300} \times 9$$

Note:
T: Irritation score H
H: Time to appear exsanguination (seconds)
L: Time for lysis to occur (seconds)
C: Time to onset of coagulation (seconds)

Table 1. Formulation of serum preparations combination of Tamanu oil and Tea tree oil

Ingredient	Use	Formula (% b/v)				
		K (-)	F0	F1	F2	F3
Tamanu oil	Active ingredient			0.5	0.75	1
Tea tree oil	Active ingredient		2	2	2	2
Carbomer	Gelling agent	0.5	0.5	0.5	0.5	0.5
TEA	Alkalizing agent	0.2	0.2	0.2	0.2	0.2
Tween 80	Emulsifying agent	2.6	2.6	2.6	2.6	2.6
Span 20	Emulsifying agent	2.4	2.4	2.4	2.4	2.4
Propylene glycol	Humectan	15	15	15	15	15
BHT	Antioxidant	0.1	0.1	0.1	0.1	0.1
Nipagin	Preservative	0.18	0.18	0.18	0.18	0.18
Nipasol	Preservative	0.02	0.02	0.02	0.02	0.02
Aqua dest	Solvent	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100

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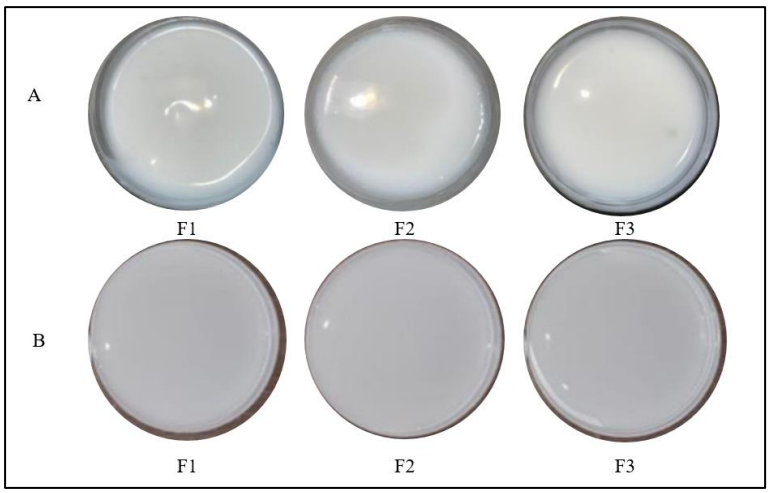

Figure 1. Serum combination of Tamanu oil 2% and Tea tree oil with levels of 0.5% (F1), 0.75% (F2), and 1% (F3) before (A) and after the stability test (B)

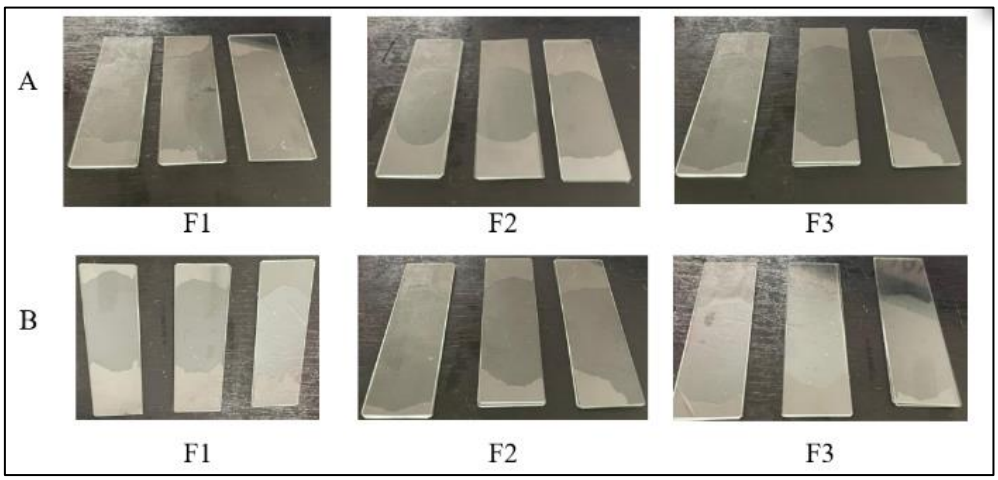

Figure 2. Homogeneity of combination serum Tamanu oil 2% and Tea tree oil with levels of 0.5% (F1), 0.75% (F2), and 1% (F3) before (A) and after stability test (B)

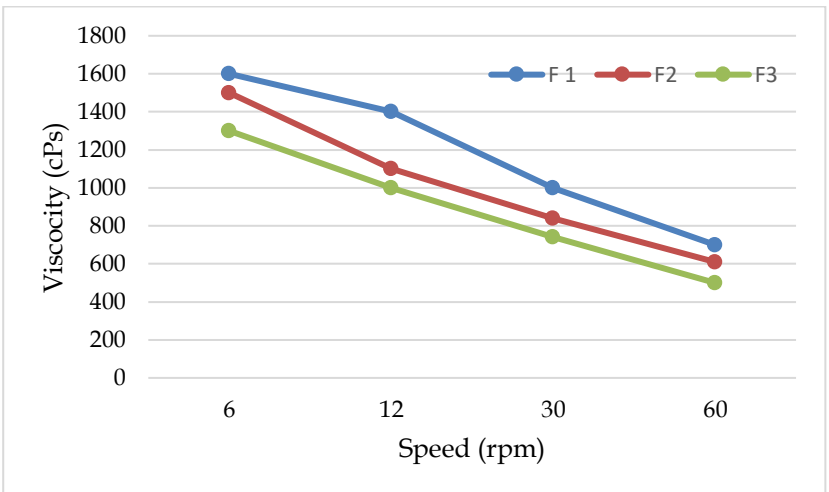

Figure 3. Flow properties of serum combination of Tea tree oil and Tamanu oil (F1: 0.5%, F2: 0.75% and, F3: 1%)

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Table 2. Characteristics of the combination serum Tea tree oil and Tamanu oil

Parameter		F1	F2	F3
Organoleptic	Before	white viscous liquid, aromatic, soft, and easy to apply		
	After	white viscous liquid, aromatic, soft, and easy to apply		
Homogeneity	Before	homogen	homogen	homogen
	After	homogen	homogen	homogen
Viscosity (cP)	Speed 6 rpm	1633±153	1467±58	1333±58
	Speed 12 rpm	1350±50	1150±50	1017±29
	Speed 30rpm	1007±31	840±40	773±31
	Speed 60 rpm	683±15	610±10	500±20
Spreadability (cm)		6.4±0.06	6.5±0.06	6.9±0.06
pH	Before	5.53 ± 0.06	5.40 ± 0.02	5.17 ± 0.05
	After	5.55 ± 0.03	5.36 ± 0.03	5.03 ± 0.06

Table 3. Antibacterial activity of serum combination of Tamanu oil and Tea tree oil

Sample	Inhibition Zone Diameter (mm)	
	Propionibacterium acnes	*Staphypococcus aureus*
F0	7.9 ± 0.6^{a}	$9.4 \pm 0.2^{*}$
F1	10.7 ± 0.6^{b}	$10.1 \pm 0.3^{*,**}$
F2	$11.7 \pm 0.4^{b,c}$	$11.1 \pm 0.7^{**,***}$
F3	12.5 ± 0.3^{c}	$11.6 \pm 0.6^{***}$
K+	16.3 ± 0.5^{d}	$15.8 \pm 0.2^{****}$
K-	0	0

Different notations indicate there are significant differences (Oneway Anova; p<0.05)

Table 4. Serum irritation score of the combination of Tamanu Oil and Tea Tree Oil using the HET-CAM method

Groups	Hemorrhage (second)	Coagulation (second)	Lysis (second)	Irritation category
K (+) (SLS)	17.07	17.56	17.86	Severely irritative
K (-) (Aquadest)	0	0	0	Nonirritant
F0	0	0	0	Nonirritant
F1	0	0	0	Nonirritant
F2	0	0	0	Nonirritant
F3	0	0	0	Nonirritant

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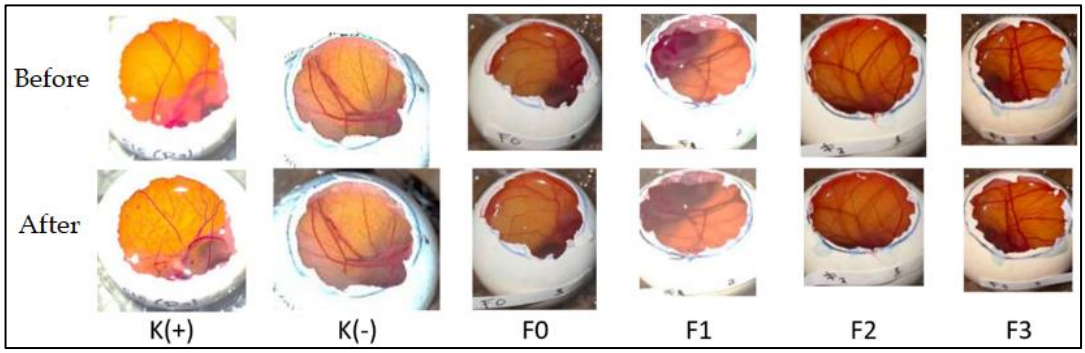

Figure 4. Effect of serum combination of Tree tea oil and Tamanu oil on HET-CAM
Note: K (+) 2% SLS solution, K (-) aquadest, F0:0%, F1:0.5 %, F2:0.75%, F3:1%

RESULT AND DISCUSSION

Organoleptic

Tamanu oil serum and tea tree oil are viscous white liquids with a smooth/soft and aromatic texture. Visuall level of serum concentration is proportional to the increase in tamanu oil levels (Figure 1).

Homogeneity

Serum Tamanu oil and Tea tree oil have good homogeneity. The sample was placed between the object glasses, and no lumps were found (Figure 2).

Viscosity

Measurement viscosity and flow properties with a Brookfield Viscometer using spindle number 63 at speeds of 6, 12, 30, 60 rpm. The results of measuring the viscosity of the serum can has seen in Table 2. In general, it can show that the viscosity of the serum tends to decrease with increasing levels of Tamanu oil (Oneway Anova; $p<0.05$).

Flow properties

As shown in Figure 3, the viscosity of the serum preparations, both F1, F2, and F3, decreased with increasing stirring speed. These results are under most of the flow properties of cosmetics in the form of emulsions or suspensions, namely with the shear thinning type of flow, meaning that the viscosity decreases as the shear rate increases. This character is also referred to as pseudoplastic and is the result of structural damage in the fluid.[14] Flow property is an important parameter in topical preparations because it has related to the ease of pouring from the package.

Spreadability

The criterion for good spreading power is around 5-7 cm. In Table 2 can be seen that F3 has a wider spreading power than F2, and F2 has a wider spreading power than F1 (Oneway Anova; $p<0.05$). All on the range of 5-7cm, so they can be categorized as having good spreading power. The spreadability area of serum is inversely proportional to its viscosity. The lower the viscosity, the wider the resulting spreading of power.

pH

The skin has a pH of 4.1-5.8,[15] and the pH for topical pharmaceutical preparations including cosmetics is 4-6.[16] The pH of serum with the increasing tamanu oil content causes the pH of the serum to decrease (Table 2), even though everything is still safe for the skin.

Stability

The parameters observed/measured after the stability test carried out using the freeze-thaw cycling method were organoleptic, homogeneity, and pH. The organoleptic serum F1, F2, and F3 did not differ from the form before the stability test was carried out, namely in the form of a thick, aromatic white liquid, which remained homogeneous and did not separate (Figure 1 and Figure 2). As shown in Table 2, the pH values in F1 and F2 both before and after the stability test were not significantly different except for F3 where after the stability test pH value decreased

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(Paired Sample t-Test; $p<0.05$). Even so, all pHs are still within the pH range is suitable for application to the skin, namely 4.5-8.6.[16] This can be stated that serum F1, F2, and F3, all remained stable after stability tests carried out.

Antibacterial activity

As shown in Table 3, the results of the antibacterial activity test against Propionibacterium acnes, F1's inhibition zone was wider than F0 but not significantly different from F2, and F2 was not significantly different from F3, but F3 had a wider inhibition zone than F1. Furthermore, for Staphylococcus aureus the results of measuring the diameter of the F1 zone were not significantly different from F0 and not different from F2, but F2 was wider than F0; F2 and F3 are not significantly different, but F3 is wider than F1. In all bacteria, when compared with K+, all inhibition zones of the serum formula were still lower (Oneway-Anova, $p<0.05$).

The inhibition zone category to Davis & Stout consists of 4 namely weak if the diameter is ≤ 5 mm, moderate in the range of 6-10 mm in diameter, strong in the range of 11-20 mm in diameter, and very strong if the diameter is ≥21 mm.[17] So based on the criteria for assessing the inhibition zone above, it stated that the antibacterial inhibition of the serum combination of Tamanu oil and tea tree oil is included in the moderate to the strong group, so this serum preparation is effective in inhibiting the growth of *Propionibacterium acnes* and *Staphylococcus aureus* bacteria as anti-acne drugs. These results prove that an increase in tamanu oil levels affects the ability of serum as an antibacterial. Compounds such as inophyllum C, inophyllum E, canalolide, and tamanolide in tamanu oil have antibacterial properties when tea tree oil contains compounds such as monoterpenes, sesquiterpenes and compounds belonging to the alcohol class also have antibacterial activity.[18] A potent antibacterial, it can even overcome resistant *Staphylococcus aureus* bacteria.[19]

Irritating effect

The results of the irritation test can show in Figure 4. Based on the scores obtained, the results of the irritation test with the HET-CAM method were categorized into 4, namely non-irritating (<0.9), weak irritation (1.0 - 4.9), moderate irritation (5.0 – 8.9), and strong irritation (9.0 – 21).[20] The results of the irritation test obtained from testing using the HET-CAM method on the three serum formulations including the serum base showed the irritation score of the preparation was 0, so the serum formula included in the non-irritating criteria (Table 4).

The serum formula was made of a 2% tea tree oil content. This concentration is in accordance with the provisions issued by the SCCP European Committee and Cosmetic Ingredient Safety, which are still within safe limits, where concentrations that indicate irritation according to SCPP are from 5% tea tree oil concentration.[21,22] The results of the serum formulation show that it has no irritating effect, so this serum is safe to apply to the skin. Tea tree oil itself has an anti-inflammatory effect, and the content of calophyllolide in Tamanu oil also has anti-inflammatory properties, which are also important in acne therapy.[23,24]

CONCLUSION

The combination of Tamanu oil and Tea tree oil in all formulas has good characteristics and stability. All the formulas show antibacterial activity against *Propionibacterium acnes* and *Staphylococcus aureus* maximum result being the serum containing the highest tamanu oil. All serum formulas do not have an irritating effect, so they are safe to use.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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