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RESEARCH ARTICLE

Development of Cinnamon bark oil (*Cinnamomum burmannii*) as an anti-acne nanoemulgel and its effectiveness against *Propionibacterium acnes*

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Abstract

Background: Acne is caused by blockage of hair follicles and skin pores due to excess sebum production on the skin. Commonly used anti-acne include typical antibiotic creams or gels of clindamycin, tetracycline, and erythromycin. The use of these drugs often causes dry skin, redness, itching, and resistance to bacteria. The cinnamon bark oil, which contains cinnamaldehyde, has been studied for antibacterial activity. **Objective:** To determine the best formula of Cinnamon bark oil nanoemulgel with good physical quality and the highest antibacterial activity against *P. acnes*. **Method:** Cinnamon bark oil was formulated as a nanoemulsion and mixed with Carbopol, a gelling agent. Nanoemulgels were produced and evaluated through organoleptic tests, pH, viscosity, antibacterial activity, and stability testing. **Result:** The results showed that the particle size, zeta potential, and % transmittance of the cinnamon bark oil emulsion were accurate for an ideal nanoemulsion. All three formulas produced a light yellow, transparent colour, had a thin and mild gel consistency, and cinnamon bark oil scent, and fulfilled the requirements of the best formula of Cinnamon bark oil nanoemulgel that had good physical quality and the highest antibacterial activity against *P.acnes*. **Conclusion:** The best formula that had antibacterial activity for *P. acnes* was Formula 3.

Introduction

Acne vulgaris is a chronic inflammatory disease of the sebaceous follicles, caused by increased sebum secretion and blockage of the follicles (Well, 2014). Acne has clinical presentations such as comedones, papules, and pustules (William *et al*., 2012). Factors that influence the occurrence of acne vulgaris include genetic, endocrine, psychological, seasonal, stress, food, activity of the sebaceous glands, bacterial infections, cosmetics, and other chemicals (Meilina & Hassanah, 2018).

Antibiotics such as clindamycin, tetracycline, and erythromycin are effective ways to treat acne (Meilina & Hassanah, 2018). However, inappropriate use of antibiotics can cause side effects such as dry skin, redness, itching, and resistance to bacteria. Hence, there is a need for alternative therapy from other sources, such as plants with high antibacterial potential.

Using natural ingredients is a safer alternative to treating acne. One natural ingredient that has antibacterial activity is cinnamon bark oil. Cinnamon bark oil contains 61.53% cinnamaldehyde and has antibacterial activity with an inhibitory diameter value of 18.773 ± 0.574 mm at a concentration of 0.1% (Aqmarina *et al.*, 2016).

However, essential oils have volatile properties. They can evaporate greatly without a carrier and provide an oily feeling, which may be uncomfortable for the user. The nanoemulgel dosage form can increase the ability of compound particles to penetrate the skin membrane. The diffusion barrier of the stratum corneum can be reduced by surfactants in the formulation, leading to high penetration of cosmetics. Nano-sized droplets dispersed in the continuous phase

of the nanoemulsion can move smoothly through the stratum corneum and distribute the active ingredients through the skin barrier (Boonme, 2009). The gel form has controlled release and good bioavailability (Jivani *et al*., 2018), is easy to apply to the skin, has a water content that can cool and moisturise the skin, and easily penetrates the skin (Sukartiningsih *et al*., 2019). Therefore, this study aimed to determine the antibacterial activity of cinnamon bark oil nanoemulgel and to determine its inhibitory power against *Propionibacterium acne*.

Methods

Preparation of cinnamon bark oil Nanoemulsion

Nanoemulsion was made by mixing tween 80 and distilled water at a speed of 300 rpm for ten minutes, then cinnamon oil was added and stirred for ten minutes. Propylene glycol and alcohol were added and stirred for 30 minutes, then left for 24 hours. Next, the carbopol base that had been developed in distilled water was added to the nanoemulsion at a ratio of 30:70.

Evaluation of cinnamon bark oil nanoemulsion

Percentage transmittance (%) of nanoemulsion

A 1 mL sample was dissolved in a 100 mL measuring flask using distilled water. The per cent transmittance of the solution was measured at a wavelength of 650 nm using UV-Vis spectrophotometry. Distilled water was used as a blank during testing (Pratiwi *et al*., 2016).

Analysis of particle size of cinnamon bark oil nanoemulsion

Particle size analysis was carried out using a particle size analyser (Horiba Scientific, Nanoparticle Analyzer SZ-100). Particle size analysis was carried out to determine the particle size, polydispersity index (PI), and zeta potential of the cinnamon bark oil nanoemulsion. The purpose of particle size analysis was to determine the size of the globules formed in the nanoemulsion.

Preparation of the cinnamon bark oil Nanoemulgel

A gel base was made by dispersing carbopol in water until homogeneous, then TEA was added until a gel base was formed. The nanoemulsion was added to the carbopol gel base and stirred until homogeneous.

Evaluation of cinnamon bark oil nanoemulgel

Organoleptic test

An organoleptic test was conducted by observing the cinnamon bark oil nanoemulgel texture, scent, and colour.

pH measurement

Exactly 10 mL of the nanoemulgel was put into a glass beaker. Then, the electrode tip was dipped to measure the pH value.

Viscosity

The viscosity of the cinnamon bark oil nanoemulgel was evaluated using a viscometer Rion VT-04F.

Stability testing

Stability testing was carried out using the Freeze-Thaw method for four cycles. Each cycle consists of storing the nanoemulgel at 4°C for 24 hours and then at room temperature for the next 24 hours (one cycle). Observations were made on organoleptic and pH values (Amna, 2020).

Antibacterial activity test

The nanoemulgel antibacterial activity test was carried out using the agar well diffusion method. Clindamycin was used as the positive control, and the negative control was nanoemulgel without cinnamon oil. Exactly 100 µL of a bacterial suspension, according to McFarland standards, was smeared onto Muller Hinton Agar (MHA) plate until it was evenly distributed. Wells were bored for F1, F2, F3, and the controls. The samples and controls were added to the wells as much as 100 µL and incubated for 24 hours at 37°C. Observations were made, and the diameter of the clear zones was measured using a calliper.

Results

The cinnamon bark oil nanoemulsion formula

The compositions of the three formulas (F1, F2, F3) are shown in Table I.

Table I: Cinnamon bark oil nanoemulsion formula

Composition	Formula		
	1	2	3
Cinnamon bark oil	1	3	5
Tween 80	35	35	35
Propylene glycol	5	5	5
Alcohol 96%	15	15	15
Methyl paraben	0.02	0.02	0.02
Propyl paraben	0.18	0.18	0.18
Butyl hydroxy toluene	0.1	0.1	0.1
Aquadest	13.7	11.7	9.7

A PSA Horiba Scientific observed the testing of per cent transmittance (%T), particle size, polydispersity index (PI), and zeta potential (ZP) of cinnamon bark oil nanoemulsion (Table II).

Table II: The characteristic of cinnamon bark oil nanoemulsion

Formula	% T	Particle size (nm)	P I	Z P
F1	99.67± 0.15	9.6	0.245	-33.0
F2	99.85 ± 0.04	11.4	0.139	-27.9
F3	99.73 ± 0.15	12.7	0.110	-19.9

The nanoemulgel (Figure 1) was a pale yellow gel with a thin texture and a cinnamon bark oil scent. Table III shows the physical quality evaluation of the nanoemulgel preparations.

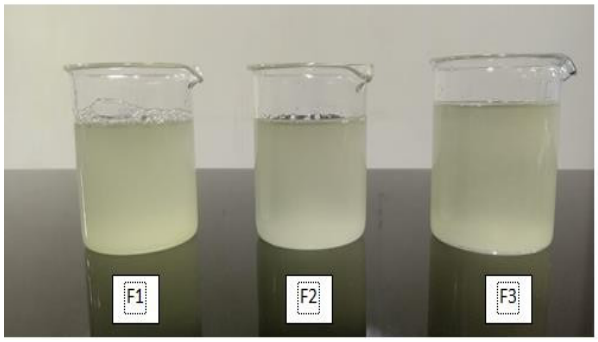

Figure 1: Cinnamon bark oil nanoemulgel

Table III: The pH value and viscosity of the cinnamon oil bark nanoemulgel

Formula	pH	Viscosity (dPas)
F1	6.20 ± 0.01	80.00 ± 0.00
F2	6.27 ± 0.01	60.00 ± 0.00
F3	6.22 ± 0.00	33.33 ± 2.89

The nanoemulgel stability test found that the nanoemulgel preparation did not experience changes in the colour, aroma, and texture of the nanoemulgel during storage. The results of the pH and viscosity test of the cinnamon bark oil nanoemulgel preparations during storage are shown in Table IV.

Table IV: Results of pH test of cinnamon bark oil nanoemulgel during storage

Formula	pH	Viscosity (dPas)
F1	5.56 ± 0.05	85.67 ± 1.15
F2	5.62 ± 0.07	71.17 ± 1.04
F3	5.65 ± 0.14	44.47 ± 0.05

The results of the antibacterial activity of the nanoemulgel against *Propionibacterium-acne* Figure 2 shows the preparation's inhibitory diameter against P. acne; Table V provides data on this.

Tabel V: Diameter of nanoemulgel inhibitory power against the growth of *P. acne*

Formula	Mean ± SD (cm)	Category
Negative control	0 ± 0	-
F1	0.87 ± 0.03	Moderate
F2	1.32 ± 0.04	Strong
F3	2.03 ± 0.06	Very strong
Positive control	3.84 ± 0.02	Very strong

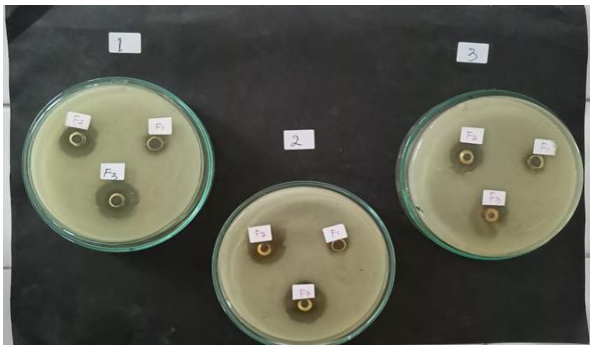

Figure 2: Nanoemulgel inhibition on the growth of *P. acne*

Discussion

In Table II, it was found that all formulas met the requirements for the percentage transmittance range. A formulation that has a percentage transmittance of 90%-100% indicates that the formulation has a clear and transparent visual appearance (Costa *et al*., 2012).

The nanoemulgel particle size in all formulas fell between 9.6-12.7 nm, which fulfils the requirement of an ideal nanoemulsion particle size of 1-100 nm (Singh *et al*., 2012). According to this study, the formula with the best zeta potential was F1 because it had a zeta potential, namely -33, which means stable. In contrast, F2 and F3 had a zeta potential value above -30, which means short-term stability (Honary, 2013). In this study, increasing the concentration of cinnamon bark oil affects the physical properties of the nanoemulgel, namely providing a distinctive scent, reducing viscosity, and increasing the activity of inhibiting the growth of *P. acne*, but does not affect the pH of these nanoemulgels.

The stability test showed that the pH value of the nanoemulgel decreased during storage. Changes in the pH value of gel-based preparations that use carbopol can be caused by the chemical reaction of the carboxylate group in carbopol with water to form H_3O^+, which is acidic (Sativa *et al*., 2014). Therefore, the pH value of the nanoemulgel decreased.

Differences in viscosity after freeze-thawing can occur due to the influence of storage temperature or hot temperature conditions during testing, which can affect the water content of the preparation, thereby affecting its viscosity (Malaka *et al*., 2021). However, before and after the test, the three formulas still had viscosity values that were within the gel viscosity requirements, which, according to Sanaji and colleagues (2019), the viscosity requirements for a good semisolid preparation are 4,000 - 40,000 cPs.

Based on the results of the antibacterial activity test, increasing the concentration of cinnamon bark oil could increase the inhibition of the growth of *P. acnes*. The positive control used was clindamycin. The nanoemulgel in formula F3 produced an inhibition zone with the broadest diameter among all the formulas and was included in the "*very strong*" category, like the positive control (Datta *et al.,* 2019).

The strong antibacterial activity of F3 was caused by the high concentration of cinnamon bark oil (5%), so its cinnamaldehyde content was also greater. The antibacterial activity of cinnamaldehyde can occur because it works by damaging the cell homeostasis process through its action on the cell membrane. Cinnamaldehyde also has a secondary effect in its action by inhibiting bacterial DNA synthesis (Pereira *et al*., 2021).

Conclusion

In this study, the cinnamon oil nanoemulgel produced a distinctive aroma and good viscosity, met the skin pH requirement, and inhibited the growth of *Propionibacterium acne*. Three distinct formulas (F1, F2 and F3) with varied concentrations were produced. The antibacterial activity of cinnamon oil nanoemulgel was highest in Formula 3, which contained 5% cinnamon bark oil, which had a zone of inhibition of 2.03 ± 0.06 cm and was classified as very strong.

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