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Research Article

Antibacterial Effect of Cinnamon and Citronella Oils Combination Against Acne-Related Bacteria

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Abstract

Acne vulgaris is a dermatological disease whose pathogenesis is due to high sebum secretion, hyperkeratinization, hormonal changes, or bacterial infections. *Staphylococcus epidermidis* and *Staphylococcus aureus* are bacteria that can induce inflammation in acne. *Cinnamomum burmannii* and *Cymbopogon nardus* essential oils have been reported to have antibacterial activity against *S. epidermidis* and *S. aureus*. This study aimed to obtain the type of interaction of a combination of *C. burmannii* and *C. nardus* oils in inhibiting bacteria associated with acne. Essential oil components were identified using gas chromatography-mass spectrometry (GCMS). Optimize the combination of *C. burmannii* and *C. nardus* oils using the checkerboard method. Furthermore, the Fractional Inhibitory Concentration Index (FICI) value is calculated to determine the effect of a combination that is synergistic, additive, not different or antagonistic. The main components of *C. burmannii* oil identified are cinnamaldehyde, eucalyptol, cinnamyl acetate, α-limonene, and α-terpineol. While *C. nardus* oil contains the five largest components: geraniol, citronellal, citronellol, citral, and geranyl acetate. *Cinnamomum burmannii* oil yielded 0.28%, with a refractive index of 1.5237. Meanwhile, the yield of *C. nardus* oil was 0.26%, with a refractive index of 1.4667. The combination of both oils yielded a FICI value of 1.5. The conclusion of this study shows that the combination of the two essential oils produces an indifferent effect against both *S. epidermidis* and *S. aureus*.

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INTRODUCTION

Recently, the development of skin care products using essential oils has gained popularity. Developing these compounds for use in skin care products is desirable to keep the skin young, healthy, and fresh and protect itself from environmental pollution. Some of their pharmacological activities, such as antibacterial, antioxidant, and anti-inflammation, can be utilized this way[1]. The stratum corneum is protected by the lipophilic qualities of essential oils, which have distinct positive values[2]. These features can also help maintain the skin microbiota, which is necessary for skin health. Topical application of essential oils, including possible incorporation into anti-acne products, can influence the normal function of skin cells[3]. They could also add antibacterial, anti-inflammatory, and antioxidant characteristics to formulas that could help skin prone to acne.

One of the most often used applications of essential oils in skin care is to limit acne outbreaks by using essential oil activities to inhibit the growth of bacteria-related pimples[4]. One of the species of bacteria implicated in the etiology of acne is *Staphylococcus* sp.[5]. Citronella (*Cymbopogon nardus*) and cinnamon (*Cinnamomum burmannii*) oils are extensively researched for their antibacterial, antioxidant, and anti-inflammatory properties. This essential oil is produced by common and reasonably easy plants to grow in Indonesia. The essential oil products are also readily available on the market, making them accessible.

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Cinnamomum burmannii oil is isolated from the bark of the genus Cinnamomum, with cinnamaldehyde as its main component (60–90%)[6]. Generally, *C. burmannii* oil is isolated from *C. burmannii* in Southeast Asia, including Indonesia. This oil is reported to have greater antibacterial activity against Gram-positive than Gram-negative bacteria. *Cinnamomum burmannii* oil has a minimum inhibitory concentration (MIC) value of 5-10 mg/mL against *Staphylococcus epidermidis* and 1 mg/mL against *Staphylococcus aureus*[6,7]. The mode of antibacterial action of *C. burmannii* oil has been reported through changes in membrane permeability and integrity[7]. In addition, *C. burmannii* oil can release and eradicate existing biofilms[8]. *Cinnamomum burmannii* oil's antibacterial effect is thought to work by altering the integrity and permeability of membranes. Several protein markers involved in tissue inflammation and inflammation can be inhibited by *C. burmannii* oil[9]. The cinnamaldehyde may contribute to the acne reduction that skin problems require[10]. Traditionally, people have used *C. burmannii* to cure skin conditions[11].

Cymbopogon nardus essential oil's ability to fight *S. aureus*, its potent antioxidant properties, and its capacity to reduce the 5-lipoxygenase enzyme activity increase the inflammatory response that leads to the development of acne[12]. According to Mahant *et al.*[13], topical use of *C. nardus* oil demonstrates excellent potential for minimizing the impacts of acne. *Cymbopogon nardus* oil is isolated from *C. nardus*, an annual herb that thrives in Indonesia and other Southeast Asia countries[14]. The major constituent in this oil was reported in various percentages. *Cymbopogon nardus* oil had antibacterial activity, with MIC of *C. nardus* oil against *S. aureus* of 2.0 µL/mL and *Propionibacterium acnes* of 0.005-0.3 µL/mL[15]. In addition, *C. nardus* essential oil has the activity to inhibit methicillin-resistant *Staphylococcus aureus in vitro*[16]. *Cymbopogon nardus* oil has lower IC_{50} antioxidant activity (2 µL/mL) than vitamin C (7.9 µL/mL). Using the 5-lipoxygenase inhibition test, *C. nardus* oil was found to have anti-inflammatory properties, with an IC_{50} value of 0.15 µL/mL[15].

According to several studies, combining essential oils improves their antibacterial, antioxidative, and anti-inflammatory benefits[17]. When examined in combination, certain essential oils have been proven to have high medicinal potential in earlier research[18-20]. However, there is still a dearth of information regarding the antibacterial effectiveness of the combined essential oils. This research was intended to investigate the interaction of *C. burmannii* and *C. nardus* oils in combination to inhibit *S. epidermidis* and *S. aureus*.

MATERIALS AND METHODS

Materials

The samples (**Figure 1**) used were stem of *C. nardus* (L.) Rendle) and bark of *C. burmannii* (Nees & T.Nees) Blume, both obtained from Beringharjo Market, Yogyakarta, Indonesia. The identification of both samples was confirmed by the Faculty of Applied Sciences and Technology, Universitas Ahmad Dahlan, Yogyakarta, Indonesia. The voucher specimens of *C. burmannii* bark (BF-LAU001) and *C. nardus* stem (BF-POA001) were kept in our Laboratory. The microorganisms used were *S. aureus* ATCC 25293 and *S. epidermidis* ATCC 12228. The bacterial growth medium used were Mueller Hinton broth (Himedia) and Mueller Hinton Agar (Himedia). The instruments used were an Abbe refractometer (Atago), GC-MS (QP2010S Shimadzu), biosafety cabinet (Monmouth), micropipette (Socorex Acura), autoclave (Shenan), incubator (Binder), oven (Binder), and 96-microwell plates (Labselect).

a **b**

Figure 1. (**a**) Bark of *C. burmannii* and (**b**) stem of *C. nardus*.

Methods

Isolation and identification of essential oils

Steam and water distillation techniques were used to separate the essential oils. The sample was distillated for 6 to 8 hours using about 2 kg. The essential oil was removed from the aqueous phase using a separatory flask. After that, the oil phase was separated and gathered. When not used, essential oils were kept in a light-protected bottle at 4°C. The yield of the oils obtained was calculated. Organoleptic examination of essential oils included visual observation of the color, odor, and flavor of the oils. An Abbe refractometer (Atago) was used to measure the refractive index of the oils.

Identification of essential oil components using GC-MS

The essential oil components were identified using GC-MS (QP2010S Shimadzu) with a stationary phase in the form of an Rtx-5 column with a length of 30 m, an ID of 0.25 mm, and a film thickness of 0.25 mm. Helium was employed as the carrier gas; the column's temperature was 50°C; injection temperature: 300°C; pressure-based flow control mode: 24.7 kPa; total flow: 90.6 mL/minute; column flow: 0.66 mL/minute; linear velocity: 29.5 cm/second; and split ratio: 129.9. Mass spectra detected by the ionization method: electron impact (70 Ev), time from 5.20 to 60 minutes, starting from m/z 20 and ending at m/z 600. By matching the mass spectra profile of the sample with those from the Wiley Library, the chemical components were identified.

Inoculum preparation

From a 24-hour culture, a bacterial colony was taken and suspended in a 0.9% saline solution. The turbidity was adjusted to 0.5 McFarland at that point. The bacterial suspension was then diluted until its density was 10^6 CFU/mL.

Minimum inhbitory concentration determination

The MIC determination of essential oils was carried out using microbroth dilution[18]. Serial concentrations of the essential oils at 0.03, 0.06, 0.12, 0.25, 0.5, 1, 2, and 4 mg/mL were applied. Then, they were added to the bacterial suspension so that the final density was 1-5 x 10^5 CFU/mL. The MIC was measured after an 18 to 24 hours incubation period at 36°C. The MIC determination was based on the smallest concentration that can inhibit bacteria (no turbidity).

Checkerboard method

Using the checkerboard method, *C. burmannii* and *C. nardus* oils were tested for their antibacterial effects[21]. Each oil was made in a series of concentrations, combined, and mixed with a bacterial suspension. The cells were then incubated at 37°C for 24 hours. MIC was obtained from the smallest concentration that can inhibit bacteria, as marked by no turbidity. The MIC determination was also confirmed by adding 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). Furthermore, the sum of FIC substances A and B generated the fractional inhibitory concentration index (FICI), as shown in **Equation 1**. FICI interpretation of the combination of two compounds was based on the following categories: FICI ≤ 0.5 is synergistic; 0.5 < FICI ≤ 1 is additive; 1 < FICI ≤ 4 is indifferent; FICI > 4.0 is an antagonistic effect[22].

$$FICI = \frac{MIC\ substance\ A\ in\ combination}{MIC\ substance\ A} + \frac{MIC\ substance\ B\ in\ combination}{MIC\ substance\ B} \quad [1]$$

Data analysis

The yield and refractive index data were expressed using the mean and standard deviation. Three replications of the antibacterial data were created.

RESULTS AND DISCUSSION

The color of the *C. burmannii* oil produced by steam and water distillation was light yellow or pale yellow (**Figure 2**). The yield produced in this study was 0.28%. This yield is smaller when compared to previous studies, which produced yields ranging from 0.36 to 0.86%[18,23]. The refractive index of *C. burmannii* bark obtained is 1.52375, less than from Indonesia's Lombok Island, which is 1.5627[23]. On the other hand, the *C. nardus* oil was brownish yellow with a yield of 0.26 and a refractive index of 1.4667 (**Table I**). This index value aligned with the *C. nardus* oil obtained from Jember, Java Island, Indonesia[24].

a **b**

Figure 2. (**a**) *Cinnamomum burmannii* and (**b**) *C. nardus oils obtained with steam and water distillation.*

Table I. Characteristics of *C. burmannii* and *C. nardus* oils.

Oil	Color	Odor	Flavor	Yield (% v/w)	Refractive index
Cinnamomum burmannii	Pale yellow	Distinctive smell	A bit sweet and spicy	0.28 ± 0.08	1.5238 ± 0.01
Cymbopogon nardus	Brownish yellow	Fresh aromatics	Bitterness	0.26 ± 0.01	1.4667 ± 0.00

Cinnamomum burmannii oil separated by gas chromatography yielded 23 components that can be identified by mass spectrometry (**Table II**). The five main components identified were cinnamaldehyde (24.14%), eucalyptol (14.09%), cinnamic (13.76%), α-limonene (9.73%), and α-terpineol (8.19%). According to earlier research, trans-cinnamaldehyde is abundant (46.31%) in *C. burmannii* bark oil[23]. Cinnamaldehyde was reported to have antimicrobial effects[9]. Unsaturated carbonyl groups in the cinnamaldehyde molecule have been demonstrated to be crucial for this advantageous effect. It has been previously documented how *C. burmannii* oil kills bacteria by modifying lipid levels, rupturing cellular membranes, blocking mobility, cell proliferation, transmembrane porin, ATPase, and inhibiting biofilm formation. It also has anti-quorum sensing properties[18,25,26].

Table II. Identification of *C. burmannii* oil components using GC-MS.

Peak No	RT (minute)	% Relative	Components
1	9.325	7.01	α–ocimene
2	9.832	2.76	α–humulene
3	10.391	1.62	Benzaldehyde
4	10.86	2.3	β–myrcene
5	11.423	0.41	Trans-geraniol
6	12.326	0.22	Allo-ocimene
7	12.833	9.73	Limonene
8	12.975	14.09	Eucalyptol
9	13.855	0.4	γ–terpinene
10	14.89	0.39	α–terpinolene
11	5.338	0.41	Farnesol
12	17.616	3.15	Isoborneol
13	17.968	2.19	1,6-octadien-3-ol, 3,7-dimethyl
14	18.488	8.19	α–terpineol
15	21.233	24.14	Cinnamaldehyde
16	21.366	2.2	Isobornyl acetate
17	23.916	2.32	Cis,cis,trans-3,3,6,6,9,9-hexamethyl-tetracyclononane
18	25.16	2.29	Trans-caryophyllen
19	25.941	13.76	Cinnamyl acetate
20	27.025	0.57	2-methyldecane
21	27.258	0.3	(+)-2-carene, 4-α-isopropenyl
22	27.617	0.17	3,5-cycloheptadienone
23	27.859	0.81	γ–cadinene

The separation of *C. nardus* oil by gas chromatography and the interpretation of the mass spectra yielded 19 components (**Table III**) with five main components: cis-geraniol (29.01%), citronellal (24.27%), citronellol (20.23%), citral (5.27%) and geranyl acetate (4.08%). Previous researchers reported that the five largest components of *C. nardus* oil were δ-elemene (4%), elemol (5%), nerol (11%), geraniol (28%), and citronellal (33%)[15,27]. These results are somewhat different from those reported by Nakahara *et al*.[14], where the main ingredients are citronellol (5%), citronellal (6%), geranyl acetate (10%), cis-citral (14%), trans-citral (23%), and geraniol (36%).

In this study, citronellal was not found to be the primary constituent of *C. nardus* oil, but geraniol was the main compound. Nakahara *et al*.[14] also reported that the major constituent of the *C. nardus* oil was geraniol. Citronellal (24.27%) was discovered as the second main compound of *C. nardus* oil in this study. Wei and Wee[27] discovered a more significant percentage of citronellal (35%), while Nakahara *et al*.[14] found a lower amount of 5.8%. The ingredients that constitute *C. nardus* essential oil, however, were discovered in various compositions in earlier publications. Some factors that can affect the differences in the components and composition of essential oils are physiological and environmental. Physiological factors, such as different harvest seasons, produce different chemical compositions. In comparison, environmental factors are caused by soil variations, nutrients, and geographical differences such as heat, sunlight, rainfall, elevation, and climate[28].

Table III. Identification of *C. nardus* oil components using GC-MS.

Peak No	RT (minute)	% Relative	Components
1	12.761	1.07	Limonene
2	15.358	1.33	1,6-octadien-3-ol, 3,7-dimethyl
3	16.915	0.87	Isopulegol
4	17.257	24.27	Citronellal
5	18.797	0.71	Dodecanal
6	19.745	20.23	Citronellol
7	20.041	3.95	Trans-citral
8	20.658	29.01	Cis-geraniol
9	20.983	5.27	Z-citral
10	23.195	3.37	7-decen-1-ol, acetate
11	24.067	4.08	Trans,cis-nona-2,6-dienyl acetate
12	24.343	0.16	Humulene
13	25.157	1.22	Trans-caryophyllene
14	26.808	0.8	Cis,cis,trans-3,3,6,6,9,9-hexamethyl-tetracyclononane
15	27.038	0.29	Tetradecane
16	27.666	2.17	Cis,cis,trans-3,3,6,6,9,9-hexamethyl-tetracyclo [6.1.0.0(2,4).0(5,7)]nonane
17	27.848	0.41	Tetracyclo[6.1.0.02,4.05,7]nonane, 3,3,6,6,9,9-hexamethyl-
18	28.566	0.51	Elemol
19	31.207	0.28	α–bisabolol

Staphylococcus epidermidis and *S. aureus* are significant in the growth and development of acne[29]. To evaluate the effectiveness of natural anti-acne medications, *S. epidermidis* and *S. aureus* were chosen as the targets. Essential oils of *C. burmannii* and *C. nardus* individually were discovered to be helpful against these troublesome microorganisms. This study investigated the antibacterial effect if these two oils were combined. *Cinnamomum burmannii* and *C. nardus* oils have been reported to have high antibacterial activity. In this study, both oils also showed antibacterial activity against *S. epidermidis*. **Table IV** shows that the MIC of *C. nardus* oil alone is 1 mg/mL and 0.06 mg/mL against *S. epidermidis* and *S. aureus*, respectively. According to Nuryastuti *et al*.[8], *C. burmannii* oil demonstrated a MIC value of 0.005 mg/mL for *S. aureus* ATCC 25923 and MIC of 0.5 to 1% for several clinical isolates of *S. epidermidis*. In our study, *C. nardus* oil showed a MIC value of 1 mg/mL against *S. epidermidis* and *S. aureus*. According to Pontes *et al*.[12], *C. nardus* oil had a MIC value of 0.5 mg/mL against *S. aureus*[6].

The inhibitory effect of the *C. burmannii* and *C. nardus* oils in combination was carried out using the checkerboard method. This method can be carried out using a relatively small amount of oil and a combination of the two oils tested in varied ratios. In addition, this method is quite simple and relatively easy to perform in the laboratory[30]—the activity results of the combination of the two oils data as shown in **Table V**. The antibacterial activity test with the checkerboard method of each oil was set at eight concentrations: 4, 2, 1, 0.5, 0.25, 0.12, 0.06, and 0.03 mg/mL. As a result of the antibacterial activity of the two oil combinations, it inhibited *S. epidermidis* with the combined MIC at one concentration ratio: 0.5 mg/mL for both *C. burmannii* and *C. nardus* oils. Whereas the test results for the two oil combinations inhibiting *S. aureus* produced combined MICs at two concentration ratios: 0.5 and 0.06 mg/mL, and 1 and 0.03 mg/mL for *C. nardus* and *C. burmannii*, respectively.

Meanwhile, the combined MIC obtained combined *C. nardus* and *C. burmannii* oils, which was lower than each of *C. nardus* and *C. burmannii*. **Table V** displays the FICI values of the combination oil of *C. nardus* and *C. burmannii* was 1.5 against *S. epidermidis* and *S. aureus*. This value indicated that combining *C. nardus* and *C. burmannii* oils produced an indifferent antibacterial effect against both *S. epidermidis* and *S. aureus*. The impact of the two oils together results in either no increase or a minor rise in inhibitory activity for the combination. More needs to be understood, however, regarding the processes via which antimicrobial interactions have indifferent effects. Chemicals targeting the same targets in microorganisms and chemical interactions (direct or indirect) between the chemicals are potential explanations.

Table IV. The MIC of *C. nardus* and *C. burmannii* againt *S. epidermidis* and *S. aureus*.

Microorganism	Essential oil	MIC (mg/mL)
Staphylococcus epidermidis	*Cymbopogon nardus*	1
	Cinnamomum burmannii	0.5
Staphylococcus aureus	*Cymbopogon nardus*	1
	Cinnamomum burmannii	0.06

Table V. Antibacterial effect of a combination of *C. nardus* and *C. burmannii* oils against *S. epidermidis* and *S. aureus* using the checkerboard method.

Microorganism	Essential oil	MIC (single; mg/mL)	MIC (combination; mg/mL)	FIC	FICI	Interaction
Staphylococcus epidermidis	*Cymbopogon nardus*	1	0.5	0.5	1.5	Indifference
	Cinnamomum burmannii	0.5	0.5	1		
Staphylococcus aureus	*Cymbopogon nardus*	1	0.5	0.5	1.5	Indifference
	Cinnamomum burmannii	0.06	0.06	1		
	Cymbopogon nardus	1	1	1	1.5	Indifference
	Cinnamomum burmannii	0.06	0.03	0.5		

Combining essential oils with additive or synergistic properties can lower the concentration needed to have the same antibacterial effect as using just one essential oil[31]. According to earlier research, combining *C. burmannii* and thyme oils had a synergistic action against *Bacillus cereus*[20]. It may be feasible to prevent the occurrence of antibiotic resistance by combining certain essential oils[32]. The combination of *C. burmannii* oil and each of the other three antimicrobial agents (gentamicin, chlorhexidine, and triclosan) showed synergistic effects against some clinical isolates of *S. epidermidis*[8]. The combination of *Rosmarinus officinalis*, *Thymus satureioides*, and piperacillin/tazobactam oils provides a strong and reproducible synergistic effect against *Salmonella typhi*. This combination seems to strengthen the antibacterial activity of essential oils and antibiotics against *S. typhi* by increasing their potential to damage the integrity of cell membranes[33].

CONCLUSION

The combination of *C. burmannii* and *C. nardus* oils slightly decreased the MIC of the combination against acne-related bacteria compared to the MIC of the individual oils, so the effect was categorized as indifference.

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AUTHORS' CONTRIBUTION

Sri Mulyaningsih: designed and coordinated the study; composed, reviewed, and approved the publication. **Arya Guna Ramadhan**: collected data. **Widyasari Putranti**: designed and reviewed article.

DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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