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## The *in vitro* antimicrobial evaluation of commercial essential oils and their combinations against acne

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### Abstract

**OBJECTIVE:** The study investigated the efficacy of commercial essential oil combinations against the two pathogens responsible for acne with the aim to identify synergy and favourable oils to possibly use in a blend.

**MATERIALS AND METHODS:** Antimicrobial activity was assessed using the minimum inhibitory concentration (MIC) assay against *Staphylococcus epidermidis* (ATCC 2223) and *Propionibacterium acnes* (ATCC 11827), and the fractional inhibitory concentration index ( $\Sigma$ FIC) was calculated. Combinations displaying synergistic interactions were further investigated at varied ratios and the results plotted on isobolograms.

**RESULTS:** From the 408 combinations investigated, 167 combinations were identified as displaying noteworthy antimicrobial activity (MIC value  $\leq 1.00$  mg mL<sup>-1</sup>). Thirteen synergistic interactions were observed against *S. epidermidis*, and three synergistic combinations were observed against *P. acnes*. It was found that not one of the synergistic interactions identified were based on the combinations recommended in the layman's aroma-therapeutic literature. Synergy was evident rather from leads based on antimicrobial activity from previous studies, thus emphasizing the importance of scientific validation. *Leptospermum scoparium* J.R.Forst. and G.Forst (manuka) was the essential oil mostly involved in synergistic interactions (four) against *S. epidermidis*. *Cananga odorata* (Lam.) Hook.f. and Thomson (ylang ylang) essential oil was also frequently involved in synergy where synergistic interactions could be observed against both pathogens. The combination with the lowest MIC value against both acne pathogens was *Vetiveria zizanioides* Stapf (vetiver) with *Cinnamomum verum* J.Presl (cinnamon bark) (MIC values 0.19–0.25 mg mL<sup>-1</sup>). *Pogostemon patchouli* Benth. (patchouli), *V. zizanioides*, *C. verum* and *Santalum* spp. (sandalwood) could be identified as the oils that contributed the most noteworthy antimicrobial activity towards the combinations. The different chemotypes of the essential oils used in the combinations predominantly resulted in similar antimicrobial activity.

**CONCLUSIONS:** The investigated essential oil combinations resulted in at least 50% of the combinations displaying noteworthy

antimicrobial activity. Most of the synergistic interactions do not necessarily correspond to the recommended layman's aromatherapeutic literature, which highlights a need for scientific validation of essential oil antimicrobial activity. No antagonism was observed.

### Résumé

**OBJECTIF:** l'étude a examiné l'efficacité d'associations d'huiles essentielles commercialisées contre les deux pathogènes responsables de l'acné dans le but d'identifier des synergies et les huiles dont le mélange pourrait être bénéfique.

**MATÉRIELS ET MÉTHODES:** l'activité antimicrobienne a été évaluée par un dosage de la concentration minimale inhibitrice (CMI) contre *Staphylococcus epidermidis* (ATCC2223) et *Propionibacterium acnes* (ATCC11827), et l'indice de concentration inhibitrice fractionnaire ( $\Sigma$ FIC) a été calculé. Les associations montrant des interactions synergiques ont été étudiées de manière plus approfondie selon différents rapports et les résultats ont été placés sur des isobogrammes.

**RÉSULTATS:** sur les 408 associations étudiées, 167 ont été identifiées comme montrant une activité antimicrobienne notable (CMI  $\leq 1.00$  mg mL<sup>-1</sup>). Treize interactions synergiques ont été observées contre *S. epidermidis* et trois associations synergiques ont été observées contre *P. acnes*. On a constaté que l'une des interactions synergiques identifiées était basée sur les associations recommandées dans la littérature aromathérapeutique grand public. La synergie était évidente plutôt à partir de pistes basées sur l'activité antimicrobienne mise en évidence dans des études antérieures, ce qui souligne ainsi l'importance de la validation scientifique. *Leptospermum scoparium* J.R.Forst. and G.Forst (manuka) était la principale huile essentielle impliquée dans des interactions synergiques (quatre) contre *S. epidermidis*. L'huile essentielle de *Cananga odorata* (Lam.) Hook.f. and Thomson (ylang ylang) était aussi souvent impliquée dans des synergies lorsque des interactions synergiques ont pu être observées contre les deux pathogènes. Les associations ayant les valeurs de CMI les plus basses contre les deux pathogènes liés à l'acné étaient *Vetiveria zizanioides* Stapf (vétiver) et *Cinnamomum verum* J.Presl (écorce de cannelle) (valeurs de CMI de 0.19 à 0.25 mg mL<sup>-1</sup>). *Pogostemon patchouli* Benth. (patchouli), *V. zizanioides*, *C. verum* et *Santalum* spp. (bois de santal) ont pu être identifiées comme les huiles qui contribuaient de façon la plus notable à l'activité antimicrobienne dans les associations.

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Les différents chémotypes des huiles essentielles utilisées dans les associations ont principalement entraîné une activité antimicrobienne similaire.

**CONCLUSIONS:** les associations d'huiles essentielles étudiées ont mis en évidence une activité antimicrobienne notable pour au moins 50 % des associations. La plupart des interactions synergiques ne correspondent pas nécessairement à la littérature aromathérapeutique grand public recommandée, ce qui met en évidence un besoin de validation scientifique de l'activité antimicrobienne des huiles essentielles. Aucun antagonisme n'a été observé.

## Introduction

Acne vulgaris, the formation of comedones, papules, pustules, nodules and/or cysts, results in a painful skin disease which affects up to 80% of teenagers and often continues into adulthood. It is a frequently encountered skin problem which causes embarrassment, social withdrawal, depression and stigmatization [1]. It is, in fact, one of the most prevalent dermatologic diseases in the world [2] and occurs mostly on the face, back and chest [3]. Although not a serious health threat, severe acne can lead to permanent scarring; which makes it a significant clinical condition that may negatively affect a person emotionally, psychologically and even socially [4–6]. Regardless of the emotional and social implications, it has also become a condition that is less seen as a disease requiring medical attention, and more designated for cosmetic intervention [7].

The cosmetic industry was estimated at 62.46 billion U.S. dollars in 2016 [8], with skin care accounting for the largest portion (36.1% in 2015 and 36.4% in 2016) of the global market. The American beauty care business reached a market value of 80 billion dollars U.S. in the year 2015 where hair (24%) and skin care products (23.7%) represented the majority of the market, reaching nearly 50% of all beauty sales [9–11]. Although cosmetic product sales have been affected by the economy, skin care products still remain one of the highest generating growth factors, especially for products containing natural ingredients and essential oils [11, 12]. Financial constraints often lead to 'do it yourself' (DIY) products being made from home [8], where a simple search on the Internet using 'DIY acne treatments' shows multiple websites advocating essential oil use for acne, especially tea tree oil.

An understanding of the pathophysiology of acne is required when selecting an acne treatment. Hormones (androgens), excessive sebum, blocked pores from dead cells and bacteria-induced inflammatory responses are factors that play a role in the development of acne [3, 13]. The skin is comprised of multiple hair follicles that are each connected to sebaceous glands. The sebaceous glands secrete sebum, which serves the skin by keeping it soft, and this sebum reaches the surface by travelling up the pore. During puberty, testosterone increases in both females and males, resulting in an increase in sebum production. This overproduction results in the pore being blocked by sebum, hair and cells inside the hair follicle (keratinocytes), creating a blocked pore. Due to the blockage, the sebum and cells that fill the pore provide an ideal environment to support the growth of the colonizing bacteria, *Propionibacterium acnes*. This increase in bacteria triggers an immune response, resulting in inflammation with interleukin-1b (IL-1b), IL-8, granulocyte-macrophage colony-stimulating factor (GM-CSF), tumour necrosis factor  $\alpha$  (TNF- $\alpha$ ) and complement deposition [14].

Current treatments comprise of an assortment of topical and systemic medication aimed at lowering sebum production, inhibiting bacterial growth, reducing inflammation or normalizing

keratinization. The current oral treatments are generally successful; however, the side effects of oral medications often result in patient discomfort and harsh side effects resulting in non-compliance. Side effects of isotretinoin, the most successful anti-acne agent, include headaches, nausea, dry skin, joint and muscle pain, depression and suicidal tendencies. The topical antimicrobial treatments are generally the preferred treatment and exert a suppressing effect on the bacterial pathogens involved in acne; however, these are limited in their use due to the development of resistance [3, 5, 6, 15–18]. This emphasizes the importance of discovering alternative acne treatments. Essential oil combinations present such an option.

Essential oils are frequently used in the treatment of acne [19–30] and have been proven in clinical studies to display anti-acne effects [17, 31]. Clinical evidence, however, is limited to *Melaleuca alternifolia* Cheel (tea tree) and *Ocimum basilicum* L. (basil), and with 18% of essential oils used in dermatology being recommended for acne, a review identified that only a fraction of the recommended combinations has been investigated *in vitro* [32]. To further investigate the potential of these essential oil combinations, it needs to be understood that essential oils are seldom used independently and more often routinely used in combination with the intention of enhancing therapeutic efficacy [20]. The intention for blending essential oils in a combination is to create therapeutic synergy; however, antimicrobial synergy does not occur as often as is believed, as shown by previous essential oil combination studies [33]. This study thus aimed to identify synergistic essential oil combinations recommended for acne treatment.

## Materials and methods

### Essential oil procurement and combination selection

The 70 selected essential oils were obtained from international flavour and fragrance industries such as Givaudan© (Dübendorf, Switzerland), Robertet© (Grasse, France) Burgess and Finch, Prana-Monde, Essentia, Scatters Oils<sup>sc</sup> (Gauteng, South Africa), Aromatics international and Subtle energies (Ayurveda aromatherapy).

The combinations were selected, firstly, on the frequency of citation in the aroma-therapeutic literature available to the layman, with specified recommendation in treating acne [19–30]. Secondly, essential oils previously proven to display noteworthy antimicrobial activity against acne pathogens [34] were also included and combined with other recommended combinations. These two approaches were decided on to compare the most cited layman combinations to that chosen by scientific studies focusing on acne pathogens and commercial essential oil combinations. Different species or suppliers of selected essential oils were analyzed to determine if combination activities are strictly limited to the chemistry of an oil regarding the type of percent of the major compounds. These oils from different suppliers are labelled with additional numbering, for example *Vetiveria zizanioides* Stapf (vetiver) **1** and *V. zizanioides* **2**.

### Chemical composition

The majority of the essential oils samples have been previously chemically characterized [34]. The oils not yet investigated are reported in this study (Table I). Gas chromatography coupled to mass spectrometry (GC-MS-FID) was used to identify the chemical profile of each essential oil. The method [34] was followed where the GC system (Agilent 6890 N GC) was coupled directly to a 5973 MS equipped with a HP-Innowax polyethylene glycol column

**Table 1** The mean MIC ( $n = 3$ ) and  $\Sigma$ FIC values of the essential oil combinations investigated against acne pathogens

Essential oil sample	MIC value (mg mL <sup>-1</sup> )		Chemical composition		
	<i>Staphylococcus epidermidis</i> (ATCC 2223)	<i>Propionibacterium acnes</i> (ATCC 11827)	Major compounds identified	Previous studies	Reference
<i>Abies balsamea</i> (L.) Mill. (balsam)	3.00	1.50	$\beta$ -pinene (30.1%) $\delta$ -3-carene (16.8%) bornyl acetate (11.4%) $\alpha$ -pinene (9.7%) limonene (7.8%) 1,8 cineole (6.9%) camphene (5.8%)	$\beta$ -pinene (31.0%) bornyl acetate (14.9%) $\delta$ -3-carene (14.2%)	[33]
<i>Cinnamomum verum</i> J.Presl (cinnamon bark)	0.25 <sup>a</sup>	0.13	Cinnamaldehyde (61.5%) $\beta$ -caryophyllene (6.8%) cinnamyl acetate (6.5%) eugenol (3.7%) $\beta$ -phellandrene (3.7%)	cinnamaldehyde (50.5%)	[55]
<i>Cinnamomum zeylanicum</i> Blume (cinnamon leaf)	0.75	0.38	Eugenol (84.7%) $\beta$ -caryophyllene (6.8%)	eugenol (78.4%)	[34]
<i>Cistus ladanifer</i> L. (rock rose) 1	2.00	1.00	Camphene (26.9%) Bornyl acetate (20.7%) $\alpha$ -pinene (12.5%)	camphene (15.5%) borneol (11.1%) orviridiflorol (19.6%) bornyl acetate (16.7%)	[56, 57]
<i>Cistus ladanifer</i> L. (rock rose) 2	1.50	0.38	$\alpha$ -pinene (29.8%) bornyl acetate (7.3%) camphene (4.4%) <i>p</i> -cymene (5.1%)	camphene (12.3%)	
<i>Cymbopogon nardus</i> (L.) Rendle (citronella)	1.00	1.00	Citronellal (42.1%) geraniol (20.6%) citronellol (18.5%)	citronellal (38.3%)geraniol (20.7%) citronellol (18.8%)	[33]
<i>Foeniculum dulce</i> Mill. (fennel)	2.00	0.50	<i>E</i> -anethole (82.0%)	<i>E</i> -anethole (79.1%)	[33]
<i>Hypericum perforatum</i> L. (St John's wort)	2.00	0.50	$\alpha$ -pinene (34.4%) $\beta$ -pinene (9.9%) $\beta$ -caryophyllene (7.7%) 3-methyl nonene (6.9%) caryophyllene oxide (3.8%)	$\alpha$ -pinene (12.5%) $\beta$ -pinene (8.3%) or germacrene D (18.6%) ( <i>E</i> )-caryophyllene (11.2%) 2-methyloctane (9.5%)	[58, 59]
<i>Matricaria recutita</i> L. (German chamomile)	1.00	0.50	Bisabolene oxide A (52.3%) $\beta$ -farnesene (19.4%) chamazulene (3.0%)	bisabolene oxide A (46.9%) $\beta$ -farnesene (19.2%)	[33]
<i>Mentha spicata</i> L. (spearmint)	2.00	0.50	carvone (78.2%) limonene (10.3%)	carvone (40.8%) limonene (20.8%) 1,8-cineole (17.0%)	[60]
<i>Nardostachys jatamansi</i> C.B.Clarke (spikenard)	1.00	0.19	$\beta$ -gurjunene (9.7%) ledene (9.1%) $\alpha$ -panasinsen (3.4%)	$\beta$ -gurjunene (29.1%) jatamansone (9.7%)	[61]
<i>Ocimum tenuiflorum</i> L. (holy basil aromatics) 1	1.00	0.50	eugenol (57.3%) $\beta$ -caryophyllene (30.9%) $\alpha$ -humulene (3.6%)	methyl eugenol (82.9%)	[62]
<i>Ocimum tenuiflorum</i> L. (holy basil SE) 2	1.00	0.50	Eugenol (30.2%) $\beta$ -caryophyllene (27.9%) $\beta$ -elemene (18.7%)		
<i>Origanum vulgare</i> L. (oregano)	0.50	0.25	Carvacrol (51.7%) thymol (22.5%) $\lambda$ -terpinene (10.2%) <i>p</i> -cymene (7.2%)	carvacrol (14.5%) $\beta$ -fenchyl alcohol (12.8%) $\gamma$ -terpinene (11.6%)	[63]
<i>Pelargonium graveolens</i> L'Hér (geranium)	1.00	0.50	Citronellol (26.7%) eudesmol (12.5%) citronellyl formate (11.5%) menthone (7.8%) linalool (7.2%) neryl formate (5.4%)	$\beta$ -citronellol (21.9%) citronellyl formate (13.2%) geraniol (11.1%)	[64]
<i>Rosa damascena</i> Mill. (rose otto) 1	1.00	0.38	Citronellol (29.9%) phenethyl alcohol (22.4%) geraniol (20.8%) nerol (10.2%)	citronellol + nerol (27.8–38.6%) geraniol (15.4–26.5%)	[38]
<i>Rosa damascena</i> Mill. (rose otto) 2	1.00	0.50	Phenyl ethyl alcohol (63.9%) citronellol (14.6%) nerol (6.8%) geraniol (7.9%)		

Table 1 (continued)

Essential oil sample	MIC value (mg mL <sup>-1</sup> )		Chemical composition		
	<i>Staphylococcus epidermidis</i> (ATCC 2223)	<i>Propionibacterium acnes</i> (ATCC 11827)	Major compounds identified	Previous studies	Reference
<i>Santalum austrocaledonicum</i> Vieill. (sandalwood)	<b>0.25</b>	<b>0.50</b>	$\alpha$ -santalol (52.7%) $\beta$ -santalol (15.7%) bergamotol (7.1%) <i>cis</i> -santalol (3.8%)	$\alpha$ -santalol (31.6%) $\beta$ -santalol (17.7%)	[65]
<i>Vetiveria zizanioides</i> Stapf (vetiver)	<b>0.25</b>	<b>0.50</b>	Not identified	zizanol (12.8%) $\beta$ -vetirenene (8.8%)	[34]
Positive control (Ciprofloxacin)	2.02 × 10 µg mL <sup>-1</sup>	7.81 × 10 µg mL <sup>-1</sup>			
Negative control (32 mg mL <sup>-1</sup> water in acetone)	>8.00 mg mL <sup>-1</sup>	>8.00 mg mL <sup>-1</sup>			

\*Noteworthy MIC value (bold).

(60 m × 250 µm i.d. × 0.25 µm film thickness). A volume of 1 µL was injected (using a split ratio of 200 : 1 in hexane) with an auto-sampler at 24.79 psi and an inlet temperature of 250°C. The GC oven temperature was maintained at a temperature of 60°C for 10 min, then 220°C at a rate of 4°C min<sup>-1</sup> for 10 min followed by a temperature of 240°C at a rate of 1°C min<sup>-1</sup>. Helium was used as the carrier gas at a constant flow of 1.2 mL min<sup>-1</sup>. Spectra were obtained on electron impact at 70 eV, scanning from 35 to 550 *m/z*. The percentage composition of the individual components was then quantified by integration measurements using flame ionization detection (FID, 250°C) and *n*-alkanes were used as reference points in the calculation of relative retention indices (RRI). Component identifications were made by comparing mass spectra from the total ion chromatogram, and retention indices using NIST<sup>®</sup> and Mass Finder<sup>®</sup> libraries [34].

#### Preparation of cultures

The micro-organisms used in this study were from the American Type Culture Collection (ATCC). Pathogens were chosen based on their relevance to acne and included *Propionibacterium acnes* (ATCC 11827) and *Staphylococcus epidermidis* (ATCC 2223) [35, 36]. *Propionibacterium acnes* was inoculated into Thioglycolate broth (TGB) (Oxoid) and incubated under anaerobic conditions using a CO<sub>2</sub> incubator for seven days at 37°C and *S. epidermidis* was grown in Tryptone Soya broth (TSB) (Oxoid), for 18 to 24 hours at 37°C. Both pathogens were streaked onto Tryptone Soya agar plates and incubated aerobically for 24 hours at 37°C to confirm purity. The absence of growth on the streak plates for *P. acnes* was indicative of purity as no growth should have been present for aerobic conditions of the anaerobe. A waiver for the use of these micro-organisms was granted by the University of the Witwatersrand Human Research Ethics Committee (Reference W-CJ-131026-3).

#### Minimum inhibitory concentration assay

The selected essential oils were tested individually and in 1 : 1 combinations using the broth microdilution assay [34]. Microtitre plates were aseptically prepared by adding 100 µL of sterile, distilled water into each of the 96 wells. The individual essential oils and combinations were added to the first row at a volume of 100 µL, and then serially diluted. Each individual oil and

combination was tested at least in triplicate. To ensure microbial susceptibility, a 100 µL volume of 0.01 mg mL<sup>-1</sup> ciprofloxacin (Sigma Aldrich<sup>®</sup>) was included as a positive control. A negative control consisting of 32.00 mg mL<sup>-1</sup> water in acetone was also included to determine if the solvent exhibited any antimicrobial effect. A culture control (TSB for *S. epidermidis* or TGB broth for *P. acnes*) was included to ensure the media supported growth.

An approximate inoculum concentration of 1 × 10<sup>6</sup> colony forming units per mL (CFU mL<sup>-1</sup>) was prepared for each micro-organism and 100 µL added to each well. The microtitre plates were then sealed with sterile adhesive sealing film and incubated under optimal growth conditions. After incubation, each well received 40 µL of 0.04% w/v *p*-iodonitrotetrazolium violet solution (INT) (Sigma Aldrich<sup>®</sup>), where a colour change from clear to pink or purple indicated microbial growth. The minimum inhibitory concentration (MIC) was taken as the lowest concentration displaying no colour change. An MIC value less or equal to 1.00 mg mL<sup>-1</sup> is considered noteworthy for essential oils [32, 34]. The values were recorded and the fractional inhibitory concentration index (ΣFIC) was calculated.

#### Fractional inhibitory concentration index (ΣFIC)

The FIC was calculated according to the review by van Vuuren and Viljoen [37], using the following equations;

$$\text{FIC (i)} = \frac{\text{MIC of (a*) combined with (b*)}}{\text{MIC of (a) independently}}$$

$$\text{FIC (ii)} = \frac{\text{MIC of (b*) combined with (a)}}{\text{MIC of (b) independently}}$$

\*Where (a) and (b) are the MIC values of each essential oil in the selection.

From these values, the FIC index was calculated accordingly: ΣFIC = FIC (i) + FIC (ii). The ΣFIC for each essential oil combination was interpreted as ≤ 0.5 indicating synergy; >0.5–1.0 as additive; >1.0–≤4.0 indicating indifference; and >4.0 indicating antagonism [37].

#### Varied ratio combinations

Combinations demonstrating synergistic or antagonistic interactions in the 1 : 1 ΣFIC analysis were further investigated at various

**Table II** The mean MIC ( $n = 3$ ) and  $\Sigma$ FIC values of the essential oil combinations investigated against acne pathogens

Essential oil combinations		Mean MIC value ( $\text{mg mL}^{-1}$ ) ( $n = 3$ ) and $\Sigma$ FIC							
		<i>Propionibacterium acnes</i> (ATCC 11827)				<i>Staphylococcus epidermidis</i> (ATCC 2223)			
Essential oil 1	Essential oil 2	MIC1 <sup>†</sup>	MIC2 <sup>†</sup>	MIC <sup>†</sup>	$\Sigma$ FIC <sup>‡</sup>	MIC1	MIC2	MIC	$\Sigma$ FIC
<i>Angelica</i>	<i>Citrus limon</i> (lemon)	2.00	2.00	2.00	1.00	2.00	2.00	1.08	0.54
<i>archangelica</i> L. (angelica)	<i>Citrus paradisi</i> (grapefruit)	2.00	2.00	2.00	1.00	2.00	2.00	1.50	0.75
	<i>Citrus reticulata</i> (mandarin)	2.00	<b>0.50</b>	2.00	2.50	2.00	4.00	<b>1.00</b>	<b>0.38</b>
<i>Anthemis nobilis</i> L. (Roman chamomile)	<i>Cananga odorata</i> (ylang ylang)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	2.00	1.00
	<i>Citrus aurantium var. amara</i> flower (neroli)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	2.00	2.00	2.00	1.00
	<i>Citrus bergamia</i> (bergamot)	<b>1.00</b>	2.00	1.50	1.13	2.00	3.00	4.00	1.67
	<i>Citrus limon</i> (lemon)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	2.00	1.00
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	1.50	1.13	2.00	2.00	2.00	1.00
	<i>Origanum majorana</i> L. (marjoram)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	2.00	2.00	2.00	1.00
	<i>Pelargonium graveolens</i> (rose geranium)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	2.00	<b>1.00</b>	1.83	1.38
	<i>Pelargonium odoratissimum</i> (geranium)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	2.00	1.25	3.00	1.95
	<i>Salvia sclarea</i> (clary sage)	<b>1.00</b>	<b>1.00</b>	2.00	2.00	2.00	2.00	2.00	1.00
	<i>Santalum album</i> (sandalwood)	<b>1.00</b>	<b>0.69</b>	<b>1.00</b>	1.23	2.00	<b>0.13</b>	<b>0.50</b>	2.13
	<i>Santalum austrocaledonicum</i> (sandalwood)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	2.00	<b>0.25</b>	<b>0.38</b>	0.84
<i>Boswellia carterii</i> Birdw. (frankincense)	<i>Allium sativum</i> L. (garlic)	2.00	<b>0.09</b>	<b>0.31</b>	1.74	1.60	2.00	<b>0.94</b>	0.53
	<i>Citrus aurantifolia</i> (lime)	2.00	<b>0.75</b>	2.00	1.83	1.60	2.00	2.00	1.13
	<i>Citrus aurantium var. amara</i> flower (neroli)	2.00	<b>1.00</b>	1.67	1.25	1.60	2.00	<b>1.00</b>	0.56
	<i>Citrus bergamia</i> (bergamot)	2.00	2.00	2.00	1.00	1.60	3.00	2.00	0.96
	<i>Citrus paradisi</i> (grapefruit)	2.00	2.00	2.00	1.00	1.60	2.00	2.00	1.13
	<i>Citrus reticulata</i> (mandarin)	2.00	<b>0.50</b>	3.00	3.75	1.60	4.00	2.00	0.88
	<i>Coriandrum sativum</i> L. (coriander)	2.00	<b>1.00</b>	2.00	1.50	1.60	2.00	2.00	1.13
	<i>Juniperus virginiana</i> (juniper)	2.00	2.00	1.50	0.75	1.60	2.00	2.00	1.13
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	1.50	0.75	1.60	2.00	2.00	1.13
	<i>Ocimum basilicum</i> (basil)	2.00	2.00	2.00	1.00	1.60	2.00	1.50	0.84
	<i>Ocimum tenuiflorum</i> (holy basil aromatics) 1	2.00	<b>0.50</b>	2.00	2.50	1.60	<b>1.00</b>	<b>1.00</b>	0.81
	<i>Ocimum tenuiflorum</i> (holy basil SE) 2	2.00	<b>0.50</b>	<b>0.78</b>	0.98	1.60	<b>1.00</b>	<b>1.00</b>	0.81
	<i>Pelargonium graveolens</i> (rose geranium)	2.00	<b>0.50</b>	1.50	1.88	1.60	<b>1.00</b>	<b>1.00</b>	0.81
	<i>Pelargonium odoratissimum</i> (geranium)	2.00	<b>1.00</b>	<b>1.00</b>	0.75	1.60	1.25	<b>1.00</b>	0.71
	<i>Pinus sylvestris</i> (pine)	2.00	1.50	4.00	2.33	1.60	2.00	1.50	0.84
	<i>Piper nigrum</i> Beyr. ex Kunth (black pepper)	2.00	2.00	4.00	2.00	1.60	2.00	<b>1.00</b>	0.56
	<i>Santalum album</i> (sandalwood)	2.00	<b>0.69</b>	<b>1.00</b>	0.98	1.60	<b>0.13</b>	<b>0.38</b>	1.62
	<i>Santalum austrocaledonicum</i> (sandalwood)	2.00	<b>0.50</b>	1.67	2.08	1.60	<b>0.25</b>	<b>0.38</b>	0.87
	<i>Syzygium aromaticum</i> (clove)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	1.60	<b>1.00</b>	<b>1.00</b>	0.81
	<i>Vetiveria zizanioides</i> (vetiver) 1	2.00	<b>0.50</b>	<b>1.00</b>	1.25	1.60	<b>0.13</b>	<b>0.75</b>	3.23
	<i>Vetiveria zizanioides</i> (vetiver) 2	2.00	<b>0.50</b>	<b>0.83</b>	1.04	1.60	<b>0.25</b>	<b>0.50</b>	1.16
	<i>Zingiber officinale</i> Roscoe (ginger)	2.00	2.00	3.00	1.50	1.60	4.00	2.00	0.88
<i>Cananga odorata</i> (Lam.) Hook.f. & Thomson (ylang ylang)	<i>Boswellia carterii</i> (frankincense)	2.00	2.00	2.00	1.00	2.00	1.60	2.00	1.13
	<i>Citrus bergamia</i> (bergamot)	2.00	2.00	5.67	2.83	2.00	3.00	4.00	1.67
	<i>Citrus limon</i> (lemon)	2.00	2.00	2.50	1.25	2.00	2.00	1.50	0.75
	<i>Citrus paradisi</i> (grapefruit)	2.00	2.00	2.00	1.00	2.00	2.00	3.00	1.50
	<i>Leptospermum scoparium</i> (manuka)	2.00	<b>0.55</b>	<b>0.94</b>	1.09	2.00	1.40	<b>0.60</b>	<b>0.36</b>
	<i>Litsea cubeba</i> Pers. (may chang)	2.00	<b>0.88</b>	<b>1.00</b>	0.82	2.00	<b>0.75</b>	<b>1.00</b>	0.92
	<i>Pogostemon patchouli</i> (patchouli)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	2.00	<b>0.25</b>	<b>1.00</b>	2.25
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	<b>1.00</b>	0.55	2.00	2.00	1.50	0.75
	<i>Santalum album</i> (sandalwood) <sup>b</sup>	2.00	<b>0.69</b>	<b>1.00</b>	0.98	2.00	<b>0.13</b>	<b>0.50</b>	2.13
	<i>Santalum austrocaledonicum</i> (sandalwood)	2.00	<b>0.50</b>	<b>0.94</b>	1.17	2.00	<b>0.25</b>	<b>0.25</b>	0.56
	<i>Vetiveria zizanioides</i> (vetiver) 1	2.00	<b>0.50</b>	<b>0.52</b>	0.64	2.00	<b>0.13</b>	<b>0.75</b>	3.19
	<i>Vetiveria zizanioides</i> (vetiver) 2	2.00	<b>0.50</b>	<b>0.83</b>	1.04	2.00	<b>0.25</b>	<b>0.75</b>	1.69
<i>Cedrus atlantica</i> (Encl.) G.Manetti ex Carrière (cedarwood)	<i>Boswellia carterii</i> (frankincense)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	2.00	1.60	2.00	1.13
	<i>Cananga odorata</i> (ylang ylang)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	2.00	2.00	1.08	0.54
	<i>Citrus aurantium var. amara</i> flower (neroli)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	2.00	2.00	1.08	0.54
	<i>Citrus bergamia</i> (bergamot)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	2.00	3.00	2.00	0.83
	<i>Cupressus sempervirens</i> (cypress)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	2.00	<b>1.00</b>	<b>1.00</b>	0.75
	<i>Juniperus virginiana</i> (juniper)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	2.00	2.00	2.00	1.00
	<i>Lavandula angustifolia</i> (lavender)	<b>0.50</b>	2.00	1.33	1.67	2.00	2.00	2.00	1.00
	<i>Melaleuca alternifolia</i> (tea tree)	<b>0.50</b>	2.00	<b>2.00</b>	2.50	2.00	4.00	3.00	1.13
	<i>Rosmarinus officinalis</i> (rosemary)	<b>0.50</b>	1.67	<b>1.50</b>	1.95	2.00	2.00	2.00	1.00
	<i>Santalum album</i> (sandalwood)	<b>0.50</b>	<b>0.69</b>	<b>1.00</b>	1.73	2.00	<b>0.13</b>	<b>0.38</b>	1.59
	<i>Santalum austrocaledonicum</i> (sandalwood)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	2.00	<b>0.25</b>	<b>0.25</b>	0.56

Table II (continued)

Essential oil combinations		Mean MIC value (mg mL <sup>-1</sup> ) (n = 3) and ΣFIC							
		<i>Propionibacterium acnes</i> (ATCC 11827)				<i>Staphylococcus epidermidis</i> (ATCC 2223)			
Essential oil 1	Essential oil 2	MIC1 <sup>†</sup>	MIC2 <sup>†</sup>	MIC <sup>†</sup>	ΣFIC <sup>‡</sup>	MIC1	MIC2	MIC	ΣFIC
<i>Citrus aurantifolia</i> (Christm.) (lime)	<i>Vetiveria zizanioides</i> (vetiver) 1	0.50	0.50	0.75	1.50	2.00	0.13	0.50	2.13
	<i>Vetiveria zizanioides</i> (vetiver) 2	0.50	0.50	0.81	1.63	2.00	0.25	1.00	2.25
	<i>Cananga odorata</i> (ylang ylang)	0.75	2.00	3.00	2.75	2.00	2.00	2.00	1.00
	<i>Citrus aurantium</i> var. <i>amara</i> flower (neroli)	0.75	1.00	3.00	3.50	2.00	2.00	2.00	1.00
	<i>Citrus bergamia</i> (bergamot)	0.75	2.00	2.00	1.83	2.00	3.00	2.00	0.83
	<i>Citrus limon</i> (lemon)	0.75	2.00	2.00	1.83	2.00	2.00	2.00	1.00
	<i>Citrus paradisi</i> (grapefruit)	0.75	2.00	2.00	1.83	2.00	2.00	2.00	1.00
	<i>Citrus reticulata</i> (mandarin)	0.75	0.50	2.00	3.33	2.00	4.00	3.00	1.13
	<i>Citrus sinensis</i> (orange)	0.75	2.00	3.00	2.75	2.00	2.00	2.00	1.00
		<i>Cupressus sempervirens</i> (cypress)	0.75	2.00	1.00	0.92	2.00	1.00	2.00
<i>Citrus aurantium</i> var. <i>amara</i> L. flower (neroli)	<i>Lavandula angustifolia</i> (lavender)	0.75	2.00	1.00	0.92	2.00	2.00	2.00	1.00
	<i>Pelargonium graveolens</i> (rose geranium)	0.75	0.50	2.00	3.33	2.00	1.00	2.00	1.50
	<i>Pelargonium odoratissimum</i> (geranium)	0.75	1.00	1.50	1.75	2.00	1.25	1.00	0.65
	<i>Rosmarinus officinalis</i> (rosemary)	0.75	1.67	4.00	3.87	2.00	2.00	2.00	1.00
	<i>Cananga odorata</i> (ylang ylang)	1.00	2.00	2.00	1.50	2.00	2.00	1.50	0.75
	<i>Citrus bergamia</i> (bergamot)	1.00	2.00	2.00	1.50	2.00	3.00	2.00	0.83
	<i>Citrus limon</i> (lemon)	1.00	2.00	2.00	1.50	2.00	2.00	1.13	0.56
	<i>Citrus paradisi</i> (grapefruit)	1.00	2.00	1.83	1.38	2.00	2.00	1.13	0.56
	<i>Citrus reticulata</i> (mandarin)	1.00	0.50	2.00	3.00	2.00	4.00	1.38	0.52
	<i>Citrus sinensis</i> (orange)	1.00	2.00	1.50	1.13	2.00	2.00	1.13	0.56
<i>Citrus aurantium</i> var. <i>amara</i> L. fruit (petitgrain)	<i>Coriandrum sativum</i> (coriander)	1.00	1.00	1.00	1.00	2.00	2.00	1.13	0.56
	<i>Lavandula angustifolia</i> (lavender)	1.00	2.00	1.00	0.75	2.00	2.00	2.00	1.00
	<i>Pogostemon patchouli</i> (patchouli)	1.00	0.50	1.00	1.50	2.00	0.25	0.50	1.13
	<i>Cananga odorata</i> (ylang ylang)	1.00	2.00	3.00	2.25	2.00	2.00	1.00	0.50
	<i>Citrus aurantium</i> var. <i>amara</i> flower (neroli)	1.00	1.00	1.00	1.00	2.00	2.00	1.13	0.56
	<i>Citrus bergamia</i> (bergamot)	1.00	2.00	2.00	1.50	2.00	3.00	1.50	0.63
	<i>Citrus sinensis</i> (orange)	1.00	2.00	3.00	2.25	2.00	2.00	1.67	0.83
	<i>Lavandula angustifolia</i> (lavender)	1.00	2.00	2.00	1.50	2.00	2.00	1.50	0.75
	<i>Pelargonium graveolens</i> (rose geranium)	1.00	0.50	1.00	1.50	2.00	1.00	2.00	1.50
	<i>Pelargonium odoratissimum</i> (geranium)	1.00	1.00	1.00	1.00	2.00	1.25	1.00	0.65
<i>Citrus bergamia</i> Risso (bergamot)	<i>Rosmarinus officinalis</i> (rosemary)	1.00	1.67	2.00	1.60	2.00	2.00	2.00	1.00
	<i>Salvia sclarea</i> (clary sage)	1.00	1.00	1.00	1.00	2.00	2.00	1.50	0.75
	<i>Santalum album</i> (sandalwood)	1.00	0.69	1.00	1.23	2.00	0.13	0.19	0.80
	<i>Santalum austrocaledonicum</i> (sandalwood)	1.00	0.50	1.00	1.50	2.00	0.25	0.73	1.64
	<i>Syzygium aromaticum</i> (clove)	1.00	0.50	1.00	1.50	2.00	1.00	1.00	0.75
	<i>Citrus limon</i> (lemon)	2.00	2.00	2.00	1.00	3.00	2.00	2.00	0.83
	<i>Citrus sinensis</i> (orange)	2.00	2.00	3.00	1.50	3.00	2.00	2.00	0.83
	<i>Coriandrum sativum</i> (coriander)	2.00	1.00	2.00	1.50	3.00	2.00	2.00	0.83
	<i>Cupressus sempervirens</i> (cypress)	2.00	2.00	2.00	1.00	3.00	1.00	2.00	1.33
	<i>Juniperus virginiana</i> (juniper)	2.00	2.00	2.00	1.00	3.00	2.00	2.00	0.83
<i>Citrus limon</i> (L.) Burm.f. (lemon)	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	2.00	1.00	3.00	2.00	3.00	1.25
	<i>Melaleuca alternifolia</i> (tea tree)	2.00	2.00	1.67	0.83	3.00	4.00	1.00	0.29
	<i>Origanum majorana</i> (marjoram)	2.00	1.00	2.00	1.50	3.00	2.00	1.50	0.63
	<i>Pelargonium graveolens</i> (rose geranium)	2.00	0.50	1.50	1.88	3.00	1.00	1.50	1.00
	<i>Pelargonium odoratissimum</i> (geranium)	2.00	1.00	2.00	1.50	3.00	1.25	2.00	1.13
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	1.00	0.55	3.00	2.00	1.50	0.63
	<i>Santalum album</i> (sandalwood)	2.00	0.69	1.00	0.98	3.00	0.13	0.50	2.08
	<i>Santalum austrocaledonicum</i> (sandalwood)	2.00	0.50	0.88	1.09	3.00	0.25	0.32	0.68
	<i>Boswellia carterii</i> (frankincense)	2.00	2.00	2.00	1.00	2.00	1.60	2.00	1.13
	<i>Citrus aurantium</i> var. <i>amara</i> leaf (petitgrain)	2.00	1.00	1.00	0.75	2.00	2.00	3.00	1.50
<i>Citrus limon</i> (L.) Burm.f. (lemon)	<i>Citrus paradisi</i> (grapefruit)	2.00	2.00	1.67	0.83	2.00	2.00	2.00	1.00
	<i>Citrus reticulata</i> (mandarin)	2.00	0.50	1.50	1.88	2.00	4.00	2.00	0.75
	<i>Citrus sinensis</i> (orange)	2.00	2.00	2.00	1.00	2.00	2.00	2.00	1.00
	<i>Eucalyptus globulus</i> (eucalyptus)	2.00	2.00	1.67	0.83	2.00	2.00	2.00	1.00
	<i>Juniperus virginiana</i> (juniper)	2.00	2.00	2.00	1.00	2.00	2.00	3.00	1.50
	<i>Laurus nobilis</i> (bay)	2.00	1.00	1.00	0.75	2.00	1.00	1.00	0.75
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	2.00	1.00	2.00	2.00	4.00	2.00
	<i>Santalum album</i> (sandalwood)	2.00	0.69	2.00	1.95	2.00	0.13	0.50	2.13
	<i>Santalum austrocaledonicum</i> (sandalwood)	2.00	0.50	1.00	1.25	2.00	0.25	0.44	0.98
	<i>Styrax benzoin</i> (benzoin)	2.00	1.00	1.00	0.75	2.00	3.00	4.00	1.67

Table II (continued)

Essential oil combinations		Mean MIC value (mg mL <sup>-1</sup> ) (n = 3) and ΣFIC								
		<i>Propionibacterium acnes</i> (ATCC 11827)				<i>Staphylococcus epidermidis</i> (ATCC 2223)				
Essential oil 1	Essential oil 2	MIC1 <sup>†</sup>	MIC2 <sup>†</sup>	MIC <sup>†</sup>	ΣFIC <sup>‡</sup>	MIC1	MIC2	MIC	ΣFIC	
<i>Citrus paradisi</i> Macfad. (grapefruit)	<i>Citrus bergamia</i> (bergamot)	2.00	2.00	2.00	1.00	2.00	3.00	2.00	0.83	
	<i>Citrus reticulata</i> (mandarin)	2.00	<b>0.50</b>	2.00	2.50	2.00	4.00	2.00	0.75	
	<i>Citrus sinensis</i> (orange)	2.00	2.00	2.67	1.33	2.00	2.00	2.00	1.00	
	<i>Cymbopogon martinii</i> (palmarosa)	2.00	<b>1.00</b>	2.00	1.50	2.00	<b>1.00</b>	<b>1.00</b>	0.75	
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	3.00	1.50	2.00	2.00	2.00	1.00	
	<i>Myrtus communis</i> (myrtle)	2.00	2.00	2.00	1.00	2.00	2.00	2.00	1.00	
	<i>Pelargonium graveolens</i> (rose geranium)	2.00	<b>0.50</b>	1.25	1.56	2.00	<b>1.00</b>	1.50	1.13	
	<i>Pelargonium odoratissimum</i> (geranium)	2.00	<b>1.00</b>	1.50	1.13	2.00	1.25	<b>1.00</b>	0.65	
	<i>Piper nigrum</i> (black pepper)	2.00	2.00	2.67	1.33	2.00	2.00	2.00	1.00	
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	2.67	1.47	2.00	2.00	2.00	1.00	
	<i>Syzygium aromaticum</i> (clove)	2.00	<b>0.50</b>	<b>0.50</b>	0.63	2.00	<b>1.00</b>	<b>1.00</b>	0.75	
	<i>Zingiber officinale</i> (ginger)	2.00	2.00	1.67	0.83	2.00	4.00	2.00	0.75	
	<i>Citrus reticulata</i> Blanco (mandarin)	<i>Cananga odorata</i> (ylang ylang)	<b>0.50</b>	2.00	1.50	1.88	4.00	2.00	1.50	0.56
		<i>Citrus bergamia</i> (bergamot)	<b>0.50</b>	2.00	2.00	2.50	4.00	3.00	2.00	0.58
<i>Coriandrum sativum</i> (coriander)		<b>0.50</b>	<b>1.00</b>	2.00	3.00	4.00	2.00	2.00	0.75	
<i>Cupressus sempervirens</i> (cypress)		<b>0.50</b>	2.00	<b>1.00</b>	1.25	4.00	<b>1.00</b>	1.50	0.94	
<i>Juniperus virginiana</i> (juniper)		<b>0.50</b>	2.00	1.50	1.88	4.00	2.00	2.00	0.75	
<i>Myrtus communis</i> (myrtle)		<b>0.50</b>	2.00	1.50	1.88	4.00	2.00	2.00	0.75	
<i>Piper nigrum</i> (black pepper)		<b>0.50</b>	2.00	1.67	2.08	4.00	2.00	<b>1.00</b>	<b>0.38</b>	
<i>Citrus sinensis</i> Pers. (orange)	<i>Boswellia carterii</i> (frankincense)	2.00	2.00	2.00	1.00	2.00	1.60	2.00	1.13	
	<i>Cinnamomum verum</i> (cinnamon bark)	2.00	<b>0.13</b>	<b>0.50</b>	2.13	2.00	<b>0.25</b>	<b>0.50</b>	1.13	
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 1	2.00	<b>1.00</b>	1.50	1.13	2.00	<b>1.00</b>	<b>1.00</b>	0.75	
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 2	2.00	<b>0.38</b>	<b>1.00</b>	1.58	2.00	<b>0.75</b>	<b>1.00</b>	0.92	
	<i>Coriandrum sativum</i> (coriander)	2.00	<b>1.00</b>	1.50	1.13	2.00	2.00	1.50	0.75	
	<i>Cupressus sempervirens</i> (cypress)	2.00	2.00	2.00	1.00	2.00	<b>1.00</b>	2.00	1.50	
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	1.50	0.75	2.00	2.00	1.50	0.75	
	<i>Salvia sclarea</i> (clary sage)	2.00	<b>1.00</b>	1.50	1.13	2.00	2.00	1.50	0.75	
	<i>Syzygium aromaticum</i> (clove)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	2.00	<b>1.00</b>	<b>1.00</b>	0.75	
	<i>Zingiber officinale</i> (ginger)	2.00	2.00	1.50	0.75	2.00	4.00	<b>1.00</b>	<b>0.38</b>	
	<i>Commiphora myrrha</i> Engl. (myrrh)	<i>Boswellia carterii</i> (frankincense)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>0.50</b>	1.60	<b>1.00</b>	1.31
		<i>Cananga odorata</i> (ylang ylang)	<b>0.50</b>	2.00	<b>0.31</b>	<b>0.39</b>	<b>0.50</b>	2.00	<b>0.50</b>	0.63
		<i>Cedrus atlantica</i> (cedarwood)	<b>0.50</b>	<b>0.50</b>	<b>0.75</b>	1.50	<b>0.50</b>	2.00	<b>1.00</b>	1.25
		<i>Citrus aurantium var. amara</i> flower (neroli)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>0.50</b>	2.00	<b>0.50</b>	0.63
<i>Cupressus sempervirens</i> (cypress)		<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	
<i>Cymbopogon martinii</i> (palmarosa)		<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>0.50</b>	<b>1.00</b>	<b>0.50</b>	0.75	
<i>Juniperus virginiana</i> (juniper)		<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>0.50</b>	2.00	<b>1.00</b>	1.25	
<i>Lavandula angustifolia</i> (lavender)		<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>0.50</b>	2.00	<b>1.00</b>	1.25	
<i>Melaleuca alternifolia</i> (tea tree)		<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>0.50</b>	4.00	<b>1.00</b>	1.13	
<i>Pelargonium graveolens</i> (rose geranium)		<b>0.50</b>	<b>0.50</b>	<b>0.75</b>	1.50	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	
<i>Pelargonium odoratissimum</i> (geranium)		<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>0.50</b>	1.25	<b>1.00</b>	1.40	
<i>Pinus sylvestris</i> (pine)		<b>0.50</b>	1.50	<b>1.00</b>	1.33	<b>0.50</b>	2.00	<b>1.00</b>	1.25	
<i>Pogostemon patchouli</i> (patchouli)		<b>0.50</b>	<b>0.50</b>	<b>0.50</b>	1.00	<b>0.50</b>	<b>0.25</b>	<b>0.50</b>	1.50	
<i>Santalum album</i> (sandalwood)		<b>0.50</b>	<b>0.69</b>	<b>0.50</b>	0.86	<b>0.50</b>	<b>0.13</b>	<b>0.50</b>	2.50	
<i>Santalum austrocaledonicum</i> (sandalwood)	<b>0.50</b>	<b>0.50</b>	<b>0.50</b>	1.00	<b>0.50</b>	<b>0.25</b>	<b>0.31</b>	0.94		
<i>Styrax benzoin</i> Dryand. (benzoin)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>0.50</b>	3.00	<b>1.00</b>	1.17		
<i>Cupressus sempervirens</i> L. (cypress)	<i>Boswellia carterii</i> (frankincense)	2.00	2.00	2.00	1.00	<b>1.00</b>	1.60	<b>1.00</b>	0.81	
	<i>Citrus limon</i> (lemon)	2.00	2.00	2.00	1.00	<b>1.00</b>	2.00	<b>1.00</b>	0.75	
	<i>Citrus paradisi</i> (grapefruit)	2.00	2.00	2.00	1.00	<b>1.00</b>	2.00	2.00	1.50	
	<i>Citrus sinensis</i> (orange)	2.00	2.00	2.00	1.00	<b>1.00</b>	2.00	2.00	1.50	
	<i>Juniperus virginiana</i> (juniper)	2.00	2.00	1.67	0.83	<b>1.00</b>	2.00	<b>1.00</b>	0.75	
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	2.00	1.00	<b>1.00</b>	2.00	2.00	1.50	
	<i>Melaleuca alternifolia</i> (tea tree)	2.00	2.00	2.00	1.00	<b>1.00</b>	4.00	2.00	1.25	
	<i>Origanum majorana</i> (marjoram)	2.00	<b>1.00</b>	<b>1.00</b>	0.75	<b>1.00</b>	2.00	<b>1.00</b>	0.75	
	<i>Pinus sylvestris</i> (pine)	2.00	1.50	<b>1.00</b>	0.58	<b>1.00</b>	2.00	<b>1.00</b>	0.75	
	<i>Salvia sclarea</i> (clary sage)	2.00	<b>1.00</b>	2.00	1.50	<b>1.00</b>	2.00	2.00	1.50	
	<i>Santalum album</i> (sandalwood)	2.00	<b>0.69</b>	1.50	1.47	<b>1.00</b>	<b>0.13</b>	<b>0.25</b>	1.13	
	<i>Santalum austrocaledonicum</i> (sandalwood)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	<b>1.00</b>	<b>0.25</b>	<b>0.34</b>	0.86	
	<i>Styrax benzoin</i> (benzoin)	2.00	<b>1.00</b>	<b>1.00</b>	0.75	<b>1.00</b>	3.00	<b>1.00</b>	0.67	
	<i>Lavandula angustifolia</i> (lavender)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>1.00</b>	2.00	<b>1.00</b>	0.75	
<i>Rosmarinus officinalis</i> (rosemary)	<b>0.50</b>	1.67	<b>1.00</b>	1.30	<b>1.00</b>	2.00	<b>1.00</b>	0.75		



Table II (continued)

Essential oil combinations		Mean MIC value (mg mL <sup>-1</sup> ) (n = 3) and ΣFIC							
		<i>Propionibacterium acnes</i> (ATCC 11827)				<i>Staphylococcus epidermidis</i> (ATCC 2223)			
Essential oil 1	Essential oil 2	MIC1 <sup>†</sup>	MIC2 <sup>†</sup>	MIC <sup>†</sup>	ΣFIC <sup>‡</sup>	MIC1	MIC2	MIC	ΣFIC
<i>Cymbopogon citratus</i> Stapf (lemongrass)	<i>Citrus reticulata</i> (mandarin)	<b>0.50</b>	<b>0.50</b>	1.50	3.00	<b>1.00</b>	4.00	<b>1.00</b>	0.63
	<i>Coriandrum sativum</i> (coriander)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Litsea cubeba</i> (may chang)	<b>0.50</b>	<b>0.88</b>	<b>1.00</b>	1.57	<b>1.00</b>	<b>0.75</b>	<b>1.00</b>	1.17
<i>Cymbopogon martinii</i> Stapf (palmarosa)	<i>Anthemis nobilis</i> (Roman chamomile)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Boswellia carterii</i> (frankincense)	<b>1.00</b>	2.00	2.00	1.50	<b>1.00</b>	1.60	<b>1.00</b>	<b>0.81</b>
	<i>Cananga odorata</i> (ylang ylang)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Cedrus atlantica</i> (cedarwood)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Citrus aurantifolia</i> (lime)	<b>1.00</b>	<b>0.75</b>	<b>1.00</b>	1.17	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Citrus aurantium</i> var. <i>amara</i> flower (neroli)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	<b>1.00</b>	2.00	<b>0.50</b>	<b>0.38</b>
	<i>Citrus aurantium</i> var. <i>amara</i> leaf (petitgrain)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Citrus bergamia</i> (bergamot)	<b>1.00</b>	2.00	2.00	1.50	<b>1.00</b>	3.00	<b>1.00</b>	0.67
	<i>Citrus reticulata</i> (mandarin)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	<b>1.00</b>	4.00	2.00	<b>1.25</b>
	<i>Citrus sinensis</i> (orange)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Matricaria recutita</i> (German chamomile)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	<b>1.00</b>	<b>1.00</b>	<b>0.75</b>	0.75
	<i>Pelargonium graveolens</i> (rose geranium)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00
	<i>Pelargonium odoratissimum</i> (geranium)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	<b>1.00</b>	1.25	<b>1.00</b>	0.90
	<i>Salvia sclarea</i> (clary sage)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Santalum album</i> (sandalwood)	<b>1.00</b>	<b>0.69</b>	<b>0.50</b>	0.61	<b>1.00</b>	<b>0.13</b>	<b>0.50</b>	2.25
	<i>Santalum austrocaledonicum</i> (sandalwood)	<b>1.00</b>	<b>0.80</b>	<b>0.83</b>	0.94	<b>1.00</b>	<b>0.25</b>	<b>0.38</b>	0.94
<i>Daucus carota</i> L. (carrot seed)	<i>Citrus aurantifolia</i> (lime)	1.50	<b>0.75</b>	1.50	1.50	<b>1.00</b>	2.00	2.00	1.50
	<i>Citrus limon</i> (lemon)	1.50	2.00	2.00	1.17	<b>1.00</b>	2.00	2.00	1.50
	<i>Citrus sinensis</i> (orange)	1.50	2.00	1.67	0.97	<b>1.00</b>	2.00	<b>1.00</b>	0.75
<i>Eucalyptus globulus</i> Labill. (eucalyptus)	<i>Cedrus atlantica</i> (cedarwood)	2.00	<b>0.50</b>	1.83	2.29	2.00	2.00	3.00	1.50
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	1.67	0.83	2.00	2.00	2.00	1.00
	<i>Melaleuca alternifolia</i> (tea tree)	2.00	2.00	1.50	0.75	2.00	4.00	<b>0.50</b>	<b>0.19</b>
	<i>Pinus sylvestris</i> (pine)	2.00	1.50	1.50	0.88	2.00	2.00	2.00	1.00
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	<b>1.00</b>	0.55	2.00	2.00	1.67	0.83
	<i>Thymus vulgaris</i> (thyme)	2.00	<b>1.00</b>	2.00	1.50	2.00	<b>0.75</b>	<b>1.00</b>	0.92
<i>Helichrysum italicum</i> (Roth) G. Don (immortelle)	<i>Anthemis nobilis</i> (Roman chamomile)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	2.00	2.00	2.00	1.00
	<i>Boswellia carterii</i> (frankincense)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	1.60	<b>1.00</b>	0.56
	<i>Citrus bergamia</i> (bergamot)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	3.00	2.00	0.83
	<i>Citrus limon</i> (lemon)	<b>1.00</b>	2.00	4.00	3.00	2.00	2.00	1.33	0.67
	<i>Citrus paradisi</i> (grapefruit)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	1.17	0.58
	<i>Citrus reticulata</i> (mandarin)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	2.00	4.00	1.67	0.63
	<i>Citrus sinensis</i> (orange)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	1.17	0.58
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	1.50	1.13	2.00	2.00	1.25	0.63
	<i>Matricaria recutita</i> (German chamomile)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	2.00	<b>1.00</b>	<b>0.75</b>	0.56
	<i>Pelargonium graveolens</i> (rose geranium)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	2.00	<b>1.00</b>	1.83	1.38
	<i>Pelargonium odoratissimum</i> (geranium)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	2.00	1.25	<b>1.00</b>	0.65
	<i>Salvia sclarea</i> (clary sage)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	2.00	2.00	1.33	0.67
<i>Hyssopus officinalis</i> L. (hyssop)	<i>Litsea cubeba</i> (may chang)	2.00	<b>0.88</b>	<b>1.00</b>	0.82	<b>0.75</b>	<b>0.75</b>	<b>1.00</b>	1.33
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	<b>1.00</b>	0.55	<b>0.75</b>	2.00	3.00	2.75
<i>Juniperus virginiana</i> L. (juniper)	<i>Citrus aurantifolia</i> (lime)	2.00	<b>0.75</b>	4.00	3.67	2.00	2.00	2.00	1.00
	<i>Citrus paradisi</i> (grapefruit)	2.00	2.00	4.00	2.00	2.00	2.00	2.00	1.00
	<i>Citrus sinensis</i> (orange)	2.00	2.00	2.00	1.00	2.00	2.00	1.50	0.75
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	1.67	0.83	2.00	2.00	2.00	1.00
	<i>Pelargonium graveolens</i> (rose geranium)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	2.00	<b>1.00</b>	<b>1.00</b>	0.75
	<i>Pelargonium odoratissimum</i> (geranium)	2.00	<b>1.00</b>	3.00	2.25	2.00	1.25	2.00	1.30
	<i>Pinus sylvestris</i> (pine)	2.00	1.50	<b>1.00</b>	0.58	2.00	2.00	1.50	0.75
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	<b>1.00</b>	0.55	2.00	2.00	1.50	0.75
	<i>Santalum album</i> (sandalwood)	2.00	<b>0.69</b>	<b>1.00</b>	0.98	2.00	<b>0.13</b>	<b>0.50</b>	2.13
	<i>Santalum austrocaledonicum</i> (sandalwood)	2.00	<b>0.50</b>	2.00	2.50	2.00	<b>0.25</b>	<b>0.38</b>	0.84
	<i>Styrax benzoin</i> (benzoin)	2.00	<b>1.00</b>	<b>1.00</b>	0.75	2.00	3.00	2.00	0.83
<i>Laurus nobilis</i> L. (bay)	<i>Citrus sinensis</i> (orange)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Coriandrum sativum</i> (coriander)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	<b>1.00</b>	2.00	1.50	1.13
	<i>Juniperus virginiana</i> (juniper)	<b>1.00</b>	2.00	<b>0.50</b>	<b>0.38</b>	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	<b>0.75</b>	0.56	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Rosmarinus officinalis</i> (rosemary)	<b>1.00</b>	1.67	<b>1.00</b>	0.80	<b>1.00</b>	2.00	1.50	1.13
	<i>Zingiber officinale</i> (ginger)	<b>1.00</b>	2.00	<b>0.83</b>	0.63	<b>1.00</b>	4.00	<b>1.00</b>	0.63

Table II (continued)

Essential oil combinations		Mean MIC value (mg mL <sup>-1</sup> ) (n = 3) and ΣFIC								
		<i>Propionibacterium acnes</i> (ATCC 11827)				<i>Staphylococcus epidermidis</i> (ATCC 2223)				
Essential oil 1	Essential oil 2	MIC1 <sup>†</sup>	MIC2 <sup>†</sup>	MIC <sup>†</sup>	ΣFIC <sup>‡</sup>	MIC1	MIC2	MIC	ΣFIC	
<i>Lavandula angustifolia</i> Mill. (lavender)	<i>Citrus reticulata</i> (mandarin)	2.00	<b>0.50</b>	2.00	2.50	2.00	4.00	2.00	0.75	
	<i>Pelargonium graveolens</i> (rose geranium)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	2.00	<b>1.00</b>	1.50	1.13	
	<i>Pelargonium odoratissimum</i> (geranium)	2.00	<b>1.00</b>	2.00	1.50	2.00	1.25	2.00	1.30	
	<i>Pinus sylvestris</i> (pine)	2.00	1.50	1.67	0.97	2.00	2.00	2.00	1.00	
	<i>Pogostemon patchouli</i> (patchouli)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	2.00	<b>0.25</b>	<b>0.50</b>	1.13	
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	<b>1.00</b>	0.55	2.00	2.00	2.00	1.00	
	<i>Salvia lavandulifolia</i> (sage)	2.00	2.00	<b>1.00</b>	<b>0.50</b>	2.00	1.50	2.00	1.17	
	<i>Tagetes minuta</i> L. (tagetes)	2.00	2.00	2.00	1.00	2.00	2.00	1.67	0.83	
	<i>Leptospermum scoparium</i> J.R.Forst. and G.Forst (manuka)	<i>Achillea millefolium</i> Ledeb. (yarrow)	<b>0.55</b>	<b>1.00</b>	<b>1.00</b>	1.41	1.40	2.00	2.00	1.21
<i>Allium sativum</i> (garlic)		<b>0.55</b>	<b>0.09</b>	<b>0.38</b>	2.34	1.40	2.00	<b>0.25</b>	<b>0.15</b>	
<i>Cedrus atlantica</i> (cedarwood)		<b>0.55</b>	<b>0.50</b>	<b>0.38</b>	0.72	1.40	2.00	<b>0.92</b>	0.56	
<i>Citrus aurantium</i> var. <i>amara</i> flower (neroli)		<b>0.55</b>	<b>1.00</b>	<b>1.00</b>	1.41	1.40	2.00	2.00	1.21	
<i>Citrus bergamia</i> (bergamot)		<b>0.55</b>	2.00	1.75	2.04	1.40	3.00	1.50	0.79	
<i>Citrus reticulata</i> (mandarin)		<b>0.55</b>	<b>0.50</b>	<b>1.00</b>	1.91	1.40	4.00	<b>0.50</b>	<b>0.24</b>	
<i>Commiphora myrrha</i> (myrrh)		<b>0.55</b>	<b>0.50</b>	<b>0.50</b>	0.96	1.40	<b>0.50</b>	<b>0.33</b>	<b>0.45</b>	
<i>Cymbopogon citratus</i> (lemongrass)		<b>0.55</b>	<b>0.50</b>	<b>1.00</b>	1.91	1.40	<b>1.00</b>	<b>0.83</b>	0.71	
<i>Kunzea ericoides</i> (A.Rich.) Joy Thomps. (kanuka)		<b>0.55</b>	2.00	<b>1.00</b>	1.16	1.40	2.00	<b>1.00</b>	0.61	
<i>Laurus nobilis</i> (bay)		<b>0.55</b>	<b>1.00</b>	<b>0.50</b>	0.71	1.40	<b>1.00</b>	<b>1.00</b>	0.86	
<i>Lavandula angustifolia</i> (lavender)		<b>0.55</b>	2.00	<b>1.00</b>	1.16	1.40	2.00	<b>1.00</b>	0.61	
<i>Litsea cubeba</i> (may chang)		<b>0.55</b>	<b>0.88</b>	<b>1.00</b>	1.49	1.40	<b>0.75</b>	<b>0.78</b>	0.80	
<i>Pelargonium graveolens</i> (rose geranium)		<b>0.55</b>	<b>0.50</b>	<b>1.00</b>	1.91	1.40	<b>1.00</b>	<b>0.92</b>	0.79	
<i>Pelargonium odoratissimum</i> (geranium)		<b>0.55</b>	<b>1.00</b>	<b>1.00</b>	1.41	1.40	1.25	<b>1.00</b>	0.76	
<i>Pogostemon patchouli</i> (patchouli)		<b>0.55</b>	<b>0.50</b>	<b>0.50</b>	0.96	1.40	<b>0.25</b>	<b>0.50</b>	1.18	
<i>Santalum album</i> (sandalwood)		<b>0.55</b>	<b>0.69</b>	<b>0.75</b>	1.23	1.40	<b>0.13</b>	<b>0.38</b>	1.63	
<i>Santalum austrocaledonicum</i> (sandalwood)		<b>0.55</b>	<b>0.50</b>	<b>0.83</b>	1.60	1.40	<b>0.25</b>	<b>0.38</b>	0.88	
<i>Vetiveria zizanioides</i> (vetiver) 1		<b>0.55</b>	<b>0.50</b>	<b>0.75</b>	1.44	1.40	<b>0.13</b>	<b>0.50</b>	2.18	
<i>Vetiveria zizanioides</i> (vetiver) 2		<b>0.55</b>	<b>0.50</b>	<b>0.83</b>	1.60	1.40	<b>0.25</b>	<b>0.50</b>	1.18	
<i>Matricaria recutita</i> L. (German chamomile)		<i>Cananga odorata</i> (ylang ylang)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Citrus aurantium</i> var. <i>amara</i> flower (neroli)	<b>0.50</b>	<b>1.00</b>	<b>0.75</b>	1.13	<b>1.00</b>	2.00	<b>1.00</b>	0.75	
	<i>Citrus bergamia</i> (bergamot)	<b>0.50</b>	2.00	1.50	1.88	<b>1.00</b>	3.00	1.50	1.00	
	<i>Citrus limon</i> (lemon)	<b>0.50</b>	2.00	1.50	1.88	<b>1.00</b>	2.00	1.25	0.94	
	<i>Lavandula angustifolia</i> (lavender)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>1.00</b>	2.00	1.75	1.31	
	<i>Origanum majorana</i> (marjoram)	<b>0.50</b>	<b>1.00</b>	1.50	2.25	<b>1.00</b>	2.00	1.25	0.94	
	<i>Pelargonium graveolens</i> (rose geranium)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	
	<i>Pelargonium odoratissimum</i> (geranium)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>1.00</b>	1.25	1.50	1.35	
	<i>Salvia sclarea</i> (clary sage)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>1.00</b>	2.00	2.00	1.50	
	<i>Santalum album</i> (sandalwood)	<b>0.50</b>	<b>0.69</b>	<b>0.75</b>	1.30	<b>1.00</b>	<b>0.13</b>	<b>0.50</b>	2.25	
	<i>Santalum austrocaledonicum</i> (sandalwood)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	<b>1.00</b>	<b>0.25</b>	<b>0.33</b>	0.83	
	<i>Melaleuca alternifolia</i> Cheel (tea tree)	<i>Citrus limon</i> (lemon)	2.00	2.00	2.00	1.00	4.00	2.00	1.75	0.66
		<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	2.00	1.00	4.00	2.00	1.50	0.56
		<i>Pelargonium graveolens</i> (rose geranium)	2.00	<b>0.50</b>	<b>1.00</b>	1.25	4.00	<b>1.00</b>	2.75	1.72
<i>Pelargonium odoratissimum</i> (geranium)		2.00	<b>1.00</b>	<b>1.00</b>	0.75	4.00	1.25	2.00	1.05	
<i>Pinus sylvestris</i> (pine)		2.00	1.50	2.50	1.46	4.00	2.00	1.50	0.56	
<i>Rosmarinus officinalis</i> (rosemary)		2.00	1.67	2.00	1.10	4.00	2.00	1.75	0.66	
<i>Santalum album</i> (sandalwood)		2.00	<b>0.69</b>	<b>1.00</b>	0.98	4.00	<b>0.13</b>	<b>0.25</b>	1.03	
<i>Santalum austrocaledonicum</i> (sandalwood)		2.00	<b>0.50</b>	<b>0.83</b>	1.04	4.00	<b>0.25</b>	<b>0.27</b>	0.58	
<i>Syzygium aromaticum</i> (clove)		2.00	<b>0.50</b>	<b>1.00</b>	1.25	4.00	<b>1.00</b>	<b>1.00</b>	0.63	
<i>Thymus vulgaris</i> (thyme)		2.00	<b>1.00</b>	2.00	1.50	4.00	<b>0.75</b>	<b>1.00</b>	0.79	
<i>Zingiber officinale</i> (ginger)		2.00	2.00	2.00	1.00	4.00	4.00	3.00	0.75	
<i>Melaleuca viridiflora</i> Gaertn. (niaouli)		<i>Citrus limon</i> (lemon)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	2.00	1.00
		<i>Juniperus virginiana</i> (juniper)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	4.00	2.00
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	4.00	2.00	
	<i>Pinus sylvestris</i> (pine)	<b>1.00</b>	1.50	<b>1.00</b>	0.83	2.00	2.00	2.00	1.00	
<i>Mentha piperita</i> L. (peppermint)	<i>Citrus limon</i> (lemon)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	1.50	0.75	
	<i>Eucalyptus globulus</i> (eucalyptus)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	<b>1.00</b>	<b>0.50</b>	
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	2.00	1.00	
	<i>Pinus sylvestris</i> (pine)	<b>1.00</b>	1.50	<b>1.00</b>	0.83	2.00	2.00	<b>1.00</b>	<b>0.50</b>	
<i>Mentha spicata</i> L. (spearmint)	<i>Citrus limon</i> (lemon)	<b>0.50</b>	1.67	2.00	2.60	2.00	2.00	2.00	1.00	
	<i>Eucalyptus globulus</i> (eucalyptus)	<b>0.50</b>	2.00	1.50	1.88	2.00	2.00	2.00	1.00	
	<i>Lavandula angustifolia</i> (lavender)	<b>0.50</b>	2.00	2.00	2.50	2.00	2.00	2.00	1.00	

Table II (continued)

Essential oil combinations		Mean MIC value (mg mL <sup>-1</sup> ) (n = 3) and ΣFIC							
		<i>Propionibacterium acnes</i> (ATCC 11827)				<i>Staphylococcus epidermidis</i> (ATCC 2223)			
Essential oil 1	Essential oil 2	MIC1 <sup>†</sup>	MIC2 <sup>†</sup>	MIC <sup>†</sup>	ΣFIC <sup>‡</sup>	MIC1	MIC2	MIC	ΣFIC
<i>Myrtus communis</i> Blanco (myrtle)	<i>Pinus sylvestris</i> (pine)	<b>0.50</b>	1.50	2.00	2.67	2.00	2.00	2.00	1.00
	<i>Citrus bergamia</i> (bergamot)	2.00	2.00	2.00	1.00	2.00	3.00	2.00	0.83
	<i>Coriandrum sativum</i> (coriander)	2.00	<b>1.00</b>	<b>1.00</b>	0.75	2.00	2.00	2.00	1.00
	<i>Lavandula angustifolia</i> (lavender)	2.00	2.00	1.67	0.83	2.00	2.00	2.00	1.00
	<i>Rosmarinus officinalis</i> (rosemary)	2.00	1.67	<b>1.00</b>	0.55	2.00	2.00	2.00	1.00
<i>Ocimum basilicum</i> L. (basil)	<i>Pelargonium graveolens</i> (rose geranium)	2.00	<b>0.50</b>	1.50	1.88	2.00	<b>1.00</b>	2.00	1.50
	<i>Pelargonium odoratissimum</i> (geranium)	2.00	<b>1.00</b>	2.00	1.50	2.00	1.25	1.50	0.98
	<i>Pelargonium graveolens</i> (rose geranium)	2.00	<b>0.50</b>	2.00	2.50	2.00	<b>1.00</b>	1.50	1.13
	<i>Pelargonium odoratissimum</i> (geranium)	2.00	<b>1.00</b>	2.00	1.50	2.00	1.25	1.67	1.08
	<i>Salvia sclarea</i> (clary sage)	2.00	<b>1.00</b>	4.00	3.00	2.00	2.00	2.00	1.00
<i>Ocimum tenuiflorum</i> L (holy basil aromatics) 1	<i>Coriandrum sativum</i> (coriander)	2.00	<b>1.00</b>	1.50	1.13	2.00	2.00	2.00	1.00
	<i>Pelargonium graveolens</i> (rose geranium)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00
	<i>Pelargonium odoratissimum</i> (geranium)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>1.00</b>	1.25	<b>1.00</b>	0.90
	<i>Salvia sclarea</i> (clary sage)	<b>0.50</b>	<b>1.00</b>	1.50	2.25	<b>1.00</b>	2.00	1.50	1.13
	<i>Coriandrum sativum</i> (coriander)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>1.00</b>	2.00	<b>1.00</b>	0.75
<i>Ocimum tenuiflorum</i> L (holy basil SE) 2	<i>Pelargonium graveolens</i> (rose geranium)	<b>0.50</b>	<b>0.50</b>	<b>0.75</b>	1.50	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00
	<i>Pelargonium odoratissimum</i> (geranium)	<b>0.50</b>	<b>1.00</b>	<b>0.75</b>	1.13	<b>1.00</b>	1.25	<b>1.00</b>	0.90
	<i>Salvia sclarea</i> (clary sage)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Coriandrum sativum</i> (coriander)	<b>0.50</b>	<b>1.00</b>	<b>0.50</b>	0.75	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Citrus aurantium var. amara</i> flower (neroli)	<b>0.50</b>	<b>1.00</b>	<b>0.75</b>	1.13	<b>1.00</b>	2.00	<b>1.00</b>	0.75
<i>Pelargonium graveolens</i> L'Hér (rose geranium)	<i>Citrus limon</i> (lemon)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>1.00</b>	2.00	1.50	1.13
	<i>Citrus sinensis</i> (orange)	<b>0.50</b>	2.00	2.00	2.50	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Rosmarinus officinalis</i> (rosemary)	<b>0.50</b>	1.67	1.50	1.95	<b>1.00</b>	2.00	1.50	1.13
	<i>Santalum album</i> (sandalwood)	<b>0.50</b>	<b>0.69</b>	<b>0.75</b>	1.30	<b>1.00</b>	<b>0.13</b>	<b>0.29</b>	1.31
	<i>Santalum austrocaledonicum</i> (sandalwood)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	<b>1.00</b>	<b>0.25</b>	<b>0.58</b>	1.46
	<i>Styrax benzoin</i> (benzoin)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>1.00</b>	3.00	<b>1.00</b>	0.67
	<i>Vetiveria zizanioides</i> (vetiver) 1	<b>0.50</b>	<b>0.50</b>	<b>0.75</b>	1.50	<b>1.00</b>	<b>0.13</b>	<b>0.58</b>	2.63
	<i>Vetiveria zizanioides</i> (vetiver) 2	<b>0.50</b>	<b>0.50</b>	<b>0.75</b>	1.50	<b>1.00</b>	<b>0.25</b>	<b>0.75</b>	1.88
	<i>Citrus aurantium var. amara</i> flower (neroli)	<b>1.00</b>	<b>1.00</b>	1.50	1.50	1.25	2.00	<b>1.00</b>	0.65
	<i>Citrus limon</i> (lemon)	<b>1.00</b>	2.00	2.00	1.50	1.25	2.00	<b>1.00</b>	0.65
<i>Pelargonium odoratissimum</i> [Soland.] (geranium)	<i>Citrus sinensis</i> (orange)	<b>1.00</b>	2.00	2.00	1.50	1.25	2.00	<b>1.00</b>	0.65
	<i>Rosmarinus officinalis</i> (rosemary)	<b>1.00</b>	1.67	<b>1.00</b>	0.80	1.25	2.00	1.67	1.08
	<i>Santalum album</i> (sandalwood)	<b>1.00</b>	<b>0.69</b>	1.38	1.69	1.25	<b>0.13</b>	<b>0.25</b>	1.10
	<i>Santalum austrocaledonicum</i> (sandalwood)	<b>1.00</b>	<b>0.50</b>	<b>1.00</b>	1.50	1.25	<b>0.25</b>	<b>0.38</b>	0.90
	<i>Styrax benzoin</i> (benzoin)	<b>1.00</b>	<b>1.00</b>	<b>1.00</b>	1.00	1.25	3.00	<b>1.00</b>	0.57
	<i>Vetiveria zizanioides</i> (vetiver) 1	<b>1.00</b>	<b>0.50</b>	<b>0.75</b>	1.13	1.25	<b>0.13</b>	<b>0.75</b>	3.30
	<i>Vetiveria zizanioides</i> (vetiver) 2	<b>1.00</b>	<b>0.50</b>	<b>0.69</b>	1.03	1.25	<b>0.25</b>	<b>0.75</b>	1.80
	<i>Cedrus atlantica</i> (cedarwood)	1.50	<b>0.50</b>	2.00	2.67	2.00	2.00	2.00	1.00
	<i>Citrus limon</i> (lemon)	1.50	2.00	2.00	1.17	2.00	2.00	2.00	1.00
	<i>Rosmarinus officinalis</i> (rosemary)	1.50	1.67	2.00	1.27	2.00	2.00	2.00	1.00
<i>Pogostemon patchouli</i> Benth. (patchouli)	<i>Boswellia carterii</i> (frankincense)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>0.25</b>	1.60	<b>1.00</b>	2.31
	<i>Cedrus atlantica</i> (cedarwood)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	<b>0.25</b>	2.00	<b>1.00</b>	2.25
	<i>Citrus bergamia</i> (bergamot)	<b>0.50</b>	2.00	2.00	2.50	<b>0.25</b>	3.00	<b>1.00</b>	2.17
	<i>Pelargonium graveolens</i> (rose geranium)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	<b>0.25</b>	<b>1.00</b>	<b>0.38</b>	0.94
	<i>Pelargonium odoratissimum</i> (geranium)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>0.25</b>	1.25	<b>1.00</b>	2.40
	<i>Salvia sclarea</i> (clary sage)	<b>0.50</b>	<b>1.00</b>	<b>1.00</b>	1.50	<b>0.25</b>	2.00	<b>1.00</b>	2.25
	<i>Santalum album</i> (sandalwood)	<b>0.50</b>	<b>0.69</b>	<b>1.00</b>	1.73	<b>0.25</b>	<b>0.13</b>	<b>0.25</b>	1.50
	<i>Santalum austrocaledonicum</i> (sandalwood)	<b>0.50</b>	<b>0.50</b>	<b>0.83</b>	1.67	<b>0.25</b>	<b>0.25</b>	<b>0.25</b>	1.00
	<i>Syzygium aromaticum</i> (clove)	<b>0.50</b>	<b>0.50</b>	<b>0.50</b>	1.00	<b>0.25</b>	<b>1.00</b>	<b>0.50</b>	1.25
	<i>Vetiveria zizanioides</i> (vetiver) 1	<b>0.50</b>	<b>0.50</b>	<b>0.35</b>	0.69	<b>0.25</b>	<b>0.13</b>	<b>0.32</b>	1.89
<i>Vetiveria zizanioides</i> (vetiver) 2	<b>0.50</b>	<b>0.50</b>	<b>0.50</b>	1.00	<b>0.25</b>	<b>0.25</b>	<b>0.50</b>	2.00	
<i>Rosmarinus officinalis</i> L. (rosemary)	<i>Boswellia carterii</i> (frankincense)	1.67	2.00	2.00	1.10	2.00	1.60	<b>1.00</b>	0.56
	<i>Citrus sinensis</i> (orange)	1.67	2.00	1.50	0.83	2.00	2.00	1.25	0.63
	<i>Mentha piperita</i> (peppermint)	1.67	<b>1.00</b>	1.50	1.20	2.00	2.00	2.00	1.00
	<i>Mentha spicata</i> (spearmint)	1.67	<b>0.50</b>	<b>1.00</b>	1.30	2.00	2.00	1.75	0.88
	<i>Ocimum basilicum</i> (basil)	1.67	2.00	<b>1.00</b>	0.55	2.00	2.00	1.67	0.83
	<i>Ocimum tenuiflorum</i> (holy basil aromatics) 1	1.67	<b>0.19</b>	<b>0.50</b>	1.48	2.00	<b>1.00</b>	<b>1.00</b>	0.75
	<i>Ocimum tenuiflorum</i> (holy basil SE) 2	1.67	<b>0.50</b>	<b>0.50</b>	0.65	2.00	<b>1.00</b>	1.50	1.13
	<i>Cananga odorata</i> (ylang ylang)	1.67	2.00	1.50	0.82	2.00	2.00	1.25	0.63
	<i>Citrus bergamia</i> (bergamot)	2.00	2.00	2.00	1.00	1.50	3.00	1.50	0.75

Table II (continued)

Essential oil combinations		Mean MIC value (mg mL <sup>-1</sup> ) (n = 3) and ΣFIC							
		<i>Propionibacterium acnes</i> (ATCC 11827)				<i>Staphylococcus epidermidis</i> (ATCC 2223)			
Essential oil 1	Essential oil 2	MIC1 <sup>*</sup>	MIC2 <sup>*</sup>	MIC <sup>†</sup>	ΣFIC <sup>‡</sup>	MIC1	MIC2	MIC	ΣFIC
<i>Salvia lavandulifolia</i> Spreng. (sage)	<i>Citrus sinensis</i> (orange)	2.00	2.00	3.00	1.50	1.50	2.00	<b>1.00</b>	0.58
<i>Salvia sclarea</i> L. (clary sage)	<i>Boswellia carterii</i> (frankincense)	<b>1.00</b>	2.00	1.50	1.13	2.00	1.60	2.00	1.13
	<i>Cedrus atlantica</i> (cedarwood)	<b>1.00</b>	<b>0.50</b>	2.00	3.00	2.00	2.00	3.00	1.50
	<i>Citrus aurantifolia</i> (lime)	<b>1.00</b>	<b>0.75</b>	<b>1.00</b>	1.17	2.00	2.00	2.00	1.00
	<i>Citrus bergamia</i> (bergamot)	<b>1.00</b>	2.00	2.00	1.50	2.00	3.00	3.00	1.25
	<i>Citrus paradisi</i> (grapefruit)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	2.00	1.00
	<i>Citrus reticulata</i> (mandarin)	<b>1.00</b>	<b>0.50</b>	1.50	2.25	2.00	4.00	2.00	0.75
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	2.00	2.00	2.00	1.00
	<i>Pelargonium graveolens</i> (rose geranium)	<b>1.00</b>	<b>0.50</b>	1.50	2.25	2.00	<b>1.00</b>	2.00	1.50
	<i>Pelargonium odoratissimum</i> (geranium)	<b>1.00</b>	<b>1.00</b>	2.00	2.00	2.00	1.25	2.00	1.30
	<i>Santalum album</i> L. (sandalwood)	<i>Citrus aurantium var. amara</i> flower (neroli)	<b>0.69</b>	<b>1.00</b>	<b>1.00</b>	1.23	<b>0.13</b>	2.00	<b>0.50</b>
<i>Citrus paradisi</i> (grapefruit)		<b>0.69</b>	2.00	<b>1.00</b>	0.98	<b>0.13</b>	2.00	<b>0.75</b>	3.19
<i>Lavandula angustifolia</i> (lavender)		<b>0.69</b>	2.00	<b>1.00</b>	0.98	<b>0.13</b>	2.00	<b>0.50</b>	2.13
<i>Piper nigrum</i> (black pepper)		<b>0.69</b>	2.00	<b>1.00</b>	0.98	<b>0.13</b>	2.00	<b>0.50</b>	2.13
<i>Styrax benzoin</i> (benzoin)		<b>0.69</b>	<b>1.00</b>	<b>0.75</b>	0.92	<b>0.13</b>	3.00	<b>0.50</b>	2.08
<i>Vetiveria zizanioides</i> (vetiver) 1		<b>0.69</b>	<b>0.50</b>	<b>0.88</b>	1.51	<b>0.13</b>	<b>0.13</b>	<b>0.25</b>	2.00
<i>Vetiveria zizanioides</i> (vetiver) 2		<b>0.69</b>	<b>0.50</b>	<b>0.63</b>	1.08	<b>0.13</b>	<b>0.25</b>	<b>0.34</b>	2.06
<i>Citrus aurantium var. amara</i> flower (neroli)		<b>0.50</b>	<b>1.00</b>	<b>0.83</b>	1.25	<b>0.25</b>	2.00	<b>0.50</b>	1.13
<i>Citrus paradisi</i> (grapefruit)		<b>0.50</b>	2.00	1.83	2.29	<b>0.25</b>	2.00	<b>1.00</b>	2.25
<i>Lavandula angustifolia</i> (lavender)		<b>0.50</b>	2.00	1.67	2.08	<b>0.25</b>	2.00	<b>0.50</b>	1.13
<i>Santalum austrocaledonicum</i> Vieill. (sandalwood)	<i>Piper nigrum</i> (black pepper)	<b>0.50</b>	2.00	1.67	2.08	<b>0.25</b>	2.00	<b>0.25</b>	0.56
	<i>Styrax benzoin</i> (benzoin)	<b>0.50</b>	<b>1.00</b>	<b>0.83</b>	1.25	<b>0.25</b>	3.00	<b>0.50</b>	1.08
	<i>Vetiveria zizanioides</i> (vetiver) 1	<b>0.50</b>	<b>0.50</b>	<b>0.83</b>	1.67	<b>0.25</b>	<b>0.13</b>	<b>0.50</b>	3.00
	<i>Vetiveria zizanioides</i> (vetiver) 2	<b>0.50</b>	<b>0.50</b>	<b>0.50</b>	1.00	<b>0.25</b>	<b>0.25</b>	<b>0.36</b>	1.43
	<i>Cinnamomum verum</i> (cinnamon bark)	<b>0.50</b>	<b>0.13</b>	<b>0.25</b>	1.25	<b>1.00</b>	<b>0.25</b>	<b>0.44</b>	1.09
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 1	<b>0.50</b>	<b>1.00</b>	<b>0.50</b>	0.75	<b>1.00</b>	<b>1.00</b>	<b>0.75</b>	0.75
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 2	<b>0.50</b>	<b>0.38</b>	<b>0.50</b>	1.17	<b>1.00</b>	<b>0.75</b>	<b>1.00</b>	1.17
	<i>Citrus bergamia</i> (bergamot)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>1.00</b>	3.00	1.50	1.00
	<i>Citrus limon</i> (lemon)	<b>0.50</b>	2.00	<b>0.75</b>	0.94	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Citrus reticulata</i> (mandarin)	<b>0.50</b>	<b>0.50</b>	<b>1.00</b>	2.00	<b>1.00</b>	4.00	<b>1.00</b>	0.63
<i>Thymus vulgaris</i> L. (thyme)	<i>Lavandula angustifolia</i> (lavender)	<b>0.50</b>	2.00	<b>1.00</b>	1.25	<b>1.00</b>	2.00	<b>1.00</b>	0.75
	<i>Litsea cubeba</i> (may chang)	<b>0.50</b>	<b>0.88</b>	<b>0.75</b>	1.18	<b>1.00</b>	<b>0.75</b>	<b>1.00</b>	1.17
	<i>Citrus bergamia</i> (bergamot)	<b>1.00</b>	2.00	1.83	1.38	<b>0.75</b>	3.00	<b>1.00</b>	0.83
	<i>Citrus limon</i> (lemon)	<b>1.00</b>	2.00	2.00	1.50	<b>0.75</b>	2.00	2.00	1.83
	<i>Lavandula angustifolia</i> (lavender)	<b>1.00</b>	2.00	<b>1.00</b>	0.75	<b>0.75</b>	2.00	<b>1.00</b>	0.92
	<i>Pinus sylvestris</i> (pine)	<b>1.00</b>	1.50	<b>1.00</b>	0.83	<b>0.75</b>	2.00	<b>1.00</b>	0.92
	<i>Rosmarinus officinalis</i> (rosemary)	<b>1.00</b>	1.67	2.00	1.60	<b>0.75</b>	2.00	<b>1.00</b>	0.92
	<i>Cinnamomum verum</i> (cinnamon bark)	<b>0.50</b>	<b>0.13</b>	<b>0.25</b>	1.25	<b>0.13</b>	<b>0.25</b>	<b>0.50</b>	3.00
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 1	<b>0.50</b>	<b>1.00</b>	<b>0.50</b>	0.75	<b>0.13</b>	<b>1.00</b>	<b>0.50</b>	2.25
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 2	<b>0.50</b>	<b>0.38</b>	<b>0.50</b>	1.17	<b>0.13</b>	<b>0.75</b>	<b>0.38</b>	1.75
<i>Vetiveria zizanioides</i> Stapf (vetiver) 1	<i>Lavandula angustifolia</i> (lavender)	<b>0.50</b>	2.00	<b>0.75</b>	0.94	<b>0.13</b>	2.00	<b>0.75</b>	3.19
	<i>Litsea cubeba</i> (may chang)	<b>0.50</b>	<b>0.88</b>	<b>0.50</b>	0.79	<b>0.13</b>	<b>0.75</b>	<b>0.50</b>	2.33
	<i>Salvia sclarea</i> (clary sage)	<b>0.50</b>	<b>1.00</b>	<b>0.75</b>	1.13	<b>0.13</b>	2.00	<b>0.75</b>	3.19
	<i>Cinnamomum verum</i> (cinnamon bark)	<b>0.05</b>	<b>0.13</b>	<b>0.25</b>	3.67	<b>0.25</b>	<b>0.25</b>	<b>0.19</b>	0.76
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 1	<b>0.50</b>	<b>1.00</b>	1.46	2.19	<b>0.25</b>	<b>1.00</b>	<b>0.75</b>	1.88
	<i>Cinnamomum zeylanicum</i> (cinnamon leaf) 2	<b>0.50</b>	<b>0.38</b>	<b>0.50</b>	1.17	<b>0.25</b>	<b>0.75</b>	<b>0.50</b>	1.33
	<i>Lavandula angustifolia</i> (lavender)	<b>0.50</b>	2.00	1.58	1.98	<b>0.25</b>	2.00	<b>1.00</b>	2.25
	<i>Litsea cubeba</i> (may chang)	<b>0.50</b>	<b>0.88</b>	<b>1.00</b>	1.57	<b>0.25</b>	<b>0.75</b>	<b>0.50</b>	1.33
	<i>Salvia sclarea</i> (clary sage)	<b>0.50</b>	<b>1.00</b>	<b>0.83</b>	1.25	<b>0.25</b>	2.00	<b>1.00</b>	2.25

\*Individual MIC value reported in this or previous study [34].

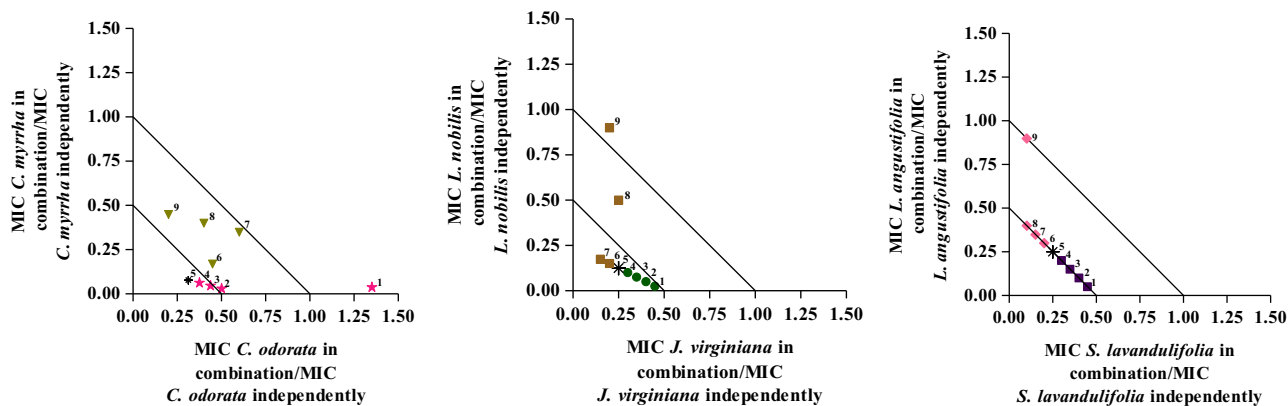
†Noteworthy MIC value of the combination (bold).

‡Synergistic interaction (bold, italics).

§Combinations recommended in the layman's aroma-therapeutic literature for the treatment of acne (shaded) [19–30].

ratios. The same method used for the 1 : 1 ratio was used, except the combinations were placed in different concentrations of 9 : 1, 8 : 2, 7 : 3, 6 : 4, 5 : 5, 4 : 6, 3 : 7, 2 : 8 and 1 : 9. The MIC

values were recorded at the various ratios on an isobologram using Graphpad Prism® (Version 5) software and the ratio points were expressed graphically.

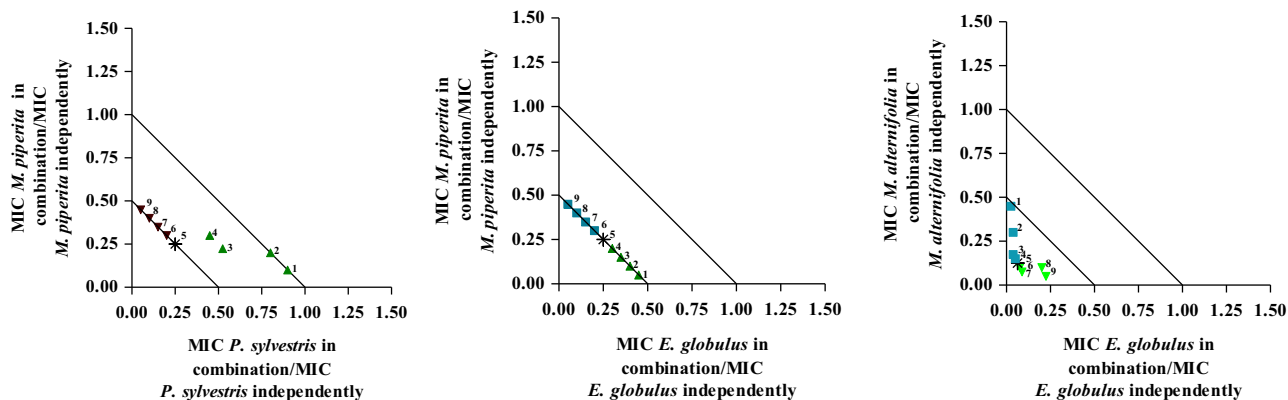


**Figure 1** Isobologram representation of essential oils in synergistic combination against *Propionibacterium acnes* (ATCC 11827). ▼ indicates *Cananga odorata*, ★ indicates *Commiphora myrrha*, ■ indicates *Juniperus virginiana*, ● indicates *Laurus nobilis*, ◆ indicates *Salvia lavandulifolia*, ■ indicates *Lavandula angustifolia* in majority volume. \* indicates equal volume of each essential oil. Points 1–9 correspond to Table III, providing the inhibitory concentrations of the essential oil ratios.

**Table III** The concentrations of essential oil and antimicrobial agent associated to the volume ratios studied against *Propionibacterium acnes* (ATCC 11827)

Plot number*	Concentrations of essential oils in combination			
	Volume ratio of essential oil 1 : essential oil 2	<i>Commiphora myrrha</i> and <i>Cananga odorata</i>	<i>Laurus nobilis</i> and <i>Juniperus virginiana</i>	<i>Lavandula angustifolia</i> and <i>Salvia lavandulifolia</i>
	μL	mg mL <sup>-1</sup>		
1	90 : 10	0.75	0.50	1.00
2	80 : 20	0.31	0.50	1.00
3	70 : 30	0.31	0.50	1.00
4	60 : 40	0.31	0.50	1.00
5	50 : 50	0.31	0.50	1.00
6	40 : 60	0.56	0.50	1.00
7	30 : 70	1.00	0.50	1.00
8	20 : 80	1.00	1.25	1.00
9	10 : 90	1.00	2.00	2.00

\*Number corresponding to isobologram matching the essential oil combination.



**Figure 2** Isobologram representations of leaf essential oils in combination against *Staphylococcus epidermidis* (ATCC 2223). ▼ indicates *Pinus sylvestris*, ▲ indicates *Mentha piperita*, ■ indicates *Eucalyptus globulus* and ▼ indicates *Melaleuca alternifolia*. \* indicates equal volume of each essential oil. Points 1–9 correspond to Table IV, providing the inhibitory concentrations of the essential oil ratios.

The connecting lines of the two axes indicate the individual doses, and the isobolograms were interpreted by inspecting the data points of the ratios. Where the data points fell beneath and inclusive of the 0.5 : 0.5 line, synergy was recorded. If the ratio points fell in the area between the 0.5 : 0.5 and 1 : 1 line, an additive interaction was observed. For data points above the 1 : 1 line and below and inclusive of the 4 : 4 line, a non-interactive (the combined effect favoured the MIC of the weaker oil) effect was observed. Antagonism (the combined effect resulted in an overall weakened MIC) is interpreted where points fall above the 4 : 4 line [37].

## Results and discussion

### Essential oil chemical composition

The results of the GC-MS profiling of a selection (not previously investigated in our other study [34]) essential oils were analysed and compared to literature (Table I) where the chemical profiles were identified. A discrepancy in the chemical profile of *Rosa damascena* Mill. (rose otto) was identified when compared to a previous study. According to Babu, Singh [38], phenyl ethyl alcohol was not reported as a major chemical constituent. This outcome may be due to the differences in harvesting, parts, origins and storage conditions of essential oils [39–41].

### Antimicrobial analysis of individual oils

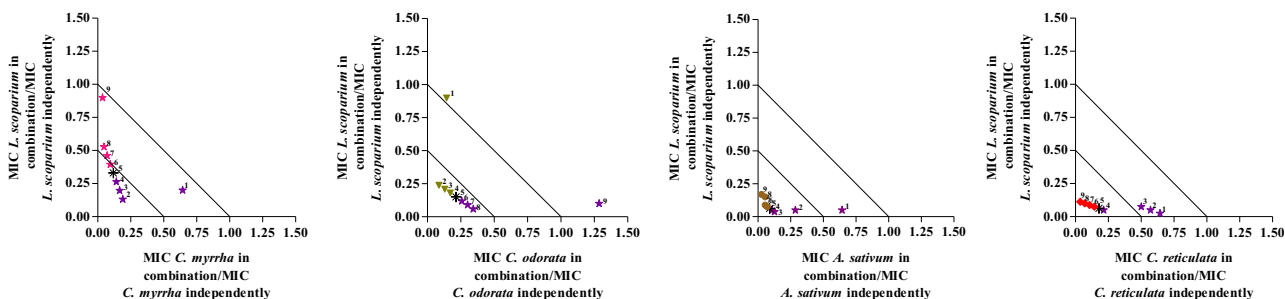
The MIC of 19 commercial essential oils was determined with results shown in Table I. The remainder of the sample oils has been previously investigated in our previous study [34]. From the results obtained, it was observed that *S. epidermidis* was inhibited at a noteworthy concentration (MIC 1.00 mg mL<sup>-1</sup> and less) by 13 of the 19 essential oils investigated, with *Vetiveria zizanioides* (vetiver), *Cinnamomum verum* J.Presl (cinnamon bark) and *Santalum austrocaledonicum* Vieill. (sandalwood) displaying the strongest activity with an MIC value of 0.25 mg mL<sup>-1</sup>. *Propionibacterium acnes* was found to be more susceptible to inhibition of the essential oils, with 18 of the 19 oils inhibiting the bacterium at a noteworthy concentration. *Nardostachys jatamansi* C.B.Clarke (spikenard) and *C. verum* displayed the strongest antimicrobial activity against *P. acnes* with MIC values of 0.19 mg mL<sup>-1</sup> and 0.13 mg mL<sup>-1</sup>, respectively.

The *Cinnamomum zeylanicum* Blume (cinnamon leaf) oil investigated in this study demonstrated higher inhibitory activity against

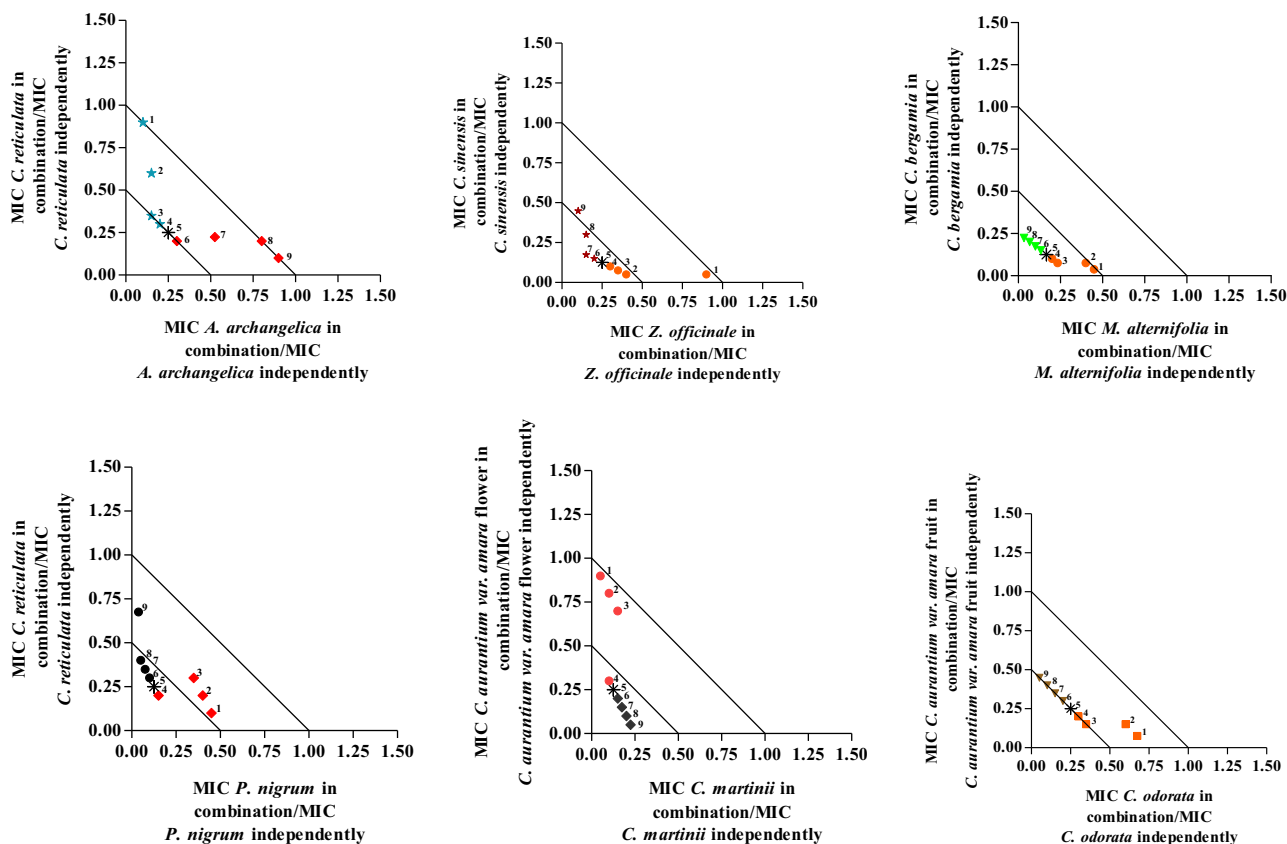
both acne pathogens, than the oil sample studied by Orchard, Sandasi [34]. This is most likely due to the higher eugenol content, a compound previously found to be responsible for antimicrobial activity [34]. The *C. verum* oil on the other hand is remarkably stronger at inhibiting the two acne pathogens than either of the *C. zeylanicum* species. This is most likely due to the presence of cinnamaldehyde, which appears to have an even stronger antimicrobial activity to that of eugenol, and could be confirmed by the noteworthy antimicrobial activity observed by Nuryastuti, van der Mei [42] against *S. epidermidis* by the major compound cinnamaldehyde contained in *C. burmannii* (cinnamon). *Cistus ladanifer* L. **2** was antimicrobially stronger than *Cistus ladanifer* **1** against both acne pathogens; however, this should not be recommended for acne treatment as noteworthy inhibition could only be observed against *P. acnes* (0.38–1.00 mg mL<sup>-1</sup>) and not against *S. epidermidis* (1.50–2.00 mg mL<sup>-1</sup>). *Cymbopogon nardus* (L.) Rendle displayed noteworthy antimicrobial activity against both the acne pathogens, and a previous study reported an MIC value of 0.13% against *P. acnes* [43]. Unfortunately, in this previous study, no GC-MS was included to allow for chemical comparison. *Matricaria recutita* L. (German chamomile) displayed noteworthy antimicrobial activity against both acne pathogens compared to the previously studied *A. nobilis* (MIC 1.00–2.00 mg mL<sup>-1</sup>), possibly making *M. recutita* a better chamomile species for treating acne. *Mentha spicata* L. (spearmint) appears to be a stronger antimicrobial than was observed for *Mentha piperita* L. (peppermint) [34] against *P. acnes*; however, both samples displayed moderate MIC values (2.00 mg mL<sup>-1</sup>) against *S. epidermidis*.

*Pelargonium graveolens* L'Hér. displayed stronger antimicrobial activity (0.50–1.00 mg mL<sup>-1</sup>) than the previously reported *Pelargonium odoratissimum* [Soland.] (1.00–1.25 mg mL<sup>-1</sup>) [34] against both acne pathogens. The *Rosa damascena* Mill. samples mostly displayed equal noteworthy antimicrobial activity when comparatively compared. Another rose species, *Rosa centifolia* L., was also previously reported to inhibit *P. acnes* at an MIC of 0.03%; however, no GC-MS data were included [44]. *Ocimum basilicum* L. was previously reported with an MIC value of 2.00 mg mL<sup>-1</sup> against both the acne pathogens [34]. The two *Ocimum tenuiflorum* L. (holy basil) samples in this study, however, inhibited *S. epidermidis* at a concentration of 1.00 mg mL<sup>-1</sup> and *P. acnes* at 0.19–0.50 mg mL<sup>-1</sup>, which may be attributed to the higher eugenol content, making this the preferred basil species for acne treatment.

*Origanum vulgare* L. (oregano) according to this study shows potential as an effective anti-acne agent supporting the results from



**Figure 3** Isobologram representations of essential oils in combination with *L. scoparium* against *Staphylococcus epidermidis* (ATCC 2223). ▼ indicates *Cananga odorata*, ★ indicates *Commiphora myrrha*, ◆ indicates *Leptospermum scoparium*, ● indicates *Citrus reticulata*, ◻ indicates *Allium sativum*. \* indicates equal volume of each essential oil. Points 1–9 correspond to Table IV, providing the inhibitory concentrations of the essential oil ratios.



**Figure 4** Isobologram representation of essential oils in combination against *Staphylococcus epidermidis* (ATCC 2223). ▼ indicates *Melaleuca alternifolia*, ★ indicates *Angelica archangelica*, ● indicates *Piper nigrum*, ◆ indicates *Citrus aurantium* var. *amara* flower, ● indicates *Cymbopogon martinii*, ▼ indicates *Cananga odorata*, ★ indicates *Zingiber officinale*, ◆ indicates *Citrus reticulata*, ● indicates *Citrus bergamia*, ● indicates *Citrus sinensis*, ■ indicates *C. aurantium* var. *amara* fruit majority volume. \* indicates equal volume of each essential oil. Points 1–9 correspond to Table IV, providing the inhibitory concentrations of the essential oil ratios.

a previous study against 22 *S. epidermidis* strains [45]. Both *Vetiveria* and *Santalum* species from this study and Orchard, Sandasi *et al.*, [34] appear to have excellent anti-acne potential. This was the first study to report on the antimicrobial activity of *M. spicata*, *C. nardus* and *O. tenuiflorum* against *S. epidermidis*, and *C. verum* and *O. vulgare* against *P. acnes*.

Antimicrobial studies on acne pathogens for *Abies koreana* E.H.Wilson (Korean fir) have been previously reported; however, this is the first report of *A. balsamea*. Other oils reported for the first time include *C. ladanifer*, *Hypericum perforatum* L. (St John's wort), *N. jatamansi*, *R. damascena* and *M. recutita*, against the two main acne pathogens.

#### Antimicrobial analysis of combinations

Previous combination studies on acne pathogens have been sorely neglected, and to the best of our knowledge, only one previous publication could be found against *S. epidermidis*. The combination included *Syzygium aromaticum* (L.) Merr. & L.M.Perry (clove) combined with *Rosmarinus officinalis* L. (rosemary) where an additive interaction was observed [46]. Table II represents the results for

the 408 investigated combinations (1 : 1) against *P. acnes* and *S. epidermidis*. Several additive and even synergistic combinations could be observed. Interestingly, the three synergistic combinations against *P. acnes*; *Commiphora myrrha* Engl. (myrrh) with *Cananga odorata* (Lam.) Hook.f. & Thomson (ylang ylang), *Laurus nobilis* L. (bay) with *Juniperus virginiana* L. (juniper) and *Lavandula angustifolia* Mill. (lavender) with *Salvia lavandulifolia* Spreng. (sage) were not specified in the aroma-therapeutic literature for acne treatment. No antagonism was observed against either pathogen and 167 combinations displayed noteworthy activity against both the acne pathogens. *Cananga odorata* was identified as being involved in synergy three times, once against *P. acnes* and twice against *S. epidermidis*. This was the only oil that was involved in synergistic combinations against both pathogens, even though interestingly it displayed poor individual antimicrobial activity when assayed singularly.

More than half (232 combinations) resulted in noteworthy antimicrobial activity against *P. acnes* and 209 combinations demonstrated noteworthy efficacy against *S. epidermidis*. The lowest MIC value ( $0.25 \text{ mg mL}^{-1}$ ), resulting from the combinations against *P. acnes*, was shown by *V. zizanioides* 1 with *C. verum*, *V. zizanioides* 2 with *C. verum* and *S. aromaticum* with *C. verum*, the

**Table IV** The concentrations of essential oil and antimicrobial agent associated to the volume ratios studied against *Staphylococcus epidermidis* (ATCC 2223)

Concentrations of essential oils in combination								
Volume ratio of essential oil 1 : essential oil 2	<i>Angelica archangelica</i> and <i>Citrus reticulata</i>	<i>Cananga odorata</i> and <i>Leptospermum scoparium</i>	<i>Citrus bergamia</i> and <i>Melaleuca alternifolia</i>	<i>Citrus reticulata</i> and <i>Piper nigrum</i>	<i>Citrus sinensis</i> and <i>Zingiber officinale</i>	<i>Cymbopogon martinii</i> and <i>Citrus aurantium var. amara</i> flower	<i>Citrus aurantium var. amara</i> fruit and <i>Cananga odorata</i>	
Plot number*	$\mu\text{L}$	$\text{mg mL}^{-1}$						
1	90 : 10	2.00	2.00	1.50	2.00	2.00	1.00	1.50
2	80 : 20	1.50	0.60	1.50	2.00	1.00	1.00	1.50
3	70 : 30	1.00	0.60	1.00	2.00	1.00	1.00	1.00
4	60 : 40	1.00	0.60	1.00	1.00	1.00	0.50	1.00
5	50 : 50	1.00	0.60	1.00	1.00	1.00	0.50	1.00
6	40 : 60	1.00	0.60	1.00	1.00	1.00	0.50	1.00
7	30 : 70	1.50	0.60	1.00	1.00	1.00	0.50	1.00
8	20 : 80	2.00	0.60	1.00	1.00	1.50	0.50	1.00
9	10 : 90	2.00	2.00	1.00	1.50	2.00	0.50	1.00

Concentrations of essential oils in combination								
Volume ratio of essential oil 1 : essential oil 2	<i>Eucalyptus globulus</i> and <i>Melaleuca alternifolia</i>	<i>Leptospermum scoparium</i> and <i>Allium sativum</i>	<i>Leptospermum scoparium</i> and <i>Commiphora myrrha</i>	<i>Leptospermum scoparium</i> and <i>Citrus reticulata</i>	<i>Mentha piperita</i> and <i>Eucalyptus globulus</i>	<i>Mentha piperita</i> and <i>Pinus sylvestris</i>		
Plot number*	$\mu\text{L}$	$\text{mg mL}^{-1}$						
1	90 : 10	1.00	1.00	1.00	1.00	1.00	2.00	
2	80 : 20	0.75	0.50	0.33	1.00	1.00	2.00	
3	70 : 30	0.50	0.25	0.33	1.00	1.00	1.50	
4	60 : 40	0.50	0.25	0.33	0.50	1.00	1.50	
5	50 : 50	0.50	0.25	0.33	0.50	1.00	1.00	
6	40 : 60	0.50	0.25	0.33	0.50	1.00	1.00	
7	30 : 70	0.50	0.25	0.33	0.50	1.00	1.00	
8	20 : 80	1.00	0.38	0.33	0.50	1.00	1.00	
9	10 : 90	1.00	0.38	0.50	0.50	1.00	1.00	

\*Number corresponding to isobologram matching the essential oil combination.

common oil being *C. verum*. The combinations of *Citrus aurantium* var. *amara* L. fruit (petitgrain) with *Santalum album* L. (sandalwood) and *V. zizanioides* **2** with *C. verum* displayed the most noteworthy MIC values ( $0.19 \text{ mg mL}^{-1}$ ) against *S. epidermidis*. Interesting to note is that *V. zizanioides* **2** with *C. verum* displayed the most noteworthy activity against both the acne pathogens. This is the first study to report on each of these combinations against acne pathogens.

The shaded results in Table II indicate combinations specified in the layman's aroma-therapeutic literature for acne [19–30]. Only a third of those combinations displayed noteworthy antimicrobial activity, and none displayed synergy. The selection of such combinations in aromatherapy, however, may be based on different trigger factors besides the antimicrobial activity in acne. There are four main triggers in acne; follicular hyperkeratinization, increase in sebum production, bacterial colonization within the follicle and inflammation. One oil may be selected for the antimicrobial activity, and another for the anti-inflammatory activity, which is plausible considering certain essential oils, such

as *Cymbopogon martinii* Stapf (palmarosa), have been proven to display anti-inflammatory activity [47–49]. The limitation of this, however, is that, although targeting two different trigger factors, if the combinations do not equate to noteworthy antimicrobial activity against the acne pathogens, it could lead to treatment failure and loss in confidence in the potential of the essential oils. This emphasizes the importance of using combinations, even if targeting two or three triggers, where both acne micro-organisms should be inhibited. These are also considerations that need to be made when selecting essential oils in cosmetic products for acne.

Different oil containing plant species were considered in the study to identify if common trends in antimicrobial activity exist in favouring a particular oil. *Ocimum tenuiflorum* (holy basil) was found to display higher antimicrobial activity than *O. basilicum*, allowing for a better *Ocimum* spp., for acne treatment. For the chamomile essential oils against *P. acnes*, *Anthemis nobilis* L. (Roman chamomile) resulted in more additive interactions than *M. recutita*; however, the latter contributes towards better antimicrobial



activity. Despite the combinations with the *Santalum* spp. and the *Vetiveria* spp. resulting in predominantly indifferent interactions, most appeared to consistently result in noteworthy MIC values. Both have been shown to display anti-inflammatory activity, and *V. zizanioides* has been mentioned as an oil with potential in the cosmetic industry [50–53].

For *Leptospermum scoparium* J.R.Forst. (manuka), synergy was observed when combined with other oils against *S. epidermidis* (four times), and the majority of the combinations with this oil displayed noteworthy antimicrobial activity against both acne pathogens. This oil has also been shown to display anti-inflammatory activity and has been noted as an oil to be recommended for medical cosmetology [54]. Ironically *M. alternifolia* is a popular essential oil in acne treatment, especially Australian *M. alternifolia*, yet *L. scoparium*, which is considered New Zealand's white tea tree, appears to be the more antimicrobially effective oil, individually and in combination for acne treatment. Furthermore, the pleasant aromatic odour would be advantageous in future cosmetic preparations. The lack of attention to this oil may be that it is one of fewer mentioned in the aroma-therapeutic literature [25, 27]. With the success shown in clinical studies of *M. alternifolia* [17, 31], one can already visualize the potential of *L. scoparium*. This is the first study to identify the effectiveness of this oil in acne combinations.

The 1 : 1 combinations that demonstrated synergy were further evaluated at different ratio combinations to determine whether different concentrations in the mixture could optimize the synergistic interactions observed. Figures 1–4 display the synergistic combinations at different ratio points (numbered 1–9) for each synergistic combination, and Table III (*P. acnes*) and Table IV (*S. epidermidis*) tabulate the concentrations and MIC values which correspond to the isobolograms.

Figure 1 shows the synergistic combinations against *P. acnes*. No pattern could be identified for either oil contributing more towards synergy against *S. epidermidis* and most of the interactions irrespective of the ratio are synergistic (Figure 2). The combinations with *L. scoparium* against *S. epidermidis* also do not follow any pattern to indicate which oil is preferable in the majority of the combinations (Figure 3). Seven synergistic combinations against *S. epidermidis* contained *Citrus* oils (Figures 3 and 4). Figure 4 displays six essential oil combinations with different *Citrus* species resulting in synergy. Synergy appeared to be predominantly dependent on the non-*Citrus* essential oil being in the majority for

synergy to occur. Four citrus species (*C. aurantium* L., *C. grandis* Hassk., *C. sinensis* Pers. and *C. limon* (L.) Burm.f.) has previously shown synergistic interactions with *L. angustifolia*, albeit against different pathogens (*S. aureus* and *C. albicans*) [33]. From these results, it would appear that the citrus species are worth taking note of when regarding essential oil combinations.

## Conclusion

With acne being one of the most popular uses for essential oils, and skin care products being a billion-dollar industry, the large body of work as presented here provides a scientific guide as to the appropriate selection of combinations for use in acne treatment. This study is the first to report on the majority of these essential oil combinations against the acne-inducing bacteria. Several promising oil combinations not previously mentioned in the aromatherapy literature are shown in this study, and the combinations generally include the essential oils *Commiphora myrrha* Engl. (myrrh), *L. scoparium*, *Pogostemon patchouli* Benth. (patchouli), *Santalum* and *Vetiveria* species. These oils should be strongly considered for future use in combination to treat acne.

This study highlights that certain essential oil species or chemotypes to preferable by used (e.g. *M. recutita* is preferred to *A. nobilis*, or *O. tenuiflorum* is preferred to *O. basilicum*) in aromatherapy; however, the different chemotypes must always be examined as this strongly affects the antimicrobial activity. Essential oil combinations are proven to have the potential to display noteworthy *in vitro* antimicrobial activity and may be beneficial in medical cosmetology use especially against acne-inducing bacteria.

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