

Rethinking Oral Infection Control: Antimicrobial Peptides and Essential Oils as Alternative Antibacterial Agents

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Rethinking Oral Infection Control: Antimicrobial Peptides and Essential Oils as Alternative Antibacterial Agents

Oral Enfeksiyonların Kontrolünü Yeniden Değerlendirmek: Alternatif Antibakteriyel Ajanlar Olarak Antimikrobiyal Peptitler ve Uçucu Yağlar

SUMMARY

Oral health has a direct impact on an individual's overall health status. Infections observed here not only affect individuals' quality of life but also decrease their productivity. Additionally, these infections can lead to systemic infections by affecting other parts of the body. Among the major causes that disrupt oral health are untreated dental caries and advanced periodontal diseases. Factors such as the loss of drug efficacy due to antimicrobial resistance, challenges in discovering new drug classes, and the limitation of existing treatment options due to observed side effects increase the need for new treatment strategies for the prevention and treatment of oral infections. The chemical composition of commercial essential oils (EO) was determined using gas chromatography-mass spectrometry (GC-MS). The antibacterial activities of antimicrobial peptides and essential oils were evaluated using the minimum inhibitory concentration method. Combinations of essential oils with antimicrobial peptides at a 1:1 ratio were prepared to investigate their efficacy. The main components of the essential oils were identified as carvacrol (82.675%) for *Thymus vulgaris* EO, eugenol (79.367%) for *Syzygium aromaticum* EO, menthol (47.199%) for *Mentha piperita* EO, and eucalyptol (63.642%) for *Eucalyptus globulus* EO. Among the essential oils, *T. vulgaris* exhibited the best antibacterial effect. The efficacy of combinations varied among the test bacteria. The most effective combination was determined with peppermint essential oil. Peppermint essential oil reduced the minimum inhibitory concentration value of both antimicrobial peptides by fourfold. The combination of lactoferrin and thyme essential oil led to a decrease in efficacy against all test bacteria. Although antimicrobial peptides alone showed limited activity, their combination with certain essential oils enhanced their antibacterial effectiveness against oral pathogens. These findings suggest that natural agent combinations exhibit species-specific efficacy and hold promise for the development of alternative therapeutic strategies.

Keywords: Essential oils, Antimicrobial peptides, pathogens, oral, thymus.

ÖZ

Ağız sağlığı, bireylerin genel sağlık durumunu doğrudan etkiler. Bu bölgede görülen enfeksiyonlar yalnızca bireylerin yaşam kalitesini azaltmakla kalmaz, aynı zamanda üretkenliklerini de düşürür. Ayrıca bu enfeksiyonlar, vücudun diğer bölgelerini etkileyerek sistemik enfeksiyonlara yol açabilir. Ağız sağlığını bozan başlıca nedenler arasında tedavi edilmemiş diş çürükleri ve ileri periodontal hastalıklar yer alır. Antimikrobiyal direnç nedeniyle ilaç etkinliğinin azalması, yeni ilaç sınıflarının keşfindeki zorluklar ve mevcut tedavi seçeneklerinin yan etkiler nedeniyle sınırlı kalması, oral enfeksiyonların önlenmesi ve tedavisi için yeni stratejilere duyulan gereksinimi artırmaktadır. Ticari uçucu yağların (EO) kimyasal bileşimi gaz kromatografisi-kütle spektrometresi (GC-MS) yöntemiyle belirlenmiştir. Antimikrobiyal peptitlerin ve uçucu yağların antibakteriyel aktiviteleri minimum inhibitör konsantrasyon (MIC) yöntemiyle değerlendirilmiştir. Etkinliklerini incelemek için uçucu yağlar ve antimikrobiyal peptitler 1:1 oranında kombine edilmiştir. Uçucu yağların başlıca bileşenleri; *Thymus vulgaris* için karvakrol (%82,675), *Syzygium aromaticum* için öjenol (%79,367), *Mentha piperita* için mentol (%47,199) ve *Eucalyptus globulus* için ökaliptol (%63,642) olarak tanımlanmıştır. Uçucu yağlar arasında en güçlü antibakteriyel etki *T. vulgaris*'te gözlenmiştir. Kombinasyonların etkinliği test edilen bakterilere göre değişiklik göstermiştir. En etkili kombinasyon nane uçucu yağı ile elde edilmiştir. Nane uçucu yağı, her iki antimikrobiyal peptitin minimum inhibitör konsantrasyon değerini dört kat azaltmıştır. Laktoferrin ve kekik uçucu yağı kombinasyonu ise tüm test bakterilerinde etkinlik azalmasına neden olmuştur. Antimikrobiyal peptitler tek başına sınırlı aktivite göstermesine rağmen, belirli uçucu yağlarla kombinasyonları oral patojenlere karşı antibakteriyel etkinliği artırmıştır. Bu bulgular, doğal ajan kombinasyonlarının tür-spesifik etkinlik sergilediğini ve alternatif tedavi stratejilerinin geliştirilmesi için umut vadettiğini göstermektedir.

Anahtar Kelimeler: Uçucu yağlar, antimikrobiyal peptitler, patojenler, oral, kekik.

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INTRODUCTION

The general health status of individuals is directly linked to oral health. A deterioration in oral health can negatively impact individuals' quality of life by affecting their daily functioning physically, emotionally, socially, and psychologically (Peres et al., 2019). Moreover, oral diseases have been associated with systemic conditions such as cardiovascular diseases, rheumatoid arthritis, and osteoporosis (Palombo, 2011).

The World Health Organization (WHO) reports that approximately 50% of the global population is affected by one or more forms of oral diseases, among which dental caries is identified as the most common oral health issue (Jain et al., 2024; Kassebaum et al., 2017). *Streptococcus mutans* is considered the primary etiological agent responsible for dental caries, while species of *Lactobacillus*, such as *L. acidophilus* and *L. casei*, are implicated in the development and progression of carious lesions. Another bacterium present in the oral cavity, *Enterococcus faecalis*, is frequently associated with endodontic infections (Alghamdi & Shakir, 2020; Wen et al., 2022).

Reducing the oral microbial load decreases the risk of infection. Although daily tooth brushing is a recommended mechanical cleaning method, it cannot reach all colonization sites of oral bacteria. Chemical mouthwashes, another group of hygiene products, have limitations such as poor long-term usability due to mucosal absorption, potential discoloration of teeth and tongue, and risk of allergic reactions (Balapanavar et al., 2013; Batista et al., 2014).

Antimicrobial peptides (AMPs) are naturally occurring molecules found across all life forms, from prokaryotes to humans. Also referred to as host defense peptides, AMPs are key components of the innate immune system that protect the host from infections in higher organisms (Mahlapuu et al., 2016). Due to their short amino acid sequences, AMPs are

notable for being easy to synthesize, for exerting broad-spectrum antimicrobial activity, and for degrading into non-toxic products such as amino acids (Rima et al., 2021).

Plants have been used for medicinal purposes for thousands of years. Natural products derived from medicinal plants form the basis for the development of numerous drugs. Essential oils obtained from plants are widely used in oral care products due to both their antimicrobial properties and their aromatic characteristics. Their low toxicity, pharmacological effects, and economic feasibility are among the main reasons for their frequent use in oral formulations (Nagy-Bota et al., 2021). Essential oils of thyme, mint, eucalyptus, and clove are widely used herbal products with various applications in the general population.

Given the limitations of current oral hygiene products in preventing oral infections and the public health significance of these infections, there is a clear need for safer and more effective products derived from natural sources (Palombo, 2011).

MATERIALS AND METHODS

Bacterial strains and growth conditions

In this study, *Streptococcus mutans* ATCC 25175, *Lactobacillus casei* RSKK 06029, and *Lactobacillus acidophilus* ATCC 11975 test bacteria were incubated on Brain Heart Infusion (BHI) and de Man Rogosa Sharp (MRS) agar media, respectively, at 37°C in a 5% CO₂ environment for 24-48 hours. The *Enterococcus faecalis* ATCC 29212 standard bacterium was incubated aerobically on BHI agar medium at 37°C for 24 hours.

Antimicrobial peptides and essential oil

In this study, commercially obtained human cathelicidin LL-37 (MedChemExpress) and human lactoferricin (Anaspec) antimicrobial peptides were used. The essential oils of *Thymus vulgaris* L. (TEO), *Mentha piperita* L. (MEO), *Eucalyptus globulus* Labill. (EEO), and *Syzygium aromaticum* L. (SEO) were used, obtained commercially.

GC and GC/MS analysis of essential oils

GC/MS analysis of the essential oil samples was performed using the Shimadzu GCMS-QP2020NX system. The analysis was performed using an Inert-Cap WAX column (30.0 m × 0.25 mm × 0.25 μm) (GL Sciences Inc., Japan) and helium as the carrier gas (1.78 ml min⁻¹). The operating conditions were: The oven temperature was set at 40°C for 5 min after injection, then increased to 240°C with a heating ramp of 4°C/min for 10 min, and then increased to 240°C with a heating ramp of 4°C/min without holding; the injector and detector (FID) temperatures were 250°C; the split ratio was set at 10:1; the injection volume was 1.0 μl. MS conditions were as follows: ion source temperature 200°C; interface temperature 250°C; mass range 35-550 atomic mass units. The compounds were identified by comparing their relative retention indices and mass spectra with the corresponding literature (Bathily et al., 2023; Bota et al., 2022; Dolghi et al., 2022; Hamdoon et al., 2024) and by comparing their mass spectra with the Wiley and NIST libraries. The percentages of the components were calculated from the GC peak areas using the normalization method.

Antibacterial activity

The Minimum Inhibitory Concentration (MIC) values of the essential oils and antimicrobial peptides against the test bacteria were determined by the broth microdilution method. Essential oils were prepared as stock solutions at 100 mg/ml in 10% DMSO and 0.1% Tween 80, while antimicrobial peptides were prepared at 1 mg/ml in sterile distilled water. In this study, Mueller-Hinton Broth was used for *E. faecalis*, BHI Broth for *S. mutans* (Galvão et al., 2012), and MRS Broth for *L. acidophilus* and *L. casei* (Anisimova & Yarullina, 2019). Serial two-fold dilutions of the samples were prepared in suitable media. Test bacteria were prepared from overnight subcultures, and the final test concentration of bacteria was adjusted to 5x10⁵ CFU/mL. Plates were incubated according to the requirements of the test bacteria. At the end of the incubation period, the concentration of the last well showing no growth was recorded as the MIC value (mg/ml). In the study, a solvent con-

taining 10% DMSO and 0.1% Tween 80 was used as a negative control, and ciprofloxacin (Merck) was used as a positive control. All experiments were performed in triplicate.

Antibacterial activity of antimicrobial peptide-essential oil combinations

Effective essential oils with antibacterial activity were mixed at a 1:1 ratio with antimicrobial peptides at stock concentration, and the antibacterial efficacy of this prepared mixture was investigated using the method described above.

RESULTS AND DISCUSSION

The general health status of individuals is associated with oral health. Oral diseases reduce the quality of life and working capacity of individuals. Oral infections affect daily life with symptoms such as pain and discomfort and have also been linked to systemic infections that impact other parts of the body. Worldwide, oral infections have a high prevalence, and there is a need for preventive measures against these infections (Palombo, 2011; Peres et al., 2019).

The results of combination experiments involving antimicrobial peptides, which did not exhibit antibacterial activity at the studied concentrations (250-1.95 μg/ml), were interpreted based on essential oils for which MIC values were determined. Due to the inability to detect MIC values for antimicrobial peptides, synergy tests involving combinations at different concentrations could not be conducted (Black et al., 2023). In this study, combinations of essential oils and antimicrobial peptides at a 1:1 ratio from stock concentrations were prepared for activity tests. In the antibacterial activity tests, the combinations were studied with TEO, MEO, and SEO, which demonstrated individual effectiveness.

Characterization of essential oils

The characterization results of the commercially obtained essential oils are shown below (Table 1.). The main components of the essential oils were identified as carvacrol for *Thymus vulgaris* EO, eugenol for *Syzygium aromaticum* EO, menthol for *Mentha piperita* EO, and eucalyptol for *Eucalyptus globulus* EO.

Table 1. Composition of the essential oil samples

NO	RRI	Compound	% Amount			
			<i>T. vulgaris</i> EO	<i>S. aromaticum</i> EO	<i>M. piperita</i> EO	<i>E. globulus</i> EO
1.	1106	α -Pinene	-	-	-	21.533
2.	1171	D-Limonene	-	-	2.390	-
3.	1179	Eucalyptol	-	-	5.095	-
4.	1233	dl-Limonene	-	-	-	4.749
5.	1240	Eucalyptol	-	-	-	63.642
6.	1270	γ -Terpinene	2.587	-	-	-
7.	1291	<i>p</i> -Cymene	5.207	-	-	1.284
8.	1452	<i>I</i> -Menthone	-	-	27.120	-
9.	1474	Menthofuran	-	-	2.234	-
10.	1480	<i>p</i> -Menthone	-	-	4.348	-
11.	1551	Linalool	6.818	-	-	-
12.	1558	Menthyl acetate	-	-	5.338	-
13.	1592	Caryophyllene	-	-	2.783	-
14.	1593	(+)-Neomenthol	-	-	3.493	-
15.	1599	<i>trans</i> -Caryophellene	-	5.932	-	-
16.	1608	Aromadendrene	-	-	-	4.435
17.	1641	Menthol	-	-	47.199	-
18.	1647	Alloaromadendrene	-	-	-	0.972
19.	1658	<i>trans</i> -Pinocarveol	-	-	-	0.908
20.	1671	α -Humulene	-	0.667	-	-
21.	1698	α -Terpinyl acetate	-	-	-	2.477
22.	1728	β -Bisabolone	2.713	-	-	-
23.	2180	Eugenol	-	79.367	-	-
24.	2223	Carvacrol	82.675	-	-	-
25.	2267	Eugenyl acetate	-	14.034	-	-
		TOTAL	100	100	100	100

Antibacterial activity

The effects of essential oils and antimicrobial peptides on test bacteria were determined using the broth microdilution method. Essential oils were tested at concentrations ranging from 250 to 0.195 μ g/ml, and antimicrobial peptides at concentrations from 250 to 0.001 μ g/ml. At the end of the incubation period, the lowest concentration with no observed bacterial growth was recorded as the MIC value (Table 2.). Among the essential oils, TEO demonstrated the highest activity against *L. casei* RSKK 06029 at a concentration of 0.78 mg/ml. Antimicrobial peptides showed no antibacterial activity against the test bacteria at the tested concentrations. Additionally, the

mixture of 10% DMSO and 0.1% Tween 80 used for dispersing the essential oils exhibited no antibacterial effect on the test bacteria.

In the study by de Oliveira Carvalho et al. (2020), which evaluated the efficacy of essential oils against oral pathogens, MIC values of SEO were reported as 0.315 mg/ml against *S. mutans* and 1.25 mg/ml against *E. faecalis*, and MIC values of TEO were reported as 0.625 mg/ml for these bacteria. Elgamily et al. (2019) reported MIC values of SEO as 15.56 mg/ml and 13.92 mg/ml against *S. mutans* and *L. acidophilus*, respectively. In another study, MIC values of SEO were reported as 2 mg/ml against *S. mutans*, 1 mg/ml against *L. casei*, and 4 mg/ml against *E. faecalis* (Agu-

iar et al., 2013). In our study, MIC values of SEO were determined as 3.12 mg/ml against *S. mutans*, 12.5 mg/ml against *E. faecalis*, and 12.5 mg/ml against *L. acidophilus*.

Fani & Kohanteb (2017) reported the MIC value of TEO as 1.9 µg/ml against clinical *S. mutans* isolates. In another study, an MIC value of 50 mg/ml was reported against the standard strain of *S. mutans* (Figueira et al., 2020). In the study by de Oliveira Carvalho et al. (2020), the MIC values of TEO were reported as 0.625 mg/ml against *S. mutans* and *E. faecalis*. In our study, MIC values of TEO were determined as 1.56 mg/ml against *S. mutans* and *E. faecalis*. It is thought that this discrepancy in MIC values may be due to the bacterial strains or the components of the essential oil used.

Goldbeck et al. (2014) reported an MIC value of 0.013 mg/ml for EEO against *S. mutans*, attributing its effect to the 1,8-cineole component. In another study, Harkat-Madouri et al. (2015) reported an MIC value of 11.4 mg/ml for EEO. In our study, EEO showed no antibacterial effect on the test bacteria at the tested concentrations.

Golestannejad et al. (2017) reported an MIC value of 10.5 µg/ml for MEO against *S. mutans* test bacteria. In another study, the MIC values of MEO were reported as 0.63 mg/ml against *S. mutans*, 0.27 mg/ml against *L. acidophilus*, and 0.23 mg/ml against *E. faecalis* (Nikolić et al., 2014). In our study, the MIC values of MEO were determined as 1.56 mg/ml against *S. mutans* and *L. acidophilus*, and 25 mg/ml against *E. faecalis*.

The antibacterial efficacy of essential oils shows significant variability in the literature. The efficacy of these oils depends on the composition and concentrations of the chemical molecules they contain.

In their study investigating the antibacterial activities of LL-37 and human lactoferricin against oral pathogens, Wuerschling et al. (2021) reported that exposure to LL-37 inhibited the growth of co-cultured bacteria by 11%-65%, and lactoferricin exposure inhibited growth by 52%-64%. In our study, no MIC value was detected against *S. mutans* for antimicrobial peptides used at the same concentrations.

Schmidtchen et al. (2002) examined the interactions of LL-37 with various pathogenic bacteria, including *E. faecalis*, reported that *E. faecalis* proteases degrade the structure of LL-37, preventing the peptide from binding to the cell and causing it to lose its effectiveness. Contrary to this study, Lima et al. (2017), in a study on endodontic infection agents, reported that LL-37 had an MIC concentration of 256 µg/ml against *E. faecalis*, and at a concentration of 128 µg/ml, it inhibited bacterial growth by 54%. The degradation of LL-37 by *E. faecalis* is likely dose-dependent. In our study, LL-37 showed no antibacterial activity against *E. faecalis* at the tested concentrations.

Enigk et al. (2020) evaluated the efficacy of five antimicrobial peptides against various pathogenic bacteria using the agar dilution method, and reported that LL-37 and lactoferrin, a precursor molecule of lactoferricin, did not affect the growth of *E. faecalis* and *S. mutans* at concentrations of 0.125-8 µg/ml. In our study, the broth microdilution method was used for the MIC test of antimicrobial peptides, and no efficacy was observed against *E. faecalis* and *S. mutans* at concentrations ranging from 250-1.95 µg/ml.

In the study by Ouhara et al. (2005), which evaluated the efficacy of antimicrobial peptides on cariogenic bacteria, two different MIC methods were used. The first method involved spreading bacteria on an agar plate after a 2-hour exposure to various concentrations of antimicrobial peptides, as reported by Midorikawa et al. (2003). In the other method, bacterial cultures were incubated with antimicrobial peptide dilutions prepared in bovine serum albumin and acetic acid phosphate buffer, as reported by Wu & Hancock (1999). Using the first method, they reported that LL-37 inhibited the growth of *S. mutans* by 80.1% and *L. casei* by 45.9% at a concentration of 1 mg/ml. Using the other method, the MIC values of LL-37 were determined as 25 µg/ml against *S. mutans* and 50 µg/ml against *L. casei*.

In our study, further research is required to investigate the growth inhibition effects of antimicrobial peptides on test bacteria, for which no MIC values were determined.

Table 2. MIC test results of essential oils and antimicrobial peptides.

		Standard Strain			
		<i>E. faecalis</i> ATCC 29212	<i>L. acidophilus</i> ATCC 11975	<i>L. casei</i> RSKK 06029	<i>S. mutans</i> ATCC 25175
Essential Oils (mg/ml)	TEO	1.56	3.15	0.78	1.56
	MEO	25	1.56	1.56	1.56
	SEO	12.5	12.5	6.25	3.12
	EEO	-	-	-	-
Antimicrobial Peptides (µg/ml)	LL-37	-	-	-	-
	Laktoferricin	-	-	-	-
Control	Ciprofloxacin (µg/ml)	2	128	8	2
	Solvent	-	-	-	-

Results of antibacterial activity tests for combinations

To evaluate the combined effects, stock concentrations of essential oils and antimicrobial peptides were mixed in equal ratios (1:1), and dilutions were prepared from this mixture. Since MIC values for antimicrobial peptides alone were not observed at the tested concentrations, synergy testing was not conducted, and the results were interpreted based on the essential oils.

The presence of LL-37 (Table 3.):

- Increased the MIC value of thyme essential oil against *L. casei* RSKK 06029 by 4-fold.
- Increased the MIC value of peppermint essential oil by 8-fold against the same bacterium.

- Reduced the MIC value of peppermint essential oil by 4-fold against *E. faecalis* ATCC 29212.
- Reduced the MIC value of clove essential oil by 4-fold against *L. acidophilus* ATCC 11975

The presence of lactoferricin (Table 4.):

- Increased the MIC values of thyme essential oil for all test bacteria.
- Increased the MIC value of clove essential oil by 4-fold against *L. casei* RSKK 06029.
- Reduced the MIC value of peppermint essential oil by 4-fold against *E. faecalis* ATCC 29212.

Table 3. MIC values (mg/ml) of LL-37 and essential oil combinations

	TEO		MEO		SEO	
	A	C	A	C	A	C
<i>E. faecalis</i> ATCC 29212	1.56	3.12	25	6.25	12.5	6.25
<i>L. acidophilus</i> ATCC 11975	3.12	3.12	1.56	3.12	12.5	3.12
<i>L. casei</i> RSKK 06029	0.78	3.12	1.56	12.5	6.25	6.25
<i>S. mutans</i> ATCC 25175	1.56	1.56	1.56	3.12	3.12	1.56

*A: Alone, C: Combination

Table 4. MIC values (mg/ml) of lactoferricin and essential oil combinations

	TEO		MEO		SEO	
	A	C	A	C	A	C
<i>E. faecalis</i> ATCC 29212	1.56	>12.5	25	6.25	12.5	12.5
<i>L. acidophilus</i> ATCC 11975	3.12	>12.5	1.56	1.56	12.5	12.5
<i>L. casei</i> RSKK 06029	0.78	>12.5	1.56	1.56	6.25	12.5
<i>S. mutans</i> ATCC 25175	1.56	12.5	1.56	3.12	3.12	12.5

*A: Alone, C: Combination

Moon et al. (2011) evaluated the efficacy of SEO alone and in combination with antibiotics against oral pathogenic bacteria. In the study, the MIC value of SEO was reported as 0.2 mg/ml against *S. mutans*, and the MIC values of its combinations with ampicillin and gentamicin were each reported as 0.05 mg/ml. In our study, the MIC value of SEO against *S. mutans* was reduced 2-fold with the LL-37 combination, while it increased 4-fold with the lactoferricin combination.

In our study, the combinations of MEO with LL-37 and lactoferricin reduced the MIC value of MEO by 4-fold against *E. faecalis*. Furthermore, the LL-37 combination reduced the MIC value of clove essential oil by 4-fold against *L. acidophilus*.

The LL-37 combination increased the MIC value of TEO by 4-fold against *L. casei* and the MIC value of MEO by 8-fold. The lactoferricin combination reduced the antibacterial activity of TEO against all test bacteria. Additionally, the lactoferricin combination increased the MIC value of SEO by 4-fold against *S. mutans*.

In the peptide and essential oil combinations prepared in the study, both increases and decreases in the MIC values of essential oils were observed in the presence of antimicrobial peptides, depending on the bacterial species. Particularly, in the combinations of MEO with LL-37 or lactoferricin peptides, a 4-fold reduction in MIC values against *E. faecalis* was detected, indicating a notable increase in activity. In contrast, a strong antagonistic effect was found in the combi-

nation of lactoferricin with TEO, where activity decreased in all tested bacteria. The data obtained from this study show that essential oils and antimicrobial peptides have a high interaction potential. At the same time, the species-specific nature of these interactions indicates the necessity of prior evaluation for therapeutic applications.

The mechanisms underlying the enhancing or reducing effects of antimicrobial peptides on the activities of essential oils may depend on various factors. For example, activity enhancement may occur due to essential oils disrupting the bacterial cell membrane, increasing permeability, and allowing peptides to reach intracellular targets. Conversely, activity reduction may develop when essential oil components affect peptide stability and structural conformation. In conclusion, further studies are needed to fully elucidate the underlying mechanisms. A literature review revealed no studies evaluating the activities of antimicrobial peptides and essential oil combinations. In this respect, the results obtained from our study will contribute to the literature.

CONCLUSION

In this study, the effects of antimicrobial peptides and essential oils on oral pathogens were evaluated both individually and in combination at stock concentrations. While the antimicrobial peptides did not exhibit antibacterial activity at the tested concentrations when used alone, their efficacy appeared to increase in the presence of certain essential oils. Moreover, it was determined that the effectiveness of the combina-

tions varied depending on the bacterial species. These variations in activity highlight the need for a detailed investigation into the interactions between essential oils and peptides. In this context, evaluating combinations of natural agents may represent an important step toward the development of alternative therapeutic approaches.

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AUTHOR CONTRIBUTION STATEMENT

MSK: Conceptualization, Data curation, Formal analysis, Writing – original draft. NA: Methodology, Project administration, Writing – review and editing. SAE: Formal analysis, Methodology, Validation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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