



ORIGINAL ARTICLE / ÖZGÜN MAKALE

## Effects of Eucalyptus Essential Oil in Post-COVID Syndrome: A Pilot Study

### Post-COVID Sendromunda Okaliptüs Uçucu Yağının Etkileri: Pilot Çalışma

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#### Abstract

**Objective:** Post-COVID syndrome is the persistence of signs and symptoms that develop during or after COVID-19 infection for longer than 12 weeks, which cannot be explained by an alternative diagnosis. This study aimed to examine the effects of eucalyptus (*Eucalyptus globulus*) aromatherapy oil on dyspnea, back pain, and anxiety in patients with post-COVID syndrome.

**Methods:** The study included patients diagnosed with post-COVID syndrome at the chest diseases outpatient clinic of Adana City Training and Research Hospital. Before and after eucalyptus oil application, as components of post-COVID syndrome, dyspnea was evaluated using the modified Medical Research Council (mMRC) scale, back pain using the Visual Analog Scale (VAS), and anxiety using the Beck Anxiety Inventory (BAI).

**Results:** A total of 15 individuals, of whom 11 were female (73.3%) and 4 were male (26.7%), were included in the study. The mean age of the patients was 45.7±10.7 years, and the mean body mass index was 24.7±3.4. The mean post-treatment values of mMRC, VAS, and BAI statistically significantly decreased compared to the pre-treatment evaluation.

**Conclusion:** Eucalyptus aromatherapy oil inhalation was found to be effective in recovery from post-COVID syndrome symptoms, such as dyspnea, back pain, and anxiety, which affect many people across the world and can cause labor and financial losses. Therefore, we recommend considering the use of this aromatherapy oil in the complementary treatment and follow-up of these patients.

**Keywords:** Post-COVID Syndrome, Eucalyptus Aromatherapy Oil, Dyspnea, Pain, Anxiety

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**Öz**

**Amaç:** Post covid sendromu Covid-19 enfeksiyonu sırasında veya sonrasında gelişen 12 haftadan uzun süren ve alternatif bir tanı ile açıklanamayan belirti ve semptomlardır. Çalışmamızın amacı post covid sendromunda nefes darlığı, sırt ağrısı, anksiyete üzerine okaliptus (Eucalyptus globulus ) aromaterapik yağının etkilerini incelemektir.

**Yöntem:** Adana Şehir Eğitim ve Araştırma Hastanesi Göğüs Hastalıkları polikliniğinde post covid sendrom tanısı alan hastalara uygulama öncesi ve 4 hafta sonrasında post covid sendrom bileşenlerinden olan nefes darlığı semptomunun takibi amacı ile mMRC (Modifiye Medical Research Council) skalası, sırt ağrısının takibi için VAS ağrı skalası, anksiyete şiddeti takibi için Beck Anksiyete Ölçeği uygulandı. Veriler uygun veri tabanında analiz edildi.

**Bulgular:** Çalışmamıza 11'i kadın ( %73.3) , 4'ü erkek (%26.7) olmak üzere toplam 15 kişi dahil edildi. Hastaların ortalama yaşı 45.7 ( +- 10.7), VKİ 37 ( +-4,4) idi. Tedavi öncesi ve sonrası mMRC, VAS, Beck anksiyete ölçeği değerlerinin ortalamaları karşılaştırıldığında istatistiksel olarak anlamlı düzeyde azalma saptandı.

**Sonuç:** Dünya üzerindeki birçok kişiyi etkileyen, işgücü ve mali kayıplara da neden olabilen post covid sendromu semptomlarından nefes darlığı, sırt ağrısı, anksiyete üzerine inhale okaliptus aromaterapik yağı iyileşmede etkili bulunmuş olup, bu hastaların tedavi ve takibinde göz önünde bulundurulması önerilir.

**Anahtar Kelimeler:** Post covid sendromu, okaliptus aromaterapik yağı, dispne, ağrı, anksiyete

**INTRODUCTION**

Due to the first pandemic of the 21st century, more than 633 million people across the world were diagnosed with coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus as of November 2022. Approximately six million cases resulted in death (1).

Many pharmacological treatments have been used since the beginning of the pandemic, but only few have been able to increase survival and prevent the development of sequelae or persistent symptoms. Unfortunately, even with no more new cases being reported and global vaccination implementation, the consequences of the COVID-19 pandemic will not be completely resolved. In particular, the long-term effective management of the effects of post-COVID syndrome is a challenge that requires increased awareness. Post-COVID syndrome, also known as long-term COVID, is defined as signs and symptoms consistent with COVID-19 that develop during or after

active infection lasting for more than 12 weeks without any possible explanation by an alternative diagnosis (National Institute for Health and Care Excellence. SIGN . Royal College of General Practitioners COVID-19 Guideline Scope). Although the prevalence of post-COVID syndrome is not clearly known, symptoms persisting after the disease have been described, with an estimated rate of 13.7% according to the data of the UK Office for National Statistics (Prevalence of Ongoing Symptoms Following Coronavirus (COVID-19) Infection in the). Accordingly, post-COVID syndrome symptoms include fatigue, headache, dyspnea, joint and muscle pain, anxiety, cognitive impairment, depression, skin rashes, and gastrointestinal complaints (2).

In the acute and post-COVID syndrome process, numerous treatment options have been offered, and new treatments have been sought. During this period, as in the past, essential oils have also been utilized in terms of their aromatherapeutic effects. An example is eucalyptus oil, which has been

frequently used by various civilizations and communities across the world since ancient times. This is an essential oil obtained by steam distillation from the leaves of different eucalyptus species. It has a characteristic, aromatic, camphor-like odor, light yellow color, and refreshing and burning taste similar to camphor. This oil contains a large quantity (at least 70%) of 1,8-cineol (eucalyptol),  $\alpha$ -pinene, phellandrene in very little amount, and other terpenes. When the antibacterial properties of *Eucalyptus globulus* essential oil were examined against 15 gram-positive and gram-negative bacteria, it was determined that this oil was very effective against *Bacillus anthracis*, *Bacillus subtilis*, and *Micrococcus glutamicus* (3). Various studies have also shown that due to their antiviral (4) and anti-inflammatory (5) activities, eucalyptus oil and its metabolites can be used against COVID-19 (6).

In this study, we examined the effects of *E. globulus* aromatherapeutic oil on the symptoms of post-COVID syndrome, such as dyspnea, back pain, and anxiety, representing the long-term effects of COVID-19.

## METHOD

Male and female patients aged over 18 years, who presented to the physiotherapy and rehabilitation outpatient clinic of Adana City Training and Research Hospital with back pain and were followed up in the chest diseases outpatient clinic with the diagnosis of post-COVID syndrome, were included in the study. Patients with a history of any chronic disease, cancer, and infection and pregnant and lactating women were excluded from the study. The sample consisted of 15 patients that were recommended aromatherapeutic eucalyptus oil (*E. globulus*) (product license/permit approval code: 008821—Istanbul Provincial Directorate of Agriculture) due to post-COVID syndrome. The analysis of the components of *E. globulus* oil used by the patients is given in Table 1.

The patients were asked to prepare the essential eucalyptus oil mixture by dropping 1 ml of eucalyptus oil into 10 ml of fixed oil (olive oil). They were recommended to apply three drops of this mixture on the wrist and inhale it from a 2-cm distance for five minutes twice a day. Before and at four weeks after this application, the patients' post-COVID syndrome symptoms were evaluated using the modified Medical Research Council (mMRC) for dyspnea, the

Visual Analog Scale for back pain, and the Beck Anxiety Inventory (BAI) for anxiety.

**Table 1. Components of Eucalyptus globulus oil used by the patients**

Component	Ratio (%)
<i>1,8-Cineole</i>	73.687
<i>Alpha-Pinene</i>	16.891
<i>Trans-pinocarveol</i>	1.336
<i>P-cymene</i>	1.330
<i>Alpha-terpineol</i>	0.599
<i>Beta-myrcene</i>	0.100
<i>Gamma-Terpinene</i>	0.309
<i>l-Phellandrene</i>	0.154
<i>Isovaleric acid, isopentyl ester</i>	0.132
<i>2-Ethylfuran</i>	0.411
<i>Beta-Pinene</i>	0.364
<i>Alloaromadendrene</i>	1.621
<i>Alpha-terpinolene</i>	1.154
<i>Aromadendrene</i>	0.314
<i>4-terpineol</i>	0.262
<i>Trans-p-Mentha-1(7),8-dien-2-ol</i>	0.131
<i>Alpha gurjunene</i>	0.258
<i>Ledene</i>	0.792
<i>Viridiflorol</i>	0.160

mMRC questions the perception of dyspnea during activities of daily living from a scale of 0 indicating no dyspnea to 4 indicating severe dyspnea (7). The VAS pain score is evaluated from 0 (no pain) to 10 (worst pain) (8). BAI consists of 21 questions used to determine the level of anxiety experienced within the past week. A score of less than 21 points in this scale indicates mild anxiety, 22-35 points moderate anxiety, and 35 points severe anxiety (9).

Statistical analyses were performed using SPSS v. 25.0 software package. Whether the data were suitable for a normal distribution was evaluated with the Shapiro-Wilk test. The mean and standard deviation values of age, gender, and body mass index (BMI) were determined using descriptive analysis methods. The pre- and post-treatment values were interpreted using the Wilcoxon

and Paired Sample T test. The effect size was calculated according to the test used (10). Values with a P value of less than 0.05 were considered statistically significant.

## RESULTS

A total of 15 individuals, of whom 11 were female (73.3%) and 4 were male (26.7%), were included in the study. The mean age of the patients was  $45.7 \pm 10.7$  years, and the mean BMI was  $24.7 \pm 3.4$  (Table 2). When the results of the mMRC scale used to evaluate dyspnea were compared before and after treatment, it was observed that there was a statistically significant decrease after treatment ( $p < 0.001$ ). In BAI, the decrease in the post-treatment scores was statistically significant compared to the pre-treatment evaluation ( $p < 0.001$ ). Using VAS, the post-

treatment back pain of the cases was also determined to statistically significantly decrease compared to the baseline ( $p < 0.001$ ). As a result of the statistical analysis, the effect of the intervention was found to be very large for mMRC, very large for VAS, and medium for BAI. The results are shown in Table 3.

Table 2. Demographic Characteristics of Patient

	n	%
Sex	Male	4
	Female	11
	$\bar{X} \pm S.D$	
Age	$45.7 \pm 10.7$	
BMI	$24.7 \pm 3.4$	

Table 3. Symptom evaluation of the patients before and after treatment

	Pre-treatment		Post-treatment		P value	Effect Size
	$\bar{X} \pm S.D$	Median (IQR)	$\bar{X} \pm S.D$	Median (IQR)		
mMRC		2 (1)		0 (1)	< 0.001*	0.95 <sup>o</sup>
VAS	$6.26 \pm 1.90$		$2.60 \pm 1.45$		< 0.001**	1.84 <sup>o</sup>
BAI	$37.33 \pm 14.74$		$25.86 \pm 13.64$		< 0.001**	0.74 <sup>o</sup>

mMRC: Modified Medical Research Council, VAS: Visual Analog Scale, BAI: Beck Anxiety Inventory

\*Wilcoxon Signed Rank Test, \*\*Paired Samples T Test

<sup>o</sup> Effect Size (r): 0.1-0.3: small, 0.3-0.5: medium,  $0.5 \leq$  large effect, <sup>oo</sup> Effect Size (Hedge's g): 0.2: small, 0.5: medium, 0.8: large effect

## DISCUSSION

Due to the side effects of pharmacological agents used in diseases, there has been an increasing interest in aromatherapy, which is one of the complementary medicine methods and continues to be the subject of many studies.

Monoterpene 1,8-cineol (eucalyptol) is the main component of *Eucalyptus* species, a frequently used aromatherapy plant, is known for its anti-inflammatory, antioxidant, bronchodilator, antiviral, antimicrobial, analgesic, and anxiolytic effects. The antiviral, anti-inflammatory, and mucolytic mechanisms of 1,8-cineol are mediated through the induction of interferon regulatory factor 3. With these properties, has been used for many years in the treatment of chronic obstructive pulmonary diseases and asthma (11,12). Furthermore, M pro inhibitors, which are important for coronavirus replication, have become a promising research topic for the control

of COVID-19, with research suggesting that essential oil components, especially 1,8-cineol can be used in the treatment of COVID-19 as a potential inhibitor without toxicity (13). Consistently, in the current study, after eucalyptus aromatherapy oil inhaler application, a statistically significant improvement was observed in mMRC measurements performed to evaluate the level of dyspnea, which also provides information about lung health.

In the content of eucalyptus aromatherapeutic oil, alpha-pinene and 1,8-cineol are antioxidants with radical scavenging activity. 1,8-cineol reduces inflammation and pain by inhibiting cytokine release from T-lymphocytes (14). In a randomized controlled study evaluating 70 patients diagnosed with rheumatoid arthritis, 1 ml of eucalyptus oil was administered to one group of patients through inhalation for three times a day for five minutes for one month, and an improvement was observed in the pain

severity ( $P < 0.05$ ) and quality of life scores of this group compared to the other group that inhaled a placebo ( $P < 0.001$ ) (15). In a study on rats, the analgesic activity of eucalyptus essential oil was considered to be related to the  $\mu$ -opioid pain pathway, and its use in the treatment of somatic, inflammatory, and visceral pain was recommended (16). Similarly, in our study, the VAS scores of back pain, a commonly observed symptom in post-COVID syndrome, decreased after four weeks of eucalyptus oil application.

Due to its lipophilic property, 1,8-cineol can cross the blood-brain barrier and affect neuronal enzyme and receptor activities in the central nervous system (17). 1 Studies have shown that 1,8-cineol can be used in the treatment of anxiety by inhibiting the acetylcholinesterase activity that catalyzes the hydrolysis of acetylcholine (18). In a randomized controlled clinical study investigating the effect of eucalyptus aromatherapeutic oil inhalation on anxiety before selective nerve root block injection in 62 patients, there was a significant improvement in the anxiety level of the 1,8-cineol inhalation group compared to the control group, and eucalyptus aromatherapy oil was recommended to reduce preoperative anxiety (19). This is supported by our study revealing a significant decrease in the BAI anxiety scores of the patients after eucalyptus inhalation. As a result of the statistical analysis, the effect of the intervention in our study was found to be very large for mMRC and VAS, medium large for BAI.

The limitations of this study include the small number of patients and the absence of a control group.

## CONCLUSION

Eucalyptus aromatherapy oil inhalation was found to be effective in recovery from post-COVID syndrome symptoms, such as dyspnea, back pain, and anxiety, which affect many people across the world and can cause labor and financial losses. Therefore, we recommend the use of this aromatherapy oil in the complementary treatment and follow-up of these patients. There is a need for randomized controlled clinical studies with a larger sample size.

## ACKNOWLEDGEMENT

### Conflict of Interest

Conflict of Interest None.

### Support Resources

No financial support was used by authors during this study

### Ethical Declaration

Ethics committee approval was not obtained because it was a pilot study and Helsinki Declaration rules were followed to conduct this study.

### Authorship Contributions

Concept: GYÖ, SBS, Design: SBS, Supervising: GYÖ, Financing and equipment: SBS Data collection and entry: SBS, GYÖ, Analysis and interpretation: SBS, Literature search: GYÖ.

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