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Original Research

The effects of aromatherapy with thyme oil on disease symptoms, vital findings, and hemodynamic parameters in COVID-19 patients[☆]

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ABSTRACT

Objective: To determine the effect of aromatherapy with thyme oil on disease symptoms, vital signs, and hemodynamic parameters in COVID-19 patients.
Methods: We conducted the randomized controlled trial with 140 (experimental group=70, control group=70) COVID-19 patients. Patients admitted to the COVID-19 service of the Batman Training and Research Hospital were included in the sample between 31.01 - 31.08 2022. Patients in the experimental group inhaled thyme oil 3 times a day during 5 days. At the end of day 5, symptoms and hemodynamic parameters were measured as posttest. Vital signs were measured 3 times a day during 5 days. The control group only received routine treatment.
Results: Thyme oil was found to be effective in relieving symptoms of shortness of breath, dizziness, secretion, diarrhea, weakness, loss of appetite, cough, headache and muscle joint pain. Although there was improvement in the symptoms of nausea-vomiting, runny nose and loss of taste-smell, the effect was not statistically significant. Thyme oil significantly decreased body temperature, pulse rate and respiratory rate ($p<0.05$), increased SPO 2 ($p<0.05$), and did not affect systolic and diastolic blood pressure ($p>0.05$). It had a significant effect on the regulation of pH, decreased CO_2 and increased O_2 significantly ($p<0.05$).
Conclusion: Thyme oil aromatherapy was effective in reducing symptoms, regulating vital signs and hemodynamic parameters. Accordingly, thyme oil is recommended as non-pharmacological treatment method in COVID-19 patients.

Introduction

Symptoms of COVID-19 infection, which occurs as pneumonia and affects the lower respiratory tract, appear after the incubation period.[1] The symptoms of the disease and the severity of the symptoms vary according to the person's immune system, age, and whether there is any underlying chronic disease. Cough, fever, sputum, fatigue, lymphopenia, dyspnea, myalgia, diarrhea, and headache are the most common symptoms reported in COVID-19 patients.[2–4]

It is known that COVID-19 has serious effects on vital signs and hemodynamics. Due to the high eosinophil count, white blood cell count, and C-reactive protein in COVID-19 patients, intermittent (febris intermittens) and fluctuating fever (febris undulans) are seen in patients.[3] In addition, the disease reduces the oxygenation capacity of the lungs and leads to a decrease in oxygen saturation in the body, resulting in insufficient oxygen supply to the cells. This situation is characterized by an increase in heart rate and respiratory rate to provide sufficient oxygen to the cells.[5]

To reduce the negative effects of the COVID-19, the use of medicinal plants along with medical antiviral treatments has become widespread.[6] Among them, thyme is a plant from the Lamiaceae family that has no known significant side effects and is used for its medicinal effects. The thyme plant belongs to the mint family and the plant contains antioxidant compounds such as phenolic, eugenol, carvacrol, and thymol.[6,7] It has been reported that thymol has beneficial effects on respiratory diseases.[7] In previous studies, it has been reported that the antispasmodic

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and antimicrobial effects of thyme oil relieve contraction, relax muscles, reduce bronchospasm and cough symptoms, and are also effective in some infectious diseases of the upper respiratory tract.[6,8–10] It has been reported that thyme stimulates immunity, increases the number of lymphocytes, and has an analgesic effect on muscle pain, headache, and joint pain.[7] There are several studies suggesting that thyme plant, which has high antioxidant properties, reduces symptoms by inducing immune system and antiviral effects[9] and may reduce the effects of the COVID-19 disease.[9,11]

Sardari et al., who examined the effect of thyme oil on symptoms in COVID-19 patients, determined that thyme oil was effective in reducing fever, cough, dyspnea, dizziness, muscle pain, anorexia, weakness, lethargy, and fatigue.[9] While there are no other studies on thyme oil and COVID-19 in the literature, Chabok et al. reported that it improves gas exchange in the respiratory tract and increases the oxygen saturation value.[12] Similarly, Schönknecht et al. determined that thyme is a spasmolytic, antimicrobial, anti-inflammatory, immunomodulatory, and antioxidant agent.[8] In addition, Oliveiro et al. reported that thyme may be an effective treatment agent for chronic diseases based on inflammatory processes in cases of morbidity and mortality in lung cancer patients.[13]

A limited number of studies in the past have investigated the effect of thyme oil generally on respiratory symptoms. Our literature review results showed that very few studies have investigated the effect of thyme oil on symptoms in COVID-19 patients. Our research is the first to investigate the effects of thyme oil on COVID-19 symptoms, vital signs, and hemodynamic parameters. Because thyme is widely used by patients, it is an easily accessible and inexpensive plant, and it has a reliable essential oil, its effect should be investigated. In this study, it is predicted that thyme oil may be effective in reducing the negative effects of COVID-19 disease.[9] For this reason, research has focused on investigating the healing effects of thyme oil in COVID-19 patients, and the aim of this study was to determine the effects of aromatherapy with thyme oil on disease symptoms, vital signs, and hemodynamic parameters in COVID-19 patients.

Three hypotheses were tested in the study:

H_1: Thyme oil is effective in relieving COVID-19 symptoms or reducing symptom severity.

H_2: Thyme oil is effective in improving the vital signs of COVID-19 patients.

H_3: Thyme oil is effective in improving the hemodynamic parameters of COVID-19 patients.

Material and method

Design

This is a randomized controlled experimental study. We adhered to

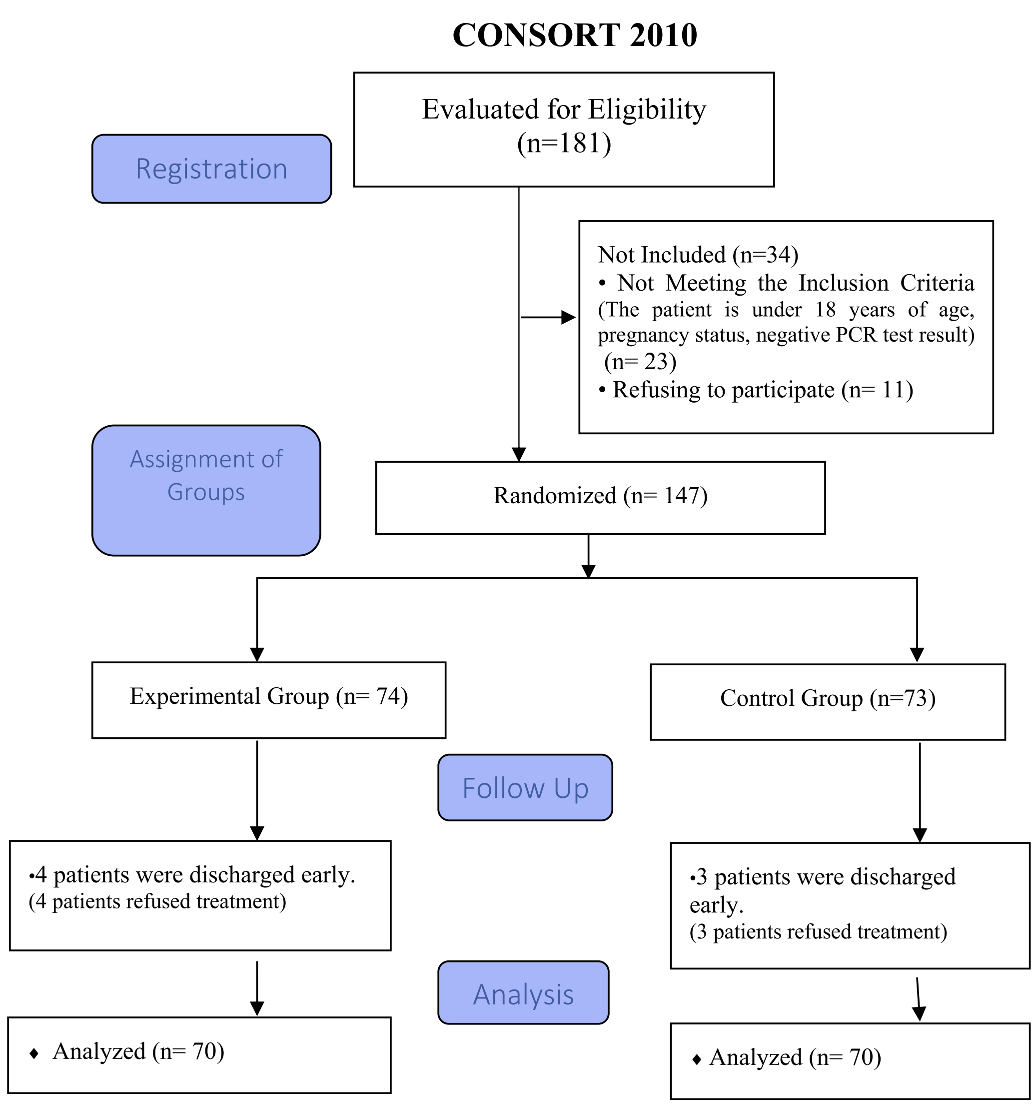

Fig. 1. CONSORT Flow Chart.

the Consort guidelines throughout the study (Fig. 1).

Population

The population of the study included patients hospitalized in XXX Training and Research Hospital COVID-19 service between 31 January 2022 and 31 July 2022. Patients who had a positive PCR test and had a lung involvement between 50 % and 80 % based on computerized tomography, who were admitted to the COVID-19 service on the 1st day of hospitalization, and stayed in the service for 5 days were included in the study. Patients who were pregnant, under the age of 18, and did not want to participate in the study were excluded. Patients who were transferred to the intensive care unit or discharged before the expected time were excluded from the study. The sample size of the study was determined based on the number of patients hospitalized in the COVID-19 service in 2020 (610 admissions). The sample size of the study was calculated as 128 individuals (experiment = 64, control = 64) using the G*power 3 program, with an effect size of 0.25, a significance level of 0.05, a confidence interval of 0.95, and a power of 0.95. The study was completed with 140 patients (experimental group = 70 control group = 70) by adding 6 patients in each group (with an increase of 9.37 %) considering that there would be losses in the study groups.

Randomization

In this study, block randomization was performed according to age and gender groups to assign the participants to the experimental and control groups. The patients were listed according to the hospitalization list and numbered up to 140. Numbers were assigned to the experimental and control groups according to the random numbers list. Thus, the probability of each patient being in either of the experimental or control groups was equalized. For the block layout, a total of 140 sets were created, with two blocks in each set. The patient distribution was made according to the order written in the group distribution. After preassignment to the groups according to the research sets, block randomization was applied according to age and gender to ensure the homogeneity of the groups.

Material

The composition of NV-2016 Coded Thyme Essential oil (GC-201,900,528) was obtained with Nature&Nurture (10 μL) macra (Barcode No: 8,697,742,121,135, Registration No: 381,751). Content of thyme oil used: 1.3 % y-Terpinene, 2.7 % p-Cymene, 5.6 % linalool, 1.2 % terpinen-4-ol, 1.2 borneol, 1.2 % β-Bisabolene Contains 3.2 % tymol and 75.7 % carvacrol. The approved ingredient composition of thyme oil is shown in Table 1. Thyme oil, whose latin name is thymus vulgaris, it is an essential oil obtained by distilling thyme, a pungent plant species that grows in the Mediterranean climate, by steam distillation.

Data collection

Data were collected between 31 January 2022 and 31 July 2022.

Table 1
Thyme Oil Analysis Results.

No	Compund	Relative Persentage (%)
1.	*y*-Terpinene	1.3
2.	*p*-Cymene	2.7
3.	Linalool	5.6
4.	Terpinen-4-ol	1.2
5.	Borneol	1.2
6.	Bisabolene	2.2
7.	Thymol	3.2
8.	Karvacrol	75.7
	Total	93.1

Data were collected at xxxxxx COVID-19 Clinic. On the first day of hospitalization in the COVID-19 clinic, the patients were met and each patient was evaluated for inclusion in the study. Then, the group to which the patient was assigned was determined and the patient was informed about the study.

Aromatherapy intervention

Thyme oil has been studied as an inhaler. Studies have mostly used essential oils for inhaled aromatherapy by dissolving them in warm water, inhaling with a nebuliser and breathing in.[12] The heavy burden of symptoms and the difficulty in providing continuous inhalation in COVID-19 patients suggested the need to facilitate inhalation. Therefore, this study is a first in this study with the idea of using an inhaler stick to provide ease of use and to use portable inhaler thyme oil. Based on all these, thyme oil aromatherapy was applied via inhaler stick. To ensure absorption, 2 cc thyme oil was dripped into the cotton wicks inside the inhaler stick. Patients randomized to the experimental group were informed about how to use the inhaler stick. The researcher showed the patient how to insert it through their nostrils by showing the first application on himself/herself. The patient was asked to administer the inhaler stick prepared for them through their nostrils. The researcher asked the patient to close the other nostril with his/her hand and inhale the thyme oil into his/ her lungs in eight breaths (Fig. 2). The patients used the inhaler stick by taking 8 breaths and inhaled three times a day for five days.

Data collection stages in the experimental and control groups

After confirming that inhaler stick was applied correctly, each patient assigned to ***experimental group*** completed the pretest part of the Demographic Characteristics Form and Visual Comparison Scale, together with the researcher. At the same time, the researcher evaluated and recorded the *COVID-19 symptoms*. Then the researcher measured and recorded the hemodynamic parameters as a pretest. Vital signs of the patients (fever, oxygen saturation, systolic-diastolic blood pressure, and pulse and respiratory rate) were measured and recorded three times a day (at 08:00, 16:00, and 24:00 h) for five days. Aromatherapy intervention was initiated after preliminary testing was completed. At 24:00 h of the 5th day of the patient's hospitalization period in the COVID-19 Clinic, the patients filled out the Visual Comparison Scale post-test part, COVID-19 symptoms and hemodynamic parameters were measured and recorded as a post-test, and repeated measurements of the vital signs were terminated.

Each patient randomized to the control group was measured simultaneously with the experimental group. No intervention was applied to the patients in this group. The control group only received routine treatment.

Data collection tools

Demographic Characteristics Form: This form, which was created by researchers, consists of a total of 13 items questioning the diagnosis, age, weight, height, gender, chronic disease status, medications used regularly, COVID-19 history, COVID-19 vaccine brand, and vaccination status.

Measurement of COVID-19 symptoms: COVID-19 symptoms were assessed and recorded. The frequency and severity of the nine most common symptoms were measured using information from the literature[9]: shortness of breath, dizziness, secretions, diarrhoea, nausea-vomiting, weakness, runny nose, change in sense of taste-smell, appetite status, cough, headache and muscle-joint pain were assessed and the severity of the symptoms measured.

Visual Comparison Scale (VCS): It is the most widely used scale for pain assessment.[14] In this study, it was used to evaluate the symptoms of COVID-19 such as headache and muscle-joint pain. The patient is

a. İnhaler Stick **b.** İnhaler Stick use

Fig. 2. Inhaler Stick and its use.

required to mark the pain from "No Pain" (0 points) to "Severe Pain" (10 points) on a 10 cm long line, which can be positioned horizontally or vertically. Since it is generally accepted that the horizontal line is easier to understand, the number format placed on the horizontal axis was used in this study.[14]

Hemodynamic Parameters and Vital Signs Follow-up Form: This form was created by the researchers and includes the pH, O_2, CO_2, SaO_2 measurement results from the measured blood gas values. The second part was created to record the temperature, pulse, respiratory rate, and systolic-diastolic blood pressure values (3 × 1 daily).

Blood pressure monitor, thermometer, and pulse oximeter: Erka brand blood pressure monitor, polygreen brand thermometer and handheld brand pulse oximeter the devices were calibrated and measurements were made by the researcher in the patient room at 08:00, 16:00 and 24:00 h for 5 days with the same brand devices in all patients.

Ethical aspects of the research

Ethics committee approval (Date: 19.10.2021 No: 2021/2631) was obtained. The scientific research platform of the Turkish Ministry of Health and the hospital where the study was carried out approved the study. Individuals who agreed to participate in the study were informed about the purpose of the study, how the research will be conducted, and how the data obtained will be used. The Declaration of Helsinki was taken as a basis.

Data analysis and evaluation

Data analysis was carried out with the SPSS (Statistical Program in Social Sciences) 25 program. The Shapiro Wilk Test was used to check whether the data conformed to normal distribution. The significance level (p) was taken as 0.05 for the comparison tests. Comparisons in paired dependent groups were made using the significance test of the difference between the two pairs. In repeated measurements, analysis of variance was used in repeated measurements to test whether there was a difference between groups. Multiple normal distribution and homogeneity of variance were controlled in the analyses. In the analysis of categorical data, the Chi-square analysis was performed by creating cross tables.

Results

In the study, 181 patients were evaluated for eligibility. Of these patients, 23 were excluded because they did not meet the inclusion criteria and 11 patients refused to participate. Four patients from the experimental group and 3 patients from the control group were excluded from the study because they were discharged early, and the study was completed with a total of 140 patients, 70 of which were in the experimental group and 70 in the control group. The participants were homogeneously distributed among the groups, in the comparison made according to the variables of age, body mass index, gender, COVID-19 transmission status, COVID-19 vaccination status, number of COVID-19 vaccine received (Table 2). All included patients received Tavanic 500 mg 2 × 1 (PO) and 7 tablets of Favipavir 200 mg for 5 days. In addition, all patients with respiratory distress received 2–4 ml 100 % O2 per hour and all patients with fever (39 and above) received Arveles 50 mg/2 ml ampoule. Patients used oxygen and Arveles as needed.

It was determined that the decrease in loss of breath score, cough, secretion, the severity of dizziness, the severity of fatigue, the severity of headache, the severity of muscle and joint pain, appetite loss, and diarrhea was statistically significant between the groups, according to time, and within the group ($p<0.05$). The percentage of explanation of time-dependent change was found to be high in dyspnea, cough, secretion and fatigue (41.6 %, 66.7 %, 55 %, 55.1 %, respectively). The percentage of explanation of time-dependent change was found to be low in dizziness, headache severity, muscle and joint pain, loss of appetite and diarrhea (10 %, 17.9 %, 22.6 %, 4.1 %, 4.7 %). Although there was improvement in the symptoms of nausea-vomiting, runny nose, and loss of taste-smell, there was no statistically significant difference (Table 3).

In the comparison of the body temperatures of the participants, it was determined that the 5th day values of the patients using thyme oil were lower than the 1st, 2nd, 3rd and 4th day values. 3.1 % (η) of the variation between groups in body temperature measurement is explained by time-dependent variation. In the comparison of blood pressure of the groups, it was determined that the decrease in systolic blood pressure measurement over time in the experimental group was statistically significant within the group ($p<0.05$). Accordingly, the mean of the 5th day in the experimental group was significantly lower than the means of the 1st and 2nd days ($p<0.05$). When the 5-day mean of the diastolic blood pressure measurements of the participants was examined, it was determined that the diastolic blood pressure means measured in the experimental group on the 2nd and 3rd days were significantly lower than those of the control group ($p<0.05$). It was determined that the change in pulse rate measurement according to time was statistically significant in both the experimental and control groups within the group ($p<0.05$). Accordingly, pulse rate values on the 5th day were found to be significantly lower than the pulse rate values on the 1st, 2nd, 3rd and 4th days in the experimental group ($p<0.05$). In the control group, pulse rate values on the 3rd and 4th days were significantly lower than the values measured on the 1st day ($p<0.05$) (Table 4).

It was determined that the SpO_2 and respiratory rate of the patients in the experimental group improved significantly compared to the patients in the control group ($p<0.05$). In the comparison within the group, it was determined that the increase in SpO_2 over time and the decrease in respiratory rate were statistically significant in both groups ($p<0.05$). In SpO_2 measurements, 33.2 % (η) of the variation between groups and 47.4 % (η) of the variation between groups in respiratory rate are explained by time-dependent variation (Table 4).

When examining pH, CO_2, and O_2 values of the patients, it was determined that there was a significant improvement in the CO_2 and O_2

Table 2
Comparison of Demographic Data in Groups.

Variable		GROUP		χ^2	p Value
		Experiment	Control		
		Mean ± SD **Min-Max**	**Mean ± SD** **Min-Max**		
Age		51.94 ± 15.88 (19 – 94)	53.34 ± 15.97 (23 – 90)	−0.520	0.604
BMI		26.09 ± 3.06 (18.29 – 33.66)	26.56 ± 3.83 (13.70 – 35.91)	−0.792	0.430
Sex	**Female**	35_a (50.0 %)	36_a (51.4 %)	0.029	0.866
	Male	35_a (50.0 %)	34_a (48.6 %)		
Status of Having a Chronic Disease	**Yes**	30_a (42.9 %)	44_b (62.9 %)	***5.657***	***0.017****
	No	40_a (57.1 %)	26_b (37.1 %)		
Name of Chronic Disease					
Heart failure	**Yes**	14_a (20.0 %)	19_a (27.1 %)	0.944	0.319
	No	56_a (80.0 %)	51_a (72.9 %)		
Hypertension	**Yes**	24_a (34.3 %)	29_a (41.4 %)	0.761	0.383
	No	46_a (65.7 %)	41_a (58.6 %)		
Diabetes	**Yes**	12_a (17.1 %)	16_a (22.9 %)	0.716	0.397
	No	58_a (82.9 %)	54_a (77.1 %)		
COPD	**Yes**	1_a (1.4 %)	9_b (12.9 %)	***5.277***	***0.022****
	No	69_a (98.6 %)	61_b (87.1 %)		
History of COVID-19	**Yes**	9_a (12.9 %)	18_a (25.7 %)	2.937	0.087
	No	61_a (87.1 %)	52_a (74.3 %)		
Number of previous COVID-19	**None**	61_a (87.1 %)	52_a (74.3 %)	2.937	0.087
	Once	9_a (12.9 %)	18_a (25.7 %)		
Status of COVID-19 Vaccination	**Yes**	49_a (70.0 %)	54_a (77.1 %)	0.912	0.341
	No	21_a (30.0 %)	16_a (22.9 %)		
Number of COVID-19 vaccination	**None**	21_a (30.0 %)	17_a (24.3 %)	0.625	0.429
	Once	8_a (11.4 %)	4_a (5.7 %)		
	Twice	28_a (40.0 %)	38_a (54.3 %)		
	Three Times	13_a (18.6 %)	11_a (15.7 %)		
Name of COVID-19 Vaccine	**None**	21_a (30.0 %)	17_a (24.3 %)	0.803	0.371
	Sinovac	20_a (28.6 %)	22_a (31.4 %)		
	Sinovac+Biontech	8_a (11.4 %)	3_a (4.3 %)		
	Biontech	21_a (30.0 %)	28_a (40.0 %)		

SD; Standard Deviation, χ^2; Chi-square Test Value, $^*p<0.05$, a-a: No difference, a-b: Difference between groups.

values of the patients in the experimental group. Accordingly, it was determined that the time-dependent decrease in the CO_2 score of the participants was statistically significant between and within the group ($p<0.05$). 14.4 % (η) of the variation between groups is explained by time-dependent variation. It was determined that the time-dependent increase in O_2 values of the participants was statistically significant between and within the group ($p<0.05$). 55.1 % (η) of the variation between groups is explained by time-dependent variation (Table 5).

Discussion

The findings regarding the benefit of using thyme oil obtained from this study contribute to the prevention of the negative effects of COVID-19.

As a result of the inhaler aromatherapy with thyme oil, it was determined that the symptoms of shortness of breath, cough, secretion, dizziness, weakness, loss of appetite, headache, and muscle joint pain decreased in the experimental group compared to the control group ($p<0.05$). Similar to our findings, Sardari et al. determined that thyme essential oil was effective in reducing symptoms such as shortness of breath, cough, dizziness, weakness, loss of appetite, headache, and muscle pain in COVID-19 patients.[9] Again, Yiagnigni et al. reported that thyme oil had an effect on shortness of breath, cough, dizziness, fatigue, and loss of appetite in patients with COVID-19.[11] Karimi et al. reported that the treatment containing thyme plant (herbs boiled or applied in the capsule form) they prepared for COVID-19 patients improved symptoms such as shortness of breath, cough, dizziness, fatigue, loss of appetite, headache, and muscle pain.[15] In addition to these limited studies on COVID-19, its use in the relief of symptoms due to different respiratory system diseases (such as asthma, bronchitis, and COPD) is supported in the literature.[8,16] The relevant literature reporting the effect of thyme oil reports that the use of thyme as a spasmolytic, antimicrobial, anti-inflammatory, immunomodulatory, and antioxidant agent in the treatment of cough is effective.[8,16,17] Some studies have shown the effect of thyme in combination with different herbs (primrose),[18] while others have shown the effect of its use in shortness of breath and secretion.[19,20] Apart from COVID-19, studies investigating the effect of thyme on pain and fatigue have shown that thyme is effective in relieving dysmenorrhea and menstrual pain[21] and pain and fatigue seen in irritable bowel syndrome.[22,23] Although the studies presented are non-COVID-19, the findings of thyme to reduce shortness of breath, cough, and secretion symptoms, muscle joint pain, headache, and fatigue support our hypothesis that these symptoms can be relieved with thyme in COVID-19. For this reason, our research findings and literature results indicate that its use in the relief of symptoms in COVID-19 may be beneficial and pioneers for a more detailed investigation.

In this study, improvement was observed in the post-test values of nausea, runny nose, and loss of taste-smell sense of the patients in the experimental and control groups. The effect of thyme on symptoms of nausea, runny nose, and loss of sense of taste and smell is not clear, since the variation seen over time and the difference between the groups were not statistically significant. It can be predicted that the improvements seen in both groups may be caused by different factors. Unlike our study, Mahboubi stated that thyme oil reduced the symptom of nausea, which is one of the symptoms of irritable bowel syndrome.[22] In viral infections such as COVID-19, the symptom of nausea is shown as an early sign of an infection of the gastrointestinal tract. COVID-19 triggers the symptom of nausea in the acute phase by causing its release from the enteroendocrine cells in the mucosa of the upper gastrointestinal tract or after the virus enters the blood directly.[24] Yianigni et al. reported that thyme oil has an effect on loss of taste and smell in patients with COVID-19.[11] It is known that the virus that causes COVID-19 has a high tendency to be

Table 3
Comparison of COVID-19 Symptoms According to Experimental and Control Groups.

Variable		Experiment Mean ± SD	Control Mean ± SD	According to Time Between Groups	Experiment-Control (p^a)
Shortness of breath	Pre-Test	7.49 ± 1.73	7.1 ± 2.08	$F = 98.348$	0.001*
	Post-Test	1.06 ± 1.41	4.11 ± 1.93	$p = 0.001$*	0.001*
		$F = 685.784$ $p = 0.001$*	$F = 147.929$ $p = 0.001$*	η = 0.416	
Cough	Pre-Test	7.73 ± 1.55	7.4 ± 1.61	$F = 289.613$	0.221
	Post-Test	1.47 ± 1.25	6.17 ± 1.23	$p = 0.001$*	0.001*
		$F = 896.832$ $p = 0.001$*	$F = 34.575$ $p = 0.001$*	η = 0.677	
Secretion	Pre-Test	6.63 ± 1.66	6.06 ± 2.63	$F = 168.507$	0.127
	Post-Test	1.21 ± 1.21	5.6 ± 1.49	$p = 0.001$*	0.001*
		$F = 402.037$ $p = 0.001$*	$F = 2.866$ $p = 0.093$	η = 0.550	
Dizziness	Pre-Test	3.36 ± 3.05	3.27 ± 3.28	$F = 1.424$	0.873
	Post-Test	0.06 ± 0.34	0.57 ± 1.45	$p = 0.001$*	0.001*
		$F = 86.129$ $p = 0.001$*	$F = 57.656$ $p = 0.001$*	η = 0.010	
Runny Nose	Pre-Test	2.29 ± 2.84	1.96 ± 2.79	$F = 1.159$	0.491
	Post-Test	0 ± 0	0.17 ± 1.01	$p = 0.284$	0.157
		$F = 48.431$ $p = 0.001$*	$F = 29.560$ $p = 0.001$*	η = 0.008	
Fatigue	Pre-Test	7.66 ± 0.98	7.61 ± 1.47	$F = 169.117$	0.839
	Post-Test	1.61 ± 1.54	5.33 ± 1.59	$p = 0.001$*	0.001*
		$F = 874.958$ $p = 0.001$*	$F = 125.183$ $p = 0.001$*	η = 0.551	
Headache	Pre-Test	6.24 ± 1.69	7.21 ± 1.9	$F = 30.186$	0.002*
	Post-Test	2.03 ± 1.19	4.86 ± 1.93	$p = 0.001$*	0.001*
		$F = 310.884$ $p = 0.001$*	$F = 97.257$ $p = 0.001$*	η = 0.179	
Muscle-Joint Pain	Pre-Test	6.64 ± 1.87	7.69 ± 1.57	$F = 40.356$	0.001*
	Post-Test	1.84 ± 1.34	4.83 ± 1.92	$p = 0.001$*	0.001*
		$F = 492.653$ $p = 0.001$*	$F = 174.551$ $p = 0.001$*	η = 0.003	
Nausea	Pre-Test	2.7 ± 3.15	1.94 ± 2.8	$F = 2.196$	0.135
	Post-Test	0.11 ± 0.58	0.09 ± 0.5	$p = 0.644$	0.756
		$F = 55.317$ $p = 0.001$*	$F = 28.536$ $p = 0.001$*	η = 0.016	
Loss of appetite	Pre-Test	6.21 ± 2.68	6.44 ± 2.41	$F = 5.882$	0.597
	Post-Test	2.64 ± 1.88	3.76 ± 2.62	$p = 0.017$*	0.005*
		$F = 191.259$ $p = 0.001$*	$F = 108.158$ $p = 0.001$*	η = 0.041	
Loss of Taste and Smell	Pre-Test	5.56 ± 4.11	5.77 ± 4.09	$F = 0.982$	0.757
	Post-Test	2.13 ± 2.15	2.77 ± 2.74	$p = 0.323$	0.125
		$F = 125.732$ $p = 0.001$*	$F = 96.264$ $p = 0.001$*	η = 0.007	
Diarrhea	Pre-Test	1.09 ± 2.35	0.26 ± 1.09	$F = 6.790$	0.008*
	Post-Test	0.06 ± 0.34	0 ± 0	$p = 0.010$*	0.157
		$F = 24.123$ $p = 0.001$*	$F = 1.509$ $p = 0.221$	η = 0.047	

SD; standard deviation, p^a; test of significance of the difference between the two means p value, η: effect size, *$p<0.05$.

found at the throat and nose area. The olfactory nerve, anatomically, appears as an extension of the brain and spreads into the nose by passing through a perforated and very thin bone structure between the brain and the nose. Because of this feature, when the virus reaches the upper respiratory tract, it can spread directly into the brain by staying at the olfactory nerve. The virus can directly damage neurons in the olfactory epithelium.[25] The sense of smell is closely related to the sense of taste. It was observed that most of the individuals who cannot smell also have a decrease in the sense of taste.[25] For this reason, it can be concluded that the effect of COVID-19 on the mechanism of taste and smell loss should be examined separately. Since the effects of thyme oil on the sense of taste-smell is limited, it may be recommended to use thyme oil for a longer period of time or to increase its frequency for future studies. In addition, it will be useful to conduct comparative studies such as applying thyme oil in different ways, such as oral use or consumption in food.

It is predicted that it is difficult to talk about the effect of aromatherapy with thyme on diarrhea, since the severity of diarrhea symptoms of the participants improved over time. In parallel with our findings, Sardari et al. and Yiagnigni et al. reported that the diarrhea symptom improved in the post-test, but there was no significant improvement.[9,11] COVID-19 is a viral infection disease, and diarrhea is seen in COVID-19 patients because it causes intestinal permeability and absorption in viral infections.[26] Studies revealing the effect of thyme plant on diarrhea other than COVID-19 stated that thyme plant can be used in the treatment of bacterial diarrhea due to its antispasmodic and antimicrobial effects.[22,23]

In this study, it was observed that the body temperature of the individuals using thyme oil on the 5th day decreased compared to the mean values on the 1st, 2nd, 3rd and 4th days, and the body temperature of the patients in the experimental group decreased compared to the control group. Sardari et al. determined that only one of the individuals using the thyme plant had fever, and Yianigni et al. determined that the thyme plant was effective on fever.[9,11] Since studies evaluating the effect of thyme oil on vital signs are limited, it is seen that the effect of thyme on fever needs to be investigated in further studies by considering the

Table 4
Comparison of Body Temperature, Blood Pressurei Pulse Rate, SpO_2 and Respiration Rate According to Experimental and Control Groups.

			Experiment	Control	According to Time Between Groups	Experiment -Control (p[a)])
Temperature	5 days Mean	Day 1	36.64 ± 0.28	37.02 ± 0.43	$F = 4.357$	0.001*
		Day 2	36.63 ± 0.24	36.96 ± 0.34	$p = 0.005$*	0.001*
		Day 3	36.58 ± 0.23	36.82 ± 0.3	η = 0.031	0.001*
		Day 4	36.52 ± 0.19	36.68 ± 0.24		0.001*
		Day 5	36.43 ± 0.18	36.61 ± 0.23		0.001*
			$F = 8.009$ $p = 0.001$* Day 5 < Days 1, 2, 3, 4	$F = 25.756$ $p = 0.001$* Days 3, 4, 5 < Day 1 Days 3 and 4 < Day 2 Days 4 and 5 < Day 3		
Systolic Blood Pressure	5 days Mean	Day 1	120.22 ± 13.73	120.44 ± 12.01	$F = 1.174$	0.922
		Day 2	118.38 ± 10.64	121.45 ± 11.58	$p = 0.319$	0.104
		Day 3	116.64 ± 10.65	119.83 ± 10.24	η = 0.008	0.0753
		Day 4	116.94 ± 10	118.35 ± 9.49		0.395
		Day 5	115.08 ± 7.13	118.13 ± 7.95		0.018
			$F = 4.053$ $p = 0.004$*	$F = 2.236$ $p = 0.068$		
Diastolic Blood Pressure	5 days Mean	Day 1	71.89 ± 6.56	72.75 ± 6.31	$F = 0.680$	0.431
		Day 2	71.8 ± 5.95	73.9 ± 5.73	$p = 0.582$	0.036*
		Day 3	71.35 ± 5.18	73.33 ± 5.55	η = 0.005	0.030*
		Day 4	71.56 ± 4.73	72.96 ± 4.25		0.068
		Day 5	71.58 ± 3.46	72.44 ± 2.89		0.114
			$F = 0.121$ $p = 0.975$	$F = 1.292$ $p = 0.276$		
Pulse	5 days Mean	Day 1	86.18 ± 11.85	85.85 ± 11.16	$F = 0.714$	0.866
		Day 2	83.12 ± 9.46	83.82±10.61	$p = 0.583$	0.681
		Day 3	82.1 ± 8.68	81.67 ± 10.43	η = 0.005	0.792
		Day 4	82.13 ± 8.49	81.64 ± 9.84		0.753
		Day 5	80.86 ± 8.33	82.2 ± 8.69		0.354
			$F = 4.835$ $p = 0001$*	$F = 3601$ $p = 0,008$*		
Saturation (SpO_2)	5 days Mean	Day 1	90.29 ± 2.85	91.67 ± 2.38	*F = 68.544*	0.002*
		Day 2	91.8 ± 2.79	92.69 ± 2.55	*p = 0.001**	0.051
		Day 3	94.23 ± 2.37	92.98 ± 2.49	*η = 0.332*	*0.003**
		Day 4	95.4 ± 2.69	93.56 ± 2.31		*0.001**
		Day 5	96.6 ± 2.02	93.58 ± 2.6		*0.001**
			$F = 125.939$ $p = 0.001$* *Days 2, 3, 4,5 > Day 1* *Day 3, 4, 5> Day 2* Day 5 > Days 3 and 4	$F = 16.193$ $p = 0.001$* *Days 2, 3, 4. 5 > Day 1* *Days 4 and 5 > Day 2*		

(*continued on next page*)

Table 4 (*continued*)

			Experiment	Control	According to Time Between Groups	Experiment -Control ($p^{a)}$)
				Days 4 and 5.> Day 3		
Respiration Rate	5 days Mean	Day 1	22.8 ± 2.3	20.1 ± 2.03	$F = 124.224$	0.001*
		Day 2	21.02 ± 2.27	19.49 ± 2.13	$p = 0.001$*	0.001*
		Day 3	18.19 ± 2.07	19.3 ± 2.49	$\eta = 0.474$	0.005*
		Day 4	16.17 ± 1.88	19.06 ± 2.82		0.001*
		Day 5	14.89 ± 1.18	18.79 ± 2.88		0.001*
			F = 114.356 p = 0.001 Days 2, 3, 4, 5 < Day 1, Days 3, 4, 5 < Day 2, Days 4 and 5 < Day 3, Day 5 < Day 4*	*F = 4.834 p = 0.001* Days 2, 3, 4, 5 < Day 1*		

SD; standard deviation, p^a; test of significance of the difference between the two means p value, $^*p<0,05$.

Table 5
Comparison of Hemodynamic Parameters According to Experimental and Control Groups.

Variable		Experimental		Control		Between Groups According to Time	Experimental-Control (p^a)
		Mean ± SD	Min-Max	Mean ± SD	Min-Max		
pH	**Pre-Test**	7.36 ± 0.06	7.21–7.53	7.35 ± 0.07	7.21–7.51	$F = 2.953$	0.619
	Post-Test	7.35 ± 0.03	7.26–7.39	7.37 ± 0.05	7.23–7.49	$p = 0.088$	0.027*
		$F = 0.101$		$F = 4.460$		$\eta = 0.021$	
		$p = 0.751$		$p = 0.036$*			
CO_2	**Pre-Test**	44.53 ± 4.02	37–51	41.13 ± 4.94	30–51	$F = 23.283$	0.001*
	Post-Test	39.14 ± 2.9	34–46	39.07 ± 3.65	33–51	$p = 0.001$*	0.898
		$F = 121.912$		$F = 17.786$		$\eta = 0.144$	
		$p = 0.001$*		$p = 0.001$*			
O_2	**Pre-Test**	78.74 ± 4.2	70–89	81.03 ± 5.03	70–91	$F = 169.153$	0.004*
	Post-Test	92.01 ± 3.25	85–98	86.04 ± 4.92	73–96	$p = 0.001$*	0.001*
		$F = 873.946$		$F = 124.758$		$\eta = 0.551$	
		$p = 0.001$*		$p = 0.001$*			

SD; standard deviation, p^a; test of significance of the difference between the two means p value, $^*p<0.05$.

factors affecting fever.

In our study, there was no difference between the groups in terms of blood pressure and pulse rate. Time-dependent changes showed that pulse rate decreased with time in both groups. In the study of Noh et al. in the improvement of menopausal symptoms in women using thyme, it was reported that there was no change in blood pressure.[27] There is only one study in the literature on blood pressure and pulse rate. It can be assumed that thyme has a diuretic effect and antihypertensive effect.[28] It is clear that the evidence we have presented needs to be further supported in order to be able to talk about the positive effects of thyme on blood pressure and pulse rate.

Our research findings showed that the SPO_2 value increased and the respiratory rate decreased with the use of thyme oil. SPO_2 and respiratory rate changes between the experimental and control groups showed significant differences according to time and groups. Ghahremani-Chabok et al. determined that thyme inhalation therapy increased oxygen saturation by decreasing the prevalence of rhonchi and the weight of air secretions in patients under mechanical ventilation.[12] Hosseinzadeh et al. reported that inhalation of thyme oil in patients with acute exacerbation of COPD was effective in reducing the intensity of wheezing and respiratory rate.[29]

In our study, it was observed that thyme caused some differences in hemodynamic parameters. Accordingly, although the pH level was lower in the experimental group, it is clear that it is difficult to explain this difference with the use of thyme oil. The CO_2 level decreased in the experimental and control groups in the posttest and depending on time, but the difference between the groups was not significant. On the other hand, the increase in O_2 level in the posttest, time-dependent changes, and changes between groups were significant. These significant differences in the O_2 level revealed the strong effect of thyme on the regulation of oxygen. While there exist no findings related to pH in previous studies, Ghahremani-Chabok et al. determined that inhalation of thyme increases oxygen saturation.[12] Alavinezhad et al. reported that thyme improves pulmonary function tests in asthmatic patients, such as FEV 1 (volume of air exhaled in the 1st second of forced expiration), MEF 25 (mean expiratory flow rate at 25 % of vital capacity), MEF 50 (mean at 50 % of vital capacity expiratory flow rate), and MEF 75 (mean expiratory flow rate at 75 % of vital capacity).[30] Ghorani et al. also stated that thyme plant provides improvement in pulmonary function tests, oxidative stress, and c-reactive protein values in COPD patients.[20] Ghorani et al. revealed that a two-month treatment with thyme in COPD patients improved the pulmonary function tests, namely, FVC (forced vital capacity), PEF (peak expiratory flow rate), and FEV 1.[19]

Strengths and limitations

The strength of the study is that the patients in the experimental and control groups were randomized according to age and gender. The investigation of COVID-19 symptoms, vital signs and hemodynamic parameters distinguishes our study from other studies in the literature. The fact that the patients in the experimental group participating in the study applied thyme oil by taking 8 breaths and smelling it from the right nostril, left nostril, and both right and left nostrils, and the fact that this could not be standardized in all patients in the experimental group may be a limitation. Since the data were collected by a single researcher, participants were not blinded. Finally, we were not able to analyse in detail all the medications each patient was taking, but only recorded the standard COVID-19 treatment protocol given to all patients. Therefore, it is recommended that all medications taken by patients be taken into account in future studies.

Contributions and conclusions

Aromatherapy with thyme oil was effective on the management of COVID-19 symptoms and the regulation of vital signs and hemodynamic parameters. The use of thyme oil in the form of inhaler sticks other than its normal use is one of the novel aspects of the research. It is recommended that inhaled aromatherapy with thyme oil be used as a non-pharmacological treatment in addition to medical treatment in the management of COVID-19 symptoms and in the regulation of vital signs and hemodynamic parameters. In addition, it may be recommended to conduct similar or further studies to examine the effect of thyme oil in the symptoms of loss of taste-smell, runny nose, and nausea and vomiting, to evaluate the effect of thyme oil in different respiratory system diseases, to support the effect of thyme oil on vital signs and hemodynamic parameters.

Ethical aspects of the research

Ethics committee approval (Date: 19.10.2021 Decision no: 2021/2631) was obtained from the Inonu University Health Sciences Non-Interventional Clinical Research Ethics Committee.

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CRediT authorship contribution statement

Uğur Öner: Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing, Methodology. **Zeliha Cengiz:** Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing.

Data availability

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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