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Research Article

Effect of *Rosmarinus Officinalis* Essential Oil On Anxiety, Depression, And Sleep Quality

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ABSTRACT

Introduction: The objective of this investigation was to evaluate the effect of *Rosmarinus officinalis* essential oil on anxiety, depression, and sleep quality. **Methods:** The essential oils were extracted by hydro-distillation using a modified Clevenger-type apparatus and the chemical composition was performed by Gas chromatography with flame ionization detection (GC-FID) and Gas chromatography mass spectrometry (GC–MS). Furthermore, a quasi-experimental study was conducted, where 81 participants were divided into two groups, comprising a waiting list control group and an experimental group treated with essential oils. Anxiety and depression indexes were evaluated using the Zung Self-Rating Anxiety Scale (SAS) and the Zung Self-Rating Depression Scale (SDS), and sleep quality was measured with the Pittsburgh Sleep Quality Inventory (PSQI). **Results:** Chemical analysis showed that 1,8 cineole (37.6%), α-pinene (19.9%), and linalool (15.8%) were the main components. Anxiety, depression, and sleep quality scores showed a decrease in the post-test study phase compared to the pre-test in the experimental group ($p<0.05$). A large size effect was found in the case of anxiety ($d = 1.491$; $g= 1.490$) with $1-\beta=0.996$, while medium size effects were observed for depression ($d = 0.581$; $g= 0.582$) with $1-\beta=0.585$; and sleep quality ($d = 0.586$; $g = 0.588$) with $1-\beta=0.638$. **Conclusion:** Essential oils extracted from *Rosmarinus officinalis* are more effective in calming anxiety and show moderate changes in depression and sleep quality.

Key words: Essential oils, Anxiety, Depression, Sleep quality, *Rosmarinus officinalis*.

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INTRODUCTION

Emotional disorders cause a considerable burden on global health, emerging evidence suggests that levels of stress and anxiety-related symptoms increased during the COVID-19 pandemic.[1,2] In fact, previous experiences have shown that infectious disease outbreaks are related to a greater number of mental health problems in survivors and affected communities.[3] In this sense, the post-pandemic era will probably be characterized by an increase in mental health problems.[4] Data suggest that high levels of anxiety, depression symptoms, and sleep problems have been prevalent during pandemic,[5] especially among young adults, showing a consistent increasing trend.[6] Literature also indicates that stress may trigger anxiety as well as sleep difficulties and depression.[7] In this context, insomnia is one of the most prevalent sleep disorders, defined as a chronic statement of difficulty falling or staying asleep.[8] In this regard, insomnia, anxiety, and depression share common etiological processes, however, evidence indicates a cyclical relationship, that is, sleep disorders impulse the development of depression[9] as well as sleep disorders induce depression.[10] Therefore, as an investigation may sustain, improving sleep quality could prevent, manage, and alleviate stress and depression symptoms.[11]

Nowadays, there is a growing trend to use herbal medicines as an alternative to treat different ailments. This is in accordance with the belief that all natural products are safer and cheaper.[12] In this sense, herbs constitute the most significant resource for the research of therapeutically effective drugs.[13] Consequently, the use of herbs in aromatherapy dates to around 1200 BC and these have been used in ancient civilizations for medical purposes, among others.[14,15]

According to National Center for Complementary and Integrative Health (NCCIH), Americans spend more than $30.2 billion per year on aromatherapy, as well as global spending is expected to grow to $5 trillion by 2050; showing how this approach has gained acceptance and popularity recently.[16] Aromatherapy uses essential oils (EOs) to cause a positive effect on mood, behavior, and wellness, in fact, several investigations have evaluated the therapeutic effects of EOs in mental health.[17] However, further studies are needed to support the use of EOs in the treatment of mental health disorders. Therefore, the aim of this study was to evaluate the effect of *Rosmarinus officinalis* essential oil on anxiety, depression, and sleep quality.

MATERIALS AND METHODS

Plant material

Fresh leaves of *Rosmarinus officinalis* were obtained from a local market and verified by Segundo Leiva Gonzales, Biol, and deposited at the Herbarium Antenor Orrego (HAO) of Antenor Orrego University.

Essential oils extraction

The leaves of *Rosmarinus officinalis* were washed with distilled water to remove dust. The samples

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were then dried using a forced air circulation stove at a temperature of 40 ° C for 24 h. Next, the samples were milled, and the powdered plant materials (100 g) were placed in a round bottom flask with 1000 ml of distilled water and connected to a modified Clevenger-type apparatus. Hydrodistillation was completed for 4 h after boiling. Finally, the oil was dried with anhydrous sodium sulphate (Na_2SO_4) and stored in a refrigerator in amber glass vials at 4°C for further use in experiments.[18]

Determination of essential oil composition

Gas chromatography analysis (GC) was performed in a Hewlett Packard 6890 gas chromatograph with a flame ionization detector (FID), using the following conditions: column temperature, 40 °C (8 min) to 180 °C at 3 °C/min, 180-230 °C at 20 °C/min, 230 °C (20 min); injector temperature 250 °C, detector temperature 250 °C; split ratio 1:50; carrier gas H2 (34 KPa). Gas chromatography mass spectrometry (GC-MS) was carried out using a Hewlett-Packard 6890 series gas chromatograph coupled with a mass selective detector Hewlett Packard MSD 5972. The system conditions were the following: fused silica capillary column HP-Innowax (30m x 0.25 mm i.d., 0.25 µm film thickness), column temperature, 40 °C (8 min) to 180 °C at 3 °C/min, 180-230 °C at 20 °C/min, 230 °C (20 min); interface 280 °C; split ratio 1:100; carrier gas He (56 KPa); EI mode 70 eV. The essential oil components were identified based on comparison of their mass spectra, retention indices (RI) with those of authentic samples and/or the NIST mass spectral library and literature.[19]

Study design and sample

This was a quasi-experimental study, using a pre-test and post-test design with an experimental group and a waiting list control group. 81 participants were divided into two groups, the first one treated with aromatherapy based on essential oil from *Rosmarinus officinalis* leaves (EG) and a waiting-list (WL) control group.

Instruments

Zung Self-Rating Anxiety Scale (SAS): This scale consists of 20 items, scored each one from 1 to 4 (1= non or a little of the time, 2 = some of the time, 3 = good part of the time, 4 = most of the time).[20] This instrument shows the validity and reliability for the population and context applied.[21]

Zung Self-Rating Depression Scale (SDS): This scale consists of 20 items. Each item is scored from 1 to 4 (1= none or a little of the time, 2 = some of the time, 3 = good part of the time, 4 = most of the time).[22] This instrument shows the validity and reliability for the population and context applied.[23]

Pittsburgh Sleep Quality Inventory (PSQI): This questionnaire contains 18 items which are grouped into seven components. The score of each item ranges from 0 to 3. The sum score of these seven components is considered as the total PSQI score which is 0–21. Scores greater than 5 show low sleep quality.[24] For the present study, the validity and reliability test for the local population and context was determined using the item test method, finding values greater than 0.42 for each item; additionally, the reliability coefficient of 0.96 was found using the split-half method.

Study procedure

A free aromatherapy course was offered to students at a private university. The course was conducted completely online, because of Peruvian government restrictions for the global pandemic. 87 undergraduate students were enrolled, and 81 took part in this research between March and April 2022. Inclusion criteria included students enrolled in the academic semester 2022-01. Meanwhile, exclusion criteria were participants with previous practice of meditation, tai chi or yoga, psychiatric or pharmacological treatment, pregnancy, flu, and loss of smell for COVID-19. The students belonged to two sections (A and B) of the same course. These sections were formed before the researchers' arrival; for this reason, there was no randomization. Section A was selected as EG and Section B as WL. After group selection, instruments were administered (pretest). Additionally, each participant received a weekly aromatherapy kit with everything they needed for oils applications, including an instruction manual. Each kit was sent each week to each student until the investigation was completed. In addition, online meetings were held weekly to monitor the applications and provide feedback. The EOs application was according to the methodology of Reza *et al.*,[25] where the participants were asked to pour two drops of EOs on a cotton ball using a dropper. Next, the cotton ball was held under the participant's nose while closed his or her eyes and took 10 deep breaths. Next, the cotton was pinned to the collar of the participant for 30 minutes. After that, the participant unpinned and disposed of the cotton ball. WL control group did not receive any intervention until the end of the application of EG. The applications were every day for 4 weeks. At the end of intervention, the instruments were administered again (posttest). (Figure 1). All participants were informed about the investigation program goals and signed a consent form in which confidentiality and anonymity were guaranteed. The study protocol was approved by Institutional Review Board (IRB). Furthermore, this investigation was carried out in accordance with the Declaration of Helsinki.

Data analysis

Data were presented as mean ± standard deviation (SD). Differences in sociodemographic and clinical data of participants were analyzed using the Pearson Chi-Square and Likelihood-ratio tests. The Mann-Whitney U test was used to determine significant differences between the groups, while the Wilcoxon test was used to determine significant differences between the study phases, in which $p < 0.05$ was considered statistically significant. These tests were used because the data did not conform to the normal distribution. Cohen's D and Hedges' G were calculated between the groups for post-test scores, as well as statistical power. Statistical analysis was performed using SPSS v.27.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Table 1 shows the chemical composition of *Rosmarinus officinalis* essential oil, where 18 components were identified, representing 98.35% (area percent) of total oil content, among which the major constituents were 1,8-Cineole (37.6%), α-pinene (19.9%), linalool (15.8%), limonene (4.12%), borneol (3.6%), camphor (2.8%), camphene (2.6%), myrcene (2.54%), and α-terpineol (2.4%). Table 2 presents socio-demographic and clinical data of analyzed undergraduate students where 34 (46.6%) were male and 39 (53.4%) were female. WL was formed by 17(47.2%) males and 19 (52.8%) females, while EG was constituted by

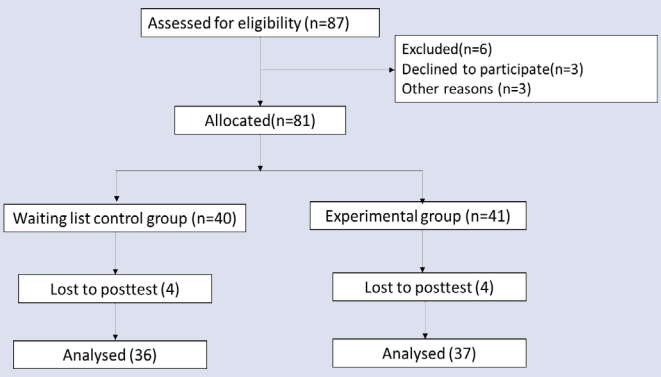


Figure 1: Flowchart of the study.

Table 1: Main chemical constituents (%) of the essential oils of *Rosmarinus officinalis*.

N°	Compounds	RI	%
1	α-pinene	935	19.9
2	Camphene	952	2.6
3	β-pinene	970	0.2
4	Myrcene	983	2.54
5	Limonene	1027	4.12
6	1,8-Cineole	1034	37.6
7	Linalool	1090	15.8
8	Camphor	1125	2.8
9	Isoborneol	1158	0.1
10	Borneol	1170	3.6
11	α-terpineol	1183	2.4
12	Bornyl acetate	1276	1.9
13	β-caryophyllene	1422	1.65
14	β-farnesene	1454	1.18
15	γ-muurolene	1483	t
16	Germacrene D	1490	0.6
17	Caryophyllene oxide	1585	0.42
18	α -Bisabolol	1671	0.94
	Total identified (%)		98.35

RI, Retention index; t= traces (<0.1%)

Table 2: Sociodemographic and clinical data of participants.

Socio-demographic data	WL	EG	Total	p-Value
Gender				
Male	17 (47.2%)	17 (45.9%)	34 (46.6 %)	0.913[a]
Female	19 (52.8%)	20 (54.1%)	39 (53.4%)	
Age(yr)				
18-25	26 (72.2%)	25 (67.6%)	51 (69.9%)	0.665[a]
26-36	10 (27.8%)	12 (32.4%)	22 (30.1%)	
Marital status				
Married	1 (2.8%)	0 (0%)	1 (1.4%)	0.232[b]
Unmarried	35 (97.2%)	37 (100.0%)	72 (98.6%)	
Divorced	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Clinical treatment provided				
Psychological	6 (16.2%)	5 (13.9%)	11 (15.1%)	0.781[b]
Pharmacological	0(0.0%)	0(0.0%)	0 (0.0%)	
None	31(83.8%)	31(86.1%)	62(84.9%)	

[a]p-value is calculated by Pearson Chi-Square test.
[b]p-value is calculated by Likelihood-ratio test.

17 (45.9%) males and 20 (54.1%) females. Besides, most participants were between 18-25 years old (n=51; 69.9 %) and the rest were between 26-36 years old (n=22; 30.1%). WL and EG were formed mostly by students between 18-25 years old (WL=72.7% and EG=67.6%). All these results show no statistically significant differences (p>0.05), using the Pearson Chi square test. Furthermore, in terms of marital status, most participants were unmarried (n=72; 98.6%) and only 1 (2%) was married. Finally, most of the participants never attended treatment, 62(84.9%) and 11(15.1%) attended psychological treatment, but there was no difference between group conformations, showing no statistically significant difference (p>0.05), using Likelihood ratio test.

Table 3 shows the mean score and SDs for stress, sleep quality, anxiety, and depression where all groups did not show differences in pretest scores (p> 0.05). However, in posttest scores there were significant differences between WL and EG (p<0.05). All these outcomes were calculated by Mann Whitney U test between groups. Besides, regarding to the study phase, WL scores did not show differences between pretest and posttest (p>0.05). Nevertheless, all variables showed differences between study phases (p<0.05). All these results were calculated using the Wilcoxon test.

Besides, Table 4 shows the scores obtained by the Cohen's D and Hedges' G test, as well as the statistical power (1-β); where values between 0.5 and 0.8 show moderate changes, as is the case of stress (d = 790; g = 0.789), sleep quality (d = 0.586; g = 0.588) and depression (d = 0.581; g = 0.582). In addition, a large size effect was found for anxiety (d = 1.491; g = 1.492). Finally, this table shows the observed power (1-β), where anxiety is the only variable with an adequate statistical power (1-β=0.996). It is noteworthy to specify that the standard for the desired power is 0.80.

DISCUSSION

The COVID-19 pandemic is considered a new stressor for mental health, therefore interventions in this area will be a priority in the next times.[26] In this context, chemical compounds from essential oils used in aromatherapy produce subtle neurological and behavioral changes, helping to improve mood states and associated disorders.[17]

In this investigation, the main components were1,8-Cineole, α-pinene, and linalool, which is in accordance with research performed in Pakistan.[19] Somehow, another research found the main components were piperitone, linalool and α-pinene.[29] At the same time, other investigations also found these compounds among the majoritarian compounds but in different ranges and quantities.[28] Therefore, the components found in our work are frequently present in rosemary Eos;[29] but the variations are due to phenological stages, that is the ontogenesis process related to morphological modifications in the structure of plant organs which influence in EOs content[30], as well as environmental factors such as altitude, soil conditions and seasonality[31]; in addition to genotype, extraction and drying methods.[28,32]

On the other hand, with respect to sociodemographic data of participants, the majority were young unmarried and female students, which is in accordance with the statistical information presented in

Table 3: Group differences of anxiety, depression, and sleep quality variables.

Groups	Pretest		Posttest		p-Value[b]
	Mean	SD	Mean	SD	
WL					
Anxiety	58.94	±5.09	58.97	±5.83	0.874
Depression	49.39	±6.69	49.81	±6.99	0.979
Sleep quality	6.14	±4.22	6.28	±5.27	0.989
EG					
Anxiety	59.03	±5.12	50.28	±5.82	0.000*
p-value[a]	0.943		0.000*		
Depression	49.65	±6.61	45.86	±6.59	0.004*
p-value[a]	0.820		0.020*		
Sleep quality	6.17	±5.53	3.70	±3.31	0.007*
p-value[a]	0.558		0.040*		

*p<0.05
[a]p-value is calculated by Mann Whitney U test between groups.
[b]p-value is calculated by Wilcoxon test between study phases.

Table 4: Cohen's D and Hedges' G between WL and EG in posttest outcomes and observed power (1-β).

Variables	Cohen's d Posttest	Glass's Δ Posttest	1-β
Anxiety	1.491	1.490	0.996
Depression	0.581	0.582	0.585
Sleep quality	0.586	0.588	0.638

Peruvian universities and the Latin American context.[33,34] In addition, an investigation affirms that university students have a good attitude towards CAM, especially herbal medicine.[35] However, this point constitutes one of the limitations because it would be needed a wider age range and sample to generalize the outcomes.

Rosmarinus officinalis EOs evidenced in animal experimental models, a potential to reduce anxiety and depression.[36] In addition, there is information that shows a positive effect in reducing stress and anxiety in experimental models with volunteers.[37] All these data are in accordance with the outcomes found in this investigation, where anxiety and depression scores decreased in the posttest phase only in EG. Indeed, rosemary EOs showed a large size effect in anxiety and a medium size effect in depression. Thus, it is more effective on anxiety, which is verified with the adequate statistical power observed for this variable, conferring the relevance of these results, which may be explained by the chemical constituents as monoterpenes presented in rosemary EOs, one of them is 1,8-Cineole which evidenced anxiolytic effects in humans.[38] Thus, some authors have suggested that 1,8-cineole may interact with the benzodiazepine site on the $GABA_A$ receptor, producing anxiolysis, however, this compound did not entirely agonize $GABA_A$ site, which means that other receptors could be involved.[39] Besides, α-pinene exerts anxiolytic activity due to its hypnotic action to modulate $GABA_A$-BZD receptors.[40] In addition, linalool, another monoterpene found in rosemary EOs is considered a mood stabilizer, which shows anxiolytic properties, and its inhalation may reduce salivary cortisol, implicated in stress, a common trigger for anxiety, however linalool may block stress and diminish anxiety due to its capacity to restore catecholamine imbalance as well to reduce stress-induced ACTH levels.[41]

In the case of depression, monoterpenes such as linalool and β-pinene exert action through their interaction with the serotonergic route through postsynaptic 5-HT_{1A} receptors and the adrenergic system through α2-receptors, which play an important role in stress-induced behavioral changes.[42] In fact, monoterpenes can be inhaled and affect directly the central nervous system, interacting with dopaminergic receptors such as D1 receptors, which the mechanism followed by most of the antidepressant drugs.[43] Nevertheless, an investigation found that a single intraperitoneal dose of 1-8 cineole did not show antidepressant effects, however, most antidepressants in the market need an average of 2 to 4 weeks of administration to get therapeutic effects,[44] in addition, a potential pathway to EOs is a direct penetration of their molecules to brain areas *via* olfactory nerve, causing a rapid effect.[45]

Regarding to sleep, EG after treatment with EOs had significantly better sleep quality than CG, establishing a medium size effect and less power than the minimal required, which means that can rosemary EOs may improve moderately sleep quality, but the outcomes cannot be generalized. In this sense, there is evidence that rosemary extracts may improve sleep quality,[46] but human data related to these EOs is limited, however, components such as α-pinene displayed a sleep-increasing behavior by direct binding to $GABA_A$-benzodiazepine ($GABA_A$-BZD) receptors modulating partially BZD binding site, causing an hypnotic effect; in fact, this monoterpene may reduce sleep latency and enhanced non-rapid eye movement sleep (NREMS), which helps the body wind down as well as fall into a deep sleep, all these without affecting the rapid eye movement sleep (REMS) and delta action.[47] Moreover; 1,8-cineole may also present the effect in question, possibly through the modulation of dopaminergic and glutamatergic systems.[48] In addition, an investigation also found that linalool acupoint application therapy improved the sleep rate, sleep latency, and sleep duration.[49] In fact, the sedative effect of linalool is dose dependent and includes the hypnotic effect, thus the most feasible hypothesis is that linalool acts as an antagonist of the excitatory neurotransmitter glutamate binding to glutamatergic N-methyl-D-aspartate (NMDA) receptors, which play a critical role in diurnal rhythmicity, sleep, and memory consolidation.[50]

Finally, these results are not definitive because of limitations, thus future studies should be elucidated to generalize the results and specify the mechanism of action as well to explain if the effects are due to a particular compound or to the synergism of all.

CONCLUSION

The essential oils extracted from *Rosmarinus officinalis* are more effective for anxiety and show moderate changes in depression and sleep quality.

CONFLICTS OF INTEREST

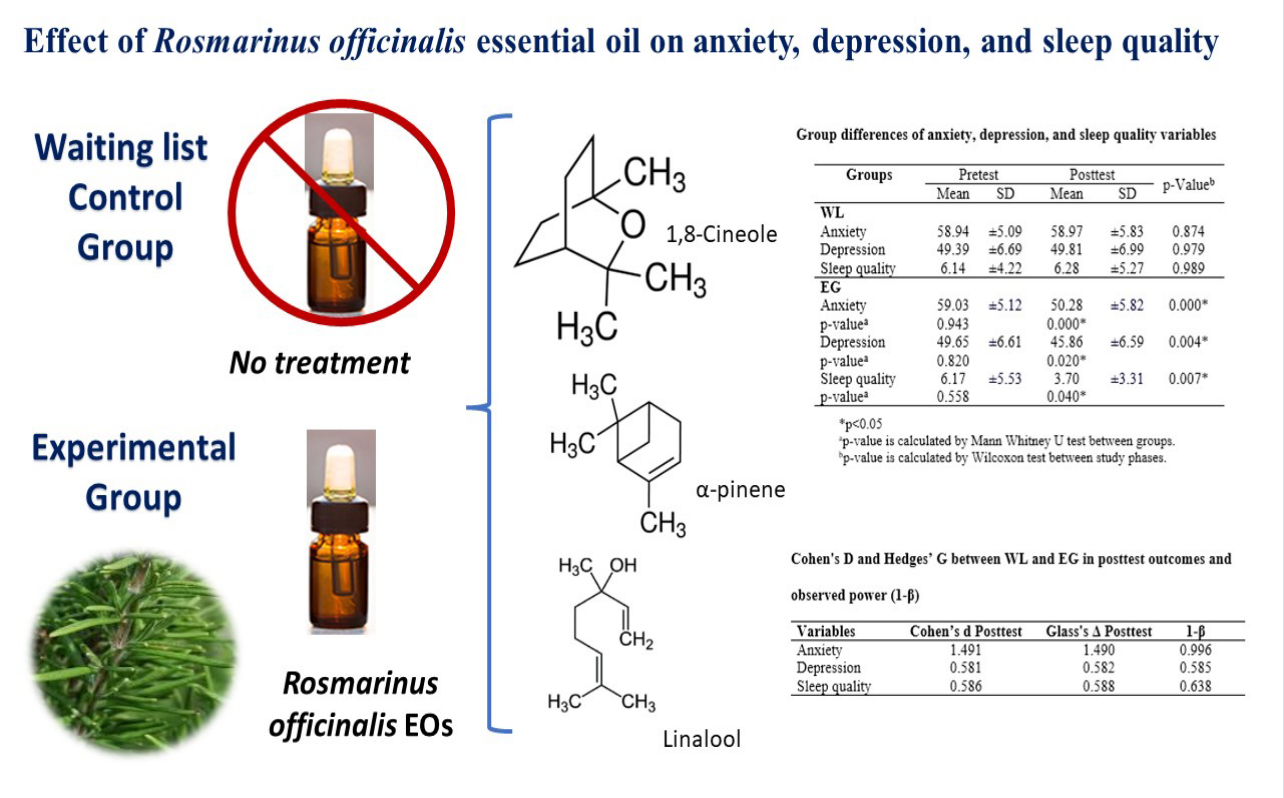
The authors declare no conflicts of interest.

REFERENCES

1. Taylor S, Landry CA, Paluszek MM, Fergus TA, McKay D, Asmundson GJG. Development and initial validation of the COVID Stress Scales. J Anxiety Disord. 2022;72:102232.
2. Qiu J, Shen B, Zhao M, Wang Z, Xie B, Xu Y. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: Implications and policy recommendations. Gen Psychiatr. 2022;33(2):e100213.
3. Cénant JM, Blais-Rochette C, Kokou-kpolou CK, Noorishad PG, Mukunzi JN, McIntee SE, *et al*. Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: A systematic review and meta-analysis. Psychiatry Res. 2021;295:113599.
4. Bill JS, Bulawa B, Swierzawski J. Mental Health and the City in the Post-COVID-19 Era. Sustainability. 2020;13(11):7533.
5. Landi G, Pakenham KL, Boccolini G, Grandi S, Tossani E. Health Anxiety and Mental Health Outcome During COVID-19 Lockdown in Italy: The Mediating and Moderating Roles of Psychological Flexibility. Front Psychol. 2020;11:2195.
6. Vahratian A, Blumberg SJ, Terlizzi EP, Schiller JS. Symptoms of Anxiety or Depressive Disorder and Use of Mental Health Care Among Adults During the COVID-19 Pandemic - United States, August 2020-February 2021. MMWR Morb Mortal Wkly Rep. 2021;70(13):490-4.
7. Kryger M, Roth T, Dement W. Principles and Practice of Sleep Medicine. 4th ed. Philadelphia: Elsevier Health Sciences. 2005.
8. Blake MJ, Trinder JA, Allen NB. Mechanisms underlying the association between insomnia, anxiety, and depression in adolescence: Implications for behavioral sleep interventions. Clin Psychol Rev. 2018;63:25-40.
9. Lovato N, Gradisar M. A meta-analysis and model of the relationship between sleep and depression in adolescents: Recommendations for future research and clinical practice. Sleep Med Rev. 2014;18(6):521-9.
10. Anconi-Israel S, Cooke JR. Prevalence and Comorbidity of Insomnia and Effect on Functioning in Elderly Populations. J Am Geriatr Soc. 2005;53(7):S264-71.
11. Lee MK, Lim S, Song JA, Kim ME, Hur MH. The effects of aromatherapy essential oil inhalation on stress, sleep quality and immunity in healthy adults: Randomized controlled trial. Eur J Integr Med. 2017;12:78-96.
12. Ahmad Khan MS, Ahmad I. Chapter 1 - Herbal Medicine: Current Trends and Future Prospects. In: Ahmad Khan MS, Ahmad I, Chattopadhyay D, editores. New Look to Phytomedicine. Academic Press; 2019;3-13.
13. Süntar I. Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. Phytochem Rev. 2020;19:1199-209.

14. Damian P, Damian K. Aromatherapy: Scent and Psyche: Using Essential Oils for Physical and Emotional Well-Being. Fairfield: Healing Arts Press. 1995.
15. Mehta S, MacGillivray M. Aromatherapy in Textiles: A Systematic Review of Studies Examining Textiles as a Potential Carrier for the Therapeutic Effects of Essential Oils. Textiles. 2022;2(1):29-49.
16. Farrar AJ, Farrar FC. Clinical Aromatherapy. Nurs Clin N Am. 2020;55(4):489-504.
17. Thangaleela S, Sivamaruthi BS, Kesika P, Bharathi M, Kunaviktikul W, Klunklin A, *et al*. Essential Oils, Phytoncides, Aromachology, and Aromatherapy—A Review. Appl Sci. 2022;12:4495.
18. Hannour K, Boughdad A, Maataoui A, Bouchelta A. Chemical composition and toxicity of Moroccan *Rosmarinus officinalis* (Lamiaceae) essential oils against the potato tuber moth, *Phthorimaea operculella* (Zeller, 1873) Zeller (Lepidoptera, Gelechiidae). J Mater Environ Sci. 2017;8(2):758-69.
19. Hussain AI, Anwar F, Chatha SLS, Jabbar A, Mahboob S, Nigam PS. *Rosmarinus officinalis* essential oil: antiproliferative, antioxidant and antibacterial activities. Braz J Microbiol. 2010;41(4):1070-8.
20. Zung WW. A rating instrument for anxiety disorders. Psychosomatics. 1971;12(6):371-9.
21. Alvarado-García PAA, Soto-Vásquez MR, Rosales-Cerquin LE, Rodrigo Villanueva EM, Jara-Aguilar DR, Tuesta-Collantes L. Anxiolytic and Antidepressant-like Effects of *Foeniculum vulgare* Essential Oil. Pharmacogn J. 2022;14(2):425-31.
22. Zung WW. A self-rating depression scale. Arch Gen Psychiatrys. 1971;12:63-70.
23. Alvarado-García PAA, Soto-Vásquez MR, Rosales LE, Rodrigo-Villanueva EM, Jara-Aguilar DR, Tuesta-Collantes L. Anxiolytic and Antidepressant-like Effects of Foeniculum vulgare Essential Oil. Pharmacogn J. 2022;14(2):425-31.
24. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.
25. Reza M, Bazeli J, Basiri M, Aalami H. Effect of aromatherapy on anxiety in patients with acute coronary syndrome hospitalized in cardiac care unit. Bali Med J. 2017;6(2):331-6.
26. Fiorillo A, Gorwood P. The consequences of the COVID-19 pandemic on mental health and implications for clinical practice. Eur Psychiatry. 2020;63(1):e32.
27. Gachkar L, Yadegari D, Rezaei MB, Taghizadeh M, Astaneh SA, Rasooli I. Chemical and biological characteristics of Cuminum cyminum and Rosmarinus officinalis essential oils. Food Chem. 2007;107:898-904.
28. Szumny A, Figiel A, Gutiérrez-Ortíz A, Carbonell-Barrachina AA. Composition of rosemary essential oil (Rosmarinus officinalis) as affected by drying method. J Food Eng. 2010;97(2):253-60.
29. Díaz-Maroto MC, Pérez-Coello MS, Sánchez-Palomo E, González-Viñas MA. Impact of drying and storage time on sensory characteristics of rosemary (Rosmarinus officinalis L.). J Sens Stud. 2007;22:34-48.
30. Alipour M, Saharkiz MJ. Phytotoxic activity and variation in essential oil content and composition of Rosemary (Rosmarinus officinalis L.) during different phenological growth stages. Biocatal Agric Biotechnol. 2016;7:271-8.
31. Bajalan I, Rouzbahani R, Pirbalouti AG, Maggi F. Quali-quantitative variation of essential oil from Iranian rosemary (Rosmarinus officinalis L.) accessions according to environmental factors. J Essent Oil Res. 2018;30:16-24.
32. Sadeh D, Nitzan N, Chaimovitsh D, Shachter A, Ghanim M, Dudai N. Ind Crops Prod. 2019;138:111419.
33. Correa-Lopez L, Morales-Romero AM, Olivera-Ruiz JE, SeguraMárquez CL, Cedillo-Ramirez L, Luna-Muñoz C. Factors associated with tobacco consumption in university students of Lima metropolitan. Rev Fac Med Hum. 2020;20(2):227-32.
34. Rodríguez-Hidalgo AJ, Pantaleón Y, Dios I, Falla D. Fear of COVID-19, Stress, and Anxiety in University Undergraduate Students: A Predictive Model for Depression. Front Psychol. 2020;11:591797.
35. Samara AM, Barabra ER, Quzaih HN, Zyoud SH. Use and acceptance of complementary and alternative medicine among medical students : a cross sectional study from Palestine. BMC Complement Med Ther. 2019;19(1):78.
36. Sasaki K, Ferdousi F, Fukumitsu S, Kuwata H, Isoda H. Antidepressant- and anxiolytic-like activities of Rosmarinus officinalis extract in rodent models: Involvement of oxytocinergic system. Biomed Pharmacother. 2021;144:112291.
37. Rahimi H, Nakhaei M, Mehrpooya N, Hatami SM, Vagharseyyedin SA. The Effect of Inhaling the Aroma of Rosemary Essential Oil on the Pre-Hospital Emergency Personnel Stress and Anxiety: A Quasi-Experimental Study. Mod Care J. 2019;16:e95082.
38. Kim KY, Seo HJ, Min SS, Park M, Seol GH. The Effect of 1,8-Cineole Inhalation on Preoperative Anxiety: A Randomized Clinical Trial. Evi Based Complementary Altern Med. 2014;2014:820126.
39. Dougnon G, Ito M. Inhalation Administration of the Bicyclic Ethers 1,8- and 1,4-cineole Prevent Anxiety and Depressive-Like Behaviours in Mice. Molecules. 2020;25(8):1884.
40. Salehi B, Upadhyay S, Orhan IE, Jugran K, Jayaweera SLD, Dias DA, *et al*. Therapeutic Potential of α- and β-Pinene: A Miracle Gift of Nature. Biomolecules. 2019;9(11):738.
41. Levenberg K, Edris W, Levine M, George DR. Considering a Potential Role of Linalool as a Mood Stabilizer for Bipolar Disorder. Curr Pharm Des. 2020;26(40):1-6.
42. Dos Santos ERQ, Maia CSF, Fontes EA, Melo AS, Pinheiro BG, Maia JGS. Linalool-rich essential oils from the Amazon display antidepressant-type effect in rodents. J Ethnopharmacol. 2018;212:43-9.
43. Cox-Georgian D, Ramadoss N, Dona C, Basu C. Therapeutic and Medicinal Uses of Terpenes. In: Joshee N, Dhekney S, Parajuli P. (eds) Medicinal Plants. Springer, Cham. 2019;349-50.
44. Ceremuga TE, McClellan CB, Green XC, Heber BE, Jolly ML, Malone TB, *et al*. Investigation of the Anxiolytic and Antidepressant Effects of Eucalyptol (1,8-Cineole), a Compound from Eucalyptus, in the Adult Male Sprague- Dawley Rat. AANA J. 2017;85(4):277-84.
45. Fung TKH, Lau BWM, Ngai SPC, Tsang HWH. Therapeutic Effect and Mechanisms of Essential Oils in Mood Disorders: Interaction between the Nervous and Respiratory Systems. Int J Mol Sci. 2021;22(9):4844.
46. Nematolahi P, Mehrabani M, Karami-Mohajeri FD. Effects of Rosmarinus officinalis L. on memory performance, anxiety, depression, and sleep quality in university students: A randomized clinical trial. Complement Ther Clin Pract. 2018;30:24-8.
47. Yang H, Woo J, Pae AN, Um MY, Cho NC, Park KD, *et al*. Alpha-Pinene, a Major Constituent of Pine Tree Oils, Enhances Non-Rapid Eye Movement Sleep in Mice through $GABA_A$-benzodiazepine Receptors. Mol Pharmacol. 2016;90(5):530-9.
48. Nóbrega de Figuêiredo SDFR, Monteiro AB, Alencar de Menezes IR, Dos Santos V, Do Nascimento EP, De Souza CK, *et al*. Effects of the *Hyptis martiusii* Benth. leaf essential oil and 1,8-cineole (eucalyptol) on the central nervous system of mice. Food Chem Toxicol. 2019;133:110802.
49. Xu L, Li X, Zhang Y, Ding M, Sun B, Su G, *et al*. The effects of linalool acupoint application therapy on sleep regulation. RSC Adv. 2021;11(11):5896.
50. Aprotosoaie AC, Hăncianu M, Costache IL, Miron A. Linalool: A review on a key odorant molecule with valuable biological properties. Flavour Fragr J. 2014;29:193-219.

GRAPHICAL ABSTRACT



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