Pharmacogn J. 2022; 14(2): 425-431
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Research Article

Anxiolytic and Antidepressant-like Effects of *Foeniculum vulgare* Essential Oil

Paul Alan Arkin Alvarado-García[1,*], Marilú Roxana Soto-Vasquez[2], Luis Enrique Rosales-Cerquin[1], Elda Maritza Rodrigo-Villanueva[2], Demetrio Rafael Jara-Aguilar[2], Lurdes Tuesta-Collantes[3]

ABSTRACT

Introduction: The aim of this research was to determine the anxiolytic and antidepressant-like effects of the essential oils from *Foeniculum vulgare* aerial parts and seeds. **Methods:** The oils were extracted by hydro-distillation using a modified Clevenger-type apparatus and chemical composition was performed by Gas chromatography with flame-ionization detection (GC-FID) and Gas chromatography-mass spectrometry (GC–MS). Furthermore, an experimental trial was conducted, where 117 participants were divided into three groups, comprising a waiting list control group and two experimental groups treated with essential oils. The anxiety and depression indexes were evaluated by Zung Self-Rating Anxiety Scale (SAS) and Zung Self-Rating Depression Scale (SDS). **Results:** chemical analysis showed that trans-Anethole was the main component, both in the essential oil from aerial parts (35.5%) and seeds (79.2%). Anxiety and depression scores showed a decrease in posttest study phase in comparison with pretest in all experimental groups ($p<0.05$), except for depression scores in the group treated with essential oil from aerial parts ($p>0.05$). Small changes were found in the case of anxiety for group treated with essential oils from aerial parts ($d = 0.41$; $\Delta = 0.40$) while moderate ($d = 0.86$; $\Delta = 0.85$) and small ($d = 0.38$; $\Delta = 0.39$) changes were found for anxiety and depression respectively, in the group treated with essential oil from seeds. **Conclusion:** The essential oil from *Foeniculum vulgare* seeds is more effective to relief anxiety than depression while the essential oil from *Foeniculum vulgare* aerial parts only exhibit small changes for anxiety.

Key words: Essential oils, Anxiety, Depression, *Foeniculum vulgare*.

Paul Alan Arkin Alvarado-García[1,*], Marilú Roxana Soto-Vasquez[2], Luis Enrique Rosales-Cerquin[1], Elda Maritza Rodrigo-Villanueva[2], Demetrio Rafael Jara-Aguilar[2], Lurdes Tuesta-Collantes[3]

[1]Escuela de Medicina. Universidad César Vallejo, Trujillo, PERÚ.
[2]Facultad de Farmacia y Bioquímica. Universidad Nacional de Trujillo, Trujillo, PERÚ.
[3]Facultad de Ciencias Biológicas. Universidad Nacional de Trujillo, Trujillo, PERÚ.

Correspondence

Paul Alan Arkin Alvarado-García

Escuela de Medicina. Universidad César Vallejo, Trujillo, PERÚ.

Email: palvaradog@ucvvirtual.edu.pe

History

- Submission Date: 25-02-2022;
- Review completed: 12-03-2022;
- Accepted Date: 17-03-2022.

DOI : 10.5530/pj.2022.14.54

Article Available online

http://www.phcogj.com/v14/i2

INTRODUCTION

Emerging international evidence indicates that COVID-19 pandemic is a major threat to population physical and mental health.[1] Anxiety, depression, and posttraumatic stress disorder symptoms were common in general population in different contagion waves of pandemic.[2] The impact of worldwide lockdown, quarantine among other restrictions to stop contagion led to maladaptive behaviors, creating a proper scenario to develop neurotic disorders as generalized anxiety disorder and obsessive-compulsive disorders, emotional outbursts especially panic, fear, anxiety, self-harm, depression, suicide, etc.[3]

Pharmacological treatment includes the use of benzodiazepines (BDZs) for anxiety as well as tricyclic Antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and selective serotonin re-uptake inhibitors (SSRIs) for depression.[4] Nevertheless, full remission of disease symptom has remained elusive; besides, the efficacy, duration of effects as side effects of these drugs are a serious concern and constitute the need for newer alternative treatments.[3]

Medicinal plants constitute the most significant source of botanical material for the research of therapeutically effective drugs.[5] According to the World Health Organization (WHO), about 70% of world population use plants to cover their primary health needs.[6] In this sense, Complementary and alternative medicine (CAM) has been integrated to conventional medicine; indeed, literature estimates that average 95% of people used biologically based therapies at one point in their lifetime.[7] This type of CAM includes the use of herbs such as in aromatherapy. This CAM modality is the science of using essential oils (EOs) from plants to utilize their therapeutic properties.[8]

EOs are aromatic oily liquids, obtained from different plants parts and comprised of multi-component mixtures that contain hundreds of chemicals.[9] Preclinical and clinical studies have confirmed that EOs can alleviate insomnia, depression, anxiety, and other mental illness; besides these oils are safe when used at an adequate concentration showing no adverse effects in comparison with commercial psychotropic drugs.[10]

Foeniculum vulgare, universally known as fennel, is a traditional and popular herb originated in the southern Mediterranean region and it grows wild throughout the Eastern, and Western hemispheres.[11] Preclinical evidence shows that EOs from *Foeniculum vulgare* aerial parts exhibited a promising anxiolytic activity.[12] In addition, an investigation found that EOs from fennel seeds induced antidepressant-like effects on mice, although its efficacy in humans has not been elucidated yet.[13] Another research also found that EOs extracted from *F. vulgare* seeds ameliorated anxiety and depression in laboratory rats, indicating an important potential for clinical applications in the management of these conditions.[14] However, there is lack of evidence about this oil in human models. In this sense, the aim of this study was to determine the anxiolytic and antidepressant-like effects of the essential oil from *Foeniculum vulgare* aerial parts and seeds.

Cite this article: 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;12(1): 425-431.

MATERIALS AND METHODS

Plant material

The aerial parts and seeds of *Foeniculum vulgare* were collected from Rosa Elena de Los Ríos Martínez medicinal plants botanical garden of Universidad Nacional de Trujillo at 34 masl; located in Trujillo district, La Libertad Region, Perú. The sample collection was conducted in the months of June to July 2021. Voucher specimens were prepared and identified by Segundo Leiva Gonzales, Biol and deposited at the Herbarium Antenor Orrego (HAO) of Antenor Orrego University.

Essential oils extraction

The aerial parts and seeds of *Foeniculum vulgare* were washed with distilled water to remove dust. Then, samples were dried using a forced air circulation stove at a temperature of 40°C for 24 h. Next, samples were milled, and the powdered plant material (100 g) were placed in a round bottom flask with 1000 ml distilled water, and then connected to a modified Clevenger-type apparatus. Hydrodistillation was completed for 3 h after boiling. Then the oil was dried over anhydrous sodium sulphate and stored in a refrigerator in amber glass vials at 4°C for further use in experiments.[15] The same procedure was carried out for aerial parts and seeds.

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 two fused silica capillary columns with two different stationary phases (SPB-1 and SupelcoWax 10, 30 m x 0.2 mm, 0.20 µm), and with the following conditions: Oven temperature, 45ºC-175°C,at 3 ºC/min, 15ºC/min up to 300ºC (10 min); injector temperature 280 ºC, detector temperature 300 ºC; split ratio 1:50; carrier gas: H, adjusted to a linear velocity of 30 cm/s. The percentage composition of the oils was computed by the normalization method from the GC peak areas. 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), Injector and oven temperatures were as above; transfer line temperature, 280°C; ion trap temperature, 220°C; carrier gas, helium, adjusted to a linear velocity of 30 cm/s; split ratio, 1:40; ionization energy, 70 eV; ionization current, 60 µA; scan range, 40-300 u; scan time, 1 s. Finally, the identification of essential oil constituents was accomplished by visual interpretation, comparing their retention indices (RI) and mass spectra with literature data and with those in the NIST 2011 mass spectra library as well as Wiley library.[16]

Study design and sample

This study utilized an experimental, pretest, and posttest design, using two experimental groups and a waiting-list control group. 117 participants were divided into three groups of 39 participants for each group, the first one treated with aromatherapy based on essential oil from *Foeniculum vulgare* aerial parts (EG1) and the second group treated with essential oil from *Foeniculum vulgare* seeds (EG2); and finally, a waiting-list (WL) control group.

Instruments

Zung Self-Rating Anxiety Scale (SAS): This scale was developed to evaluate the frequency of anxiety symptoms. It 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).[17] For the present study, the validity and reliability test for the local population were determined using the item-test method, finding values above 0.40 for each item, additionally, the reliability coefficient of 0.89 was found using the split-half method.

Zung Self-Rating Depression Scale (SDS): This scale consists of 20 items, constructed based on the clinical diagnostic criteria used to characterize depressive disorders. 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).[18] For the present study, the validity and reliability test for the local population was determined using the item test method, finding values above 0.30 for each item; additionally, the reliability coefficient of 0.94 was found using the split-half method.

Study procedure

A free aromatherapy course was offered to students belonged to a private university. The course was conducted entirely online, due to Peruvian government restrictions for global pandemic. 132 undergraduate students were enrolled and 117 took part in this investigation between September and October 2021. Inclusion criteria included students enrolled in the academic semester 2021-02. They were required to have a score of greater than 45 in both instruments; meanwhile exclusion criteria were participants with previous practice of meditation, tai chi or yoga, psychiatric or pharmacological treatment, and pregnancy. Participants for each group were randomized by a person not involved in the study by utilization of a random number table. After groups were formed, instruments were administered (pretest). Besides, each participant received weekly an aromatherapy kit with everything they needed for oils applications, including an instruction manual. Each kit was sent each week to each participant until the research was completed. In addition, weekly online meetings were held to monitor the applications and provide feedback. The EOs applications were according to the methodology of Reza et al.,[19] 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 the cotton ball. WL control group did not receive any intervention until applications in all experimental groups ended. The applications were every day for 4 weeks. At the end of interventions, the two instruments were administered again (posttest) (Figure 1). When the offered course finished, 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). Besides, this investigation was performed in accordance with the Declaration of Helsinki.

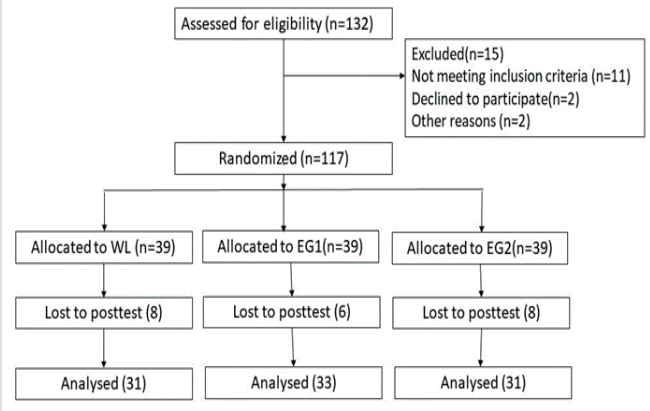


Figure 1: Flowchart of the study.

Data analysis

Data were presented as mean ± standard deviation (SD). Differences in sociodemographic and clinical data from participants were analyzed using the Pearson Chi-Square and Likelihood-ratio tests. Kruskal-Wallis test was used to determine significant differences between groups, while Wilcoxon test was used to determine significant differences between the study phases. These tests were used because data did not conform to the normal distribution. Cohen's D, Glass's delta and Percentage Change were calculated between pretest and posttest scores. All statistical analysis was performed using SPSS v.25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Table 1 shows the results from samples analyzed by GC/MS, where 31 components were identified in the essential oil from *Foeniculum vulgare* aerial parts, representing 98.8% (area percent) of total oil content, among which the major constituents were trans-Anethole (35.5%), α-Pinene (14.3%), limonene (13.1%), p-cymene (7.3%), α-fenchone (6.4%), α-Phellandrene (5.1%), β-Pinene (4.7%), myrcene (3.9%), myrtenol (2.4%) and carvacrol (1.9%). Besides, 30 components were identified in the case of the essential oil from *Foeniculum vulgare* seeds, representing 99.5% (area percent) of total oil content. The major components were trans-Anethole (79.2%), limonene (11.3%), fenchone (3.2%) and α-Pinene (1.9%).

Table 2 presents socio-demographic and clinical data of analyzed undergraduate students where 42 (44%) were male and 53 (56%) were female. WL was formed by 14(45%) male and 17(55%) female, while EG1 was formed by 15(46%) male and 18 (54%) female, and there were 13(42%) male and 18 (58%) female in EG2. These results show no statistically significant differences ($p>0.05$), using the Chi square test. Besides, most participants were between 18-25 years old (n=67; 71%) and the rest between 26-38 years old (n=28; 29%). In relation to their marital status, 92(97%) were unmarried, 2 (2%) were married and only 1 (1%) was divorced. Finally, most of the participants never attended treatment, 88(93%) and only 7(7%) attended psychological treatment, and there was no difference between groups conformation, showing no statistically significant differences ($p>0.05$), using Likelihood ratio test.

Table 3 shows the mean score and SDs for anxiety and depression based on Zung Self-Rating Anxiety and Depression Scales, where all groups did not show differences in pretest scores ($p> 0.05$ for anxiety and depression). The same can be observed in posttest scores ($p>0.05$ for depression) except for anxiety scores ($p<0.05$). All these results were calculated by Kruskal-Wallis test. In relation with study phases, WL scores did not show differences between pretest and posttest ($p>0.05$), while only anxiety scores shown differences in EG1 ($p<0.05$) except for depression scores ($p>0.05$). Nevertheless, all EG2 scores shown differences between study phases ($p<0.05$). All these results were calculated by Wilcoxon test.

Besides, Table 4 shows the scores obtained by the Cohen's D and Glass's delta test, as well as the percentage of change found; where values between 0.2 and 0.5 show small changes, as is the case of anxiety in EG1($d = 0.41$; $\Delta= 0.40$) and depression in EG2 ($d = 0.38$; $\Delta = 0.39$). Besides, it was found moderate changes in EG2 scores for anxiety ($d = 0.86$; $\Delta = 0.85$). Likewise, In EG1, anxiety obtained a percentage of change of -4.51%, in addition, anxiety and depression in EG2 obtained a percentage of change of -8.09%, and -4.72% respectively.

DISCUSSION

It is well known that anxiety and depression symptoms have been dramatically increased in recent years because of COVID-19 pandemic.[20] In this sense, traditional herbal medicine can help to improve mental health conditions.[21] *F. vulgare* has been used

Table 1: Main chemical constituents (%) of the essential oils from *Foeniculum vulgare* aerial parts and seeds.

Components	RI	Foeniculum vulgare	
		Aerial parts	Seeds
α-Thujene	922	0.2	t
α-Pinene	931	14.3	1.9
Camphene	940	0.9	0.2
Sabinene	959	0.2	0.1
1-octen-3-ol	962	t	-
β-Pinene	970	4.7	0.4
Dehydro 1,8-cineol	974	0.4	0.2
Myrcene	978	3.9	0.5
α-Phellandrene	997	5.1	0.1
p-cymene	1012	7.3	0.2
Limonene	1025	13.1	11.3
Cis-β-ocimene	1032	0.8	0.5
γ-Terpinene	1038	0.2	0.6
Fenchone	1051	6.4	3.2
Terpinolene	1060	0.2	t
Terpinen-4-ol	1150	0.5	0.2
α-Terpineol	1158	0.1	-
Myrtenol	1165	2.4	0.3
Borneol acetate	1184	0.1	t
Trans-Carveol	1190	0.2	0.1
Carvone	1210	0.1	0.1
cis-Anethole	1222	t	t
Geraniol	1240	0.1	-
trans-Anethole	1255	35.5	79.2
Carvacrol	1298	1.9	0.1
α-Copaene	1380	-	0.1
trans-Caryophyllene	1420	-	t
α-Bergamotene	1443	t	t
β-Sesquiphellandrene	1511	0.1	-
γ-cadinene	1516	-	0.1
δ-cadinene	1525	0.1	-
(E)-Nerolidol	1560	-	t
Geraniol isovalerate	1597	t	t
Palustrol	1741	-	0.1
Phytol acetate	2044	t	t
Total identified (%)		98.8	99.5

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

Table 2: Socio-demographic and clinical data of participants.

Socio-demographic data	WL	EG1	EG2	Total	p-Value
Gender					
Male	14 (45%)	15 (46%)	13 (42%)	42 (44 %)	0.953[a]
Female	17 (55%)	18 (54%)	18 (58%)	53 (56%)	
Age(yr)					
18-25	21 (55%)	24(58%)	22(61%)	67 (71%)	0.907[a]
26-38	10(39%)	9(39%)	9(36%)	28 (29%)	
Marital status					
Married	1(3%)	0 (0%)	1 (3%)	2 (2%)	0.431[b]
Unmarried	30 (97%)	32 (97%)	30 (97%)	92 (97%)	
Divorced	0 (0%)	1 (3%)	0 (0%)	1 (1%)	
Clinical treatment provided					
Psychological	2(6%)	2(6%)	3(10%)	7 (7%)	0.840[b]
Pharmacological	0(0%)	0(0%)	0(0%)	0 (0%)	
None	29(94%)	31(94%)	28(90%)	88(93%)	

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

Table 3: Group differences of anxiety and depression variables according to Zung Self-Rating Anxiety and Depression Scales.

Groups	Pretest		Posttest		p-Value[b]
	Mean	SD	Mean	SD	
WL					
Anxiety	61.48	±5.30	61.88	±6.06	0.922
Depression	53.90	±6.42	54.16	±6.89	0.576
EG 1					
Anxiety	62.03	±6.14	59.23	±5.71	0.016*
Depression	54.00	±7.26	53.30	±5.09	0.359
EG 2					
Anxiety	61.45	±7.66	56.48	±5.94	0.002*
	0.841		0.005*		
Depression	53.97	±6.98	51.32	±7.37	0.038*
p-value[a]	0.990		0.342		

*p < 0.05
[a]p-value is calculated by Kruskal-Wallis test between groups
[b]p-value is calculated by Wilcoxon test between study phases

Table 4: Cohen's D, Hedges' G and Percentage Change in intervention groups.

Group	Cohen's d Posttest	Glass's Δ Posttest	% Of change Pretest-Posttest
EG1			
Anxiety	0.41	0.40	-4.51
Depression	0.14	0.12	-1.30
EG2			
Anxiety	0.86	0.85	-8.09
Depresion	0.38	0.39	-4.72

traditionally for its carminative properties, but it is also known for its essential oil with a characteristic anise odor.[22] According to literature, the major component for *F. vulgare* seeds essential oil can vary from methyl chavicol (estragole) to trans-anethole, fenchone, a-phellandrene, among others.[22-24] This is agreed with our results where the main component was also trans-anethole. In the case of *F. vulgare* aerial parts essential oil, the major component found was trans-Anethole what is in accordance with other investigations where the monoterpene fraction was dominant and the main component was also trans-anethole.[23,25] Indeed, fennel EOs show a considerable chemodiversity and the chemical composition can vary depending on the phenological state, different maturation stages and geographical origin.[26,27]

Regarding socio-demographic data of participants, the majority were young and female. This is in concordance with some studies which confirm that young, young adults and women conform the major population in Peruvian universities.[28] It is remarkable to say that the sample is conform for health science students. In this sense, an investigation affirm these students have a good attitude towards CAM, especially herbal medicine.[29] Nevertheless, this point constitutes one of the limitations because it would be needed a wider age range to generalize results.

Evidence in animal models shows that fennel EOs from aerial parts and seeds attenuate anxiogenic and depressive behavior.[12,13,30] In relation to human trials on the effects of fennel on anxiety and depression, it was found two studies where patients with depression or anxiety showed a slight or significant improvement. It´s remarkable to say that no significant differences were found between groups in these studies.[31,32] This agrees with the results of our work. In the case of anxiety, EG1 and EG2 EOs diminished anxiety scores, nevertheless the group treated with EOs from seeds had a greater size effect and percentage of change.

In the case of depression, the group treated with EOs from aerial parts did not have a statistical difference while EG2 showed small changes. In summary, EOs from seeds showed better results than EOs from aerial parts. This may be because the amount of anethole was greater in the seeds than in the aerial parts. In fact, evidence indicates that this compound may decrease the anxiogenic and depressogenic behaviors by increasing 5-HT levels and facilitating 5-HT neurotransmission;[30,33] a similar mechanism to SSRIs.[34] Moreover, other findings suggest that dopaminergic (D_1 and D_2 receptors), serotonergic ($5\text{-}HT_{1A}$, $5\text{-}HT_{2A}$ receptors), and noradrenergic (α_1 and α_2 adrenoceptors) systems could be partly involved in antidepressant effect of anethole.[35]

In addition, there is growing evidence that suggest the role of free radicals in the pathogenesis of anxiety and depression.[36] In this regard, increased oxidative stress has been reported because of increasing catabolism of 5-HT by monoamine oxidase B (MAO-B), but anethole inhibits the activity of MAO-B enzyme, alleviating psychiatric disorders as anxiety and depression.[33]

Other compound present in these EOs is limonene, where evidence reports its anxiolytic effect similar to diazepam, indeed, this monoterpene may regulate the DAergic and GABAergic neuronal pathways via the modulation of A2A receptor activity, generating an anti-anxiety activity.[37] Besides, literature indicates that limonene exhibits antidepressant effects that is related to modulation of monoaminergic system.[38] Furthermore, other constituent found was α-Pinene that have a potent action at the benzodiazepine (BZD) site of $GABA_A$ receptors causing sedation,[39] consequently a central nervous system depression.[40] This action may explain why EG1 did not present a significant antidepressant effect since the content of α-Pinene in the aerial parts was greater than seeds thus it can block partly the antidepressant effect. In this respect, different components of fennel EOs may be interacting, causing a synergistic action[41] or antagonism.

CONCLUSION

According to our investigation, the essential oils extracted from *Foeniculum vulgare* aerial parts exhibit small changes for anxiety but no changes for depression while the essential oils extracted from *Foeniculum vulgare* seeds show moderate changes for anxiety and small changes for depression.

CONFLICTS OF INTEREST

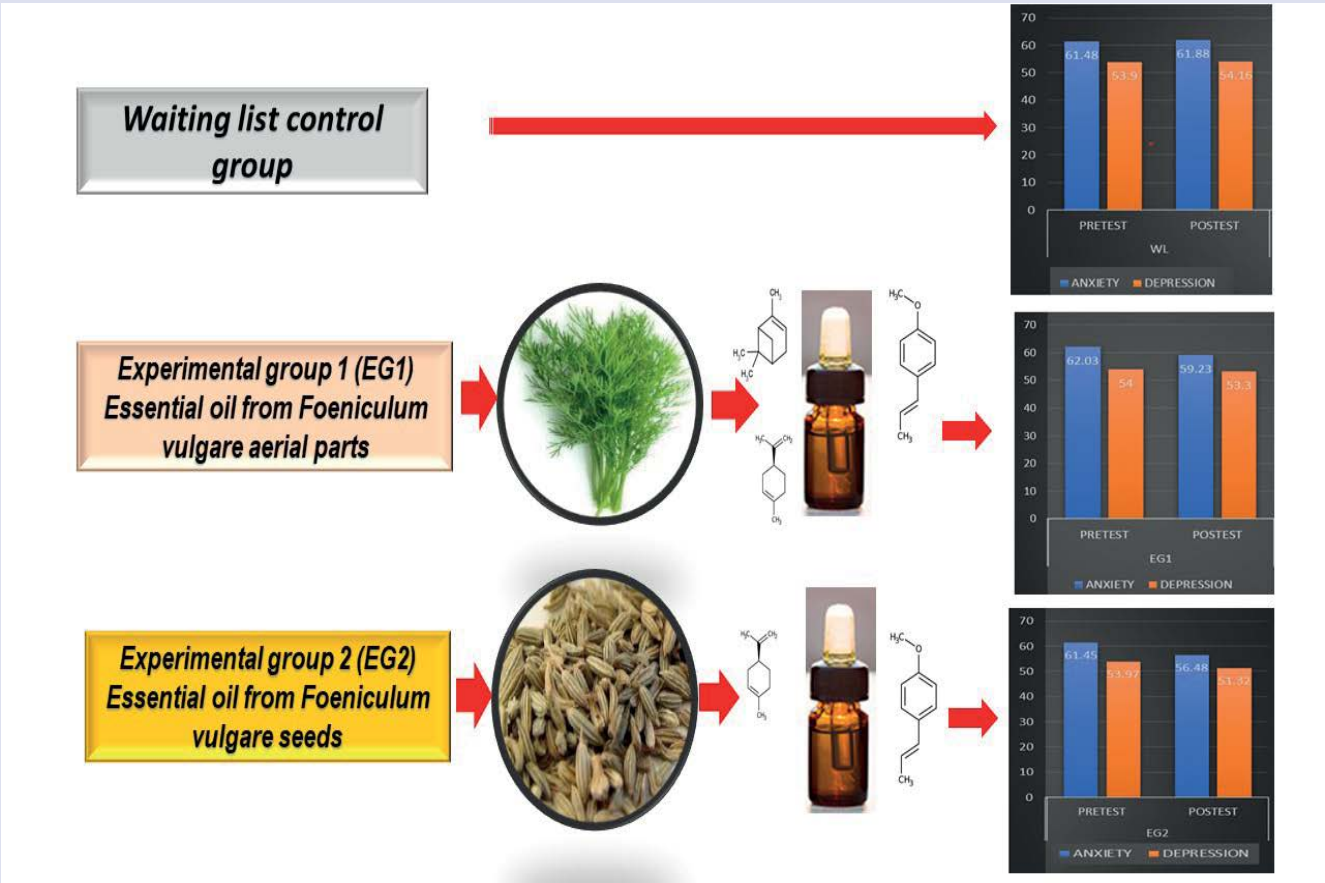
The authors declare no conflicts of interest.

REFERENCES

1. Ghebreyesus TA. Addressing mental health needs: An integral part of COVID-19 response. World Psychiatry. 2020;19(2):129-130.
2. Wang C, Pan R, Wan X. A Longitudinal Study on the Mental Health of General Population during the COVID-19 Epidemic in China. Brain Behav Immun. 2020;87:40-48.
3. Fajemiroye JO, Da Silva DM, Oliveira DR, Costa EA. Treatment for anxiety and depression: medicinal plants in retrospect. Fundam Clin Pharmacol. 2016;30(3):198-215.
4. Liu S, Yang L, Zhang C, Xiang Y, Liu Z, Hu S, *et al.* Online mental health services in China during the COVID-19 outbreak. Lancet Psychiat. 2020;7(4):e17-e18.
5. Süntar I. Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. Phytochem Rev. 2020;19:1199-1209.
6. World Health Organization (WHO). WHO Traditional Medicine Strategy. 2013;54:2014-2023.
7. Koithan M. Introducing Complementary and Alternative Therapies. J Nurse Pract. 2009;5(1):18-20.

8. Tanvisut R, Traisrisilp K, Tongsong T. Efficacy of aromatherapy for reducing pain during labor: a randomized controlled trial. Arch Gynecol. 2018;297(5):1145-1150.
9. Aziz AAA, Ahmad A, Setapar SHM, Karakucuk A, Azim MM, Lokhat D, *et al*. Essential Oils: Extraction Techniques, Pharmaceutical And Therapeutic Potential - A Review. Curr Drug Metab. 2018;19(3):1100-1110.
10. Lizarraga-Valderrama LR. Effects of essential oils on central nervous system: Focus on mental health. Phytother Res. 2021;35(2):657-679.
11. Badgujar SB, Patel VV, Bandivdekar AH. FoeniculumvulgareMill: a review of its botany, phytochemistry, pharmacology, contemporary application, and toxicology. Biomed Res Int. 2014;2014:1-32.
12. Mesfin M, Asres K, Shibesni W. Evaluation of anxiolytic activity of the essential oil of the aerial part of *Foeniculum vulgare* Miller in mice. BMC Complement Altern Med. 2014;14:30.
13. Abbasi-Maleki S, Maleki SG. Antidepressant-like effects of *Foeniculum vulgare* essential oil and potential involvement of dopaminergic and serotonergic systems on mice in the forced swim test. Pharma Nutrition. 2015;15:100241.
14. Cionca O, Hancianu M, Mircea C, Trifan A, Hritcu L. Essential oils from *Apiaceae* as valuable resources in neurological disorders: *Foeniculi vulgare* aetheroleum. Ind Crops Prod. 2016;88:51-57.
15. Abdellaoui M, Tariq ED, Derouich M, El-Rhaffari L. Essential oil and chemical composition of wild and cultivated fennel (*Foeniculum vulgare* Mill.): A comparative study. S Afr J Bot. 2020;135:93-100.
16. Miguel MG, Cruz C, Faleiro L, Simões TF, Figueiredo AC, Barroso JG, *et al*. *Foeniculum vulgare* Essential Oils: Chemical Composition, Antioxidant and Antimicrobial Activities. Nat Prod Commun. 2010;5(2):319-328.
17. Zung WW. A rating instrument for anxiety disorders. Psychosomatics. 1971;12:371-379.
18. Zung WW. A self-rating depression scale. Arch Gen Psychiatrys. 1971;12:63-70.
19. 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;6:331-336.
20. Hawkes MT, Szenczy AK, Klein DN, Hajcak G, Nelson BD. Increases in depression and anxiety symptoms in adolescents and young adults during the COVID-19 pandemic. Psychol Med. 2021:1-9.
21. Shahrajabian MH, Sun W, Soleymani A, Cheng Q. Traditional herbal medicines to overcome stress, anxiety and improve mental health in outbreaks of human coronaviruses. Phytother Res. 2021;35(3):1237-1247.
22. Rather MA, Dar BA, Sofi SN, Bhat BA, Qurishi MA. *Foeniculum vulgare*: A comprehensive review of its traditional use, phytochemistry, pharmacology, and safety. Arab J Chem. 2016;9:S1574-S1583.
23. Graça MG, Cruz C, Faleiro L, Simões MTF, Figueiredo AC, Barroso JG, *et al*. *Foeniculum vulgare* Essential Oils: Chemical Composition, Antioxidant and Antimicrobial Activities. Nat Prod Commun. 2010;5(2):319-328.
24. Díaz-Maroto MC, Díaz-Maroto IJ, Sánchez-Palomo E, Perez-Coello S. Volatile Components and Key Odorants of Fennel (*Foeniculum vulgare* Mill.) and Thyme (*Thymus vulgaris* L.) Oil Extracts Obtained by Simultaneous Distillation–Extraction and Supercritical Fluid Extraction. J Agri Food Chem. 2005;53(13):5385-5389.
25. Pavela R, Zabka M, Bednár J, Tríska J, Vrchotová N. New knowledge for yield, composition and insecticidal activity of essential oils obtained from the aerial parts or seeds of fennel (*Foeniculum vulgare* Mill.). Ind Crops Prod. 2016;83:275-282.
26. Diaaz-Maroto MC, Pearez-Coello MS, Esteban J, Sanz J. Comparison of the volatile composition of wild fennel samples (*Foeniculum vulgare* Mill.) from Central Spain. J Agric Food Chem. 2006;54(18):68146818.
27. Telci I, Demirtas I, Sachin A. Variation in plant properties and essential oil composition of sweet fennel (*Foeniculum vulgare* Mill.) fruit during stages of maturity. Ind Crops Prod. 2009;30:126-130.
28. Correa-Lopez L, Morales-Romero AM, Olivera-Ruiz JE, Segura-Márquez CL, Cedillo-Ramirez L, Luna-Muñoz C. Factors associated with tobacco consumption in university students of Lima metropolitan. Rev Fac Med Hum. 2020;20:227-232.
29. 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.
30. Perveen T, Yousuf S, Razi F, Zuberi NA, Tabassum S, Haider S. Involvement of altered serotonergic responses in fennel oil induced antidepressant, anxiolytic and antinociceptive effects in rats. World J Pharm Res. 2014;2:493-498.
31. Ghazanfarpour M, Mohammadzadeh F, Shokrollahi P, Khadivzadeh T, Najafi MN, Hajirezaee H, *et al*. Effect of *Foeniculum vulgare* (fennel) on symptoms of depression and anxiety in postmenopausal women: a double-blind randomised controlled trial. J Obstet Gynaecol. 2018;38(1):121-126.
32. Ghazanfarpour M, Najafi MN, Sharghi NB, Mousavi MS, Babakhanian M, Rakhshandeh H. A double-blind, placebo-controlled trial of Fennel (*Foeniculum vulgare*) on menopausal symptoms: A high placebo response. J Turk Ger Gynecol Assoc. 2018;19(3):122-127.
33. Perveen T, Emad S, Ahmad S, Batool Z, Yousuf S, Sheikh S, *et al*. Fennel Oil Treatment Mimics the Anti-Depressive and Anxiolytic Effects of Fluoxetine without Altering the Serum Cholesterol Levels in Rats. Pakistan J Zool. 2017;49:2291-2297.
34. García-García A, Newman-Tancredi A, Leonardo ED. 5-HT1A receptors in mood and anxiety: recent insights into autoreceptor versus heteroreceptor function. Psychopharmacology. 2014;231(4):623-636.
35. Hassanzadeh SA, Abbasi-Maleki S, Mousavi Z. Anti-depressive-like effect of monoterpene trans-anethole *via* monoaminergic pathways. Saudi J Biol Sci. 2022.
36. Xu Y, Wang C, Klabnik JJ, O'Donnell JM. Novel therapeutic targets in depression and anxiety: Antioxidants as a candidate treatment. Curr Neuropharmacol. 2014;12(2):108-119.
37. Song Y, Seo S, Lamichhane S, Seo J, Hong JT, Cha HJ, *et al*. Limonene has anti-anxiety activity *via* adenosine A2A receptor-mediated regulation of dopaminergic and GABAergic neuronal function in the striatum. Phytomedicine. 2021;83:153474.
38. Zhang LL, Yang ZY, Fan G, Ren JN, Yin KJ, Pan SY. Antidepressant-like Effect of Citrus sinensis (L.) Osbeck Essential Oil and Its Main Component Limonene on Mice. J Agric Food Chem. 2019;67(50):13817-13828.
39. Yang H, Woo J, Pae AN, Um MY, Cho N, Park KD, *et al*. Cho S. α-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):530-539.
40. Nielsen GD, Larsen ST, Hougaard KS, Hammer M, Wolkoff P, Clausen PA, *et al*. Mechanisms of Acute Inhalation Effects of (+) and (-)-α-Pinene in BALB/c Mice. Basic Clin Pharmacol Toxicol. 2005;96(6):420-428.
41. Okano S, Honda Y, Kodama T, Kimura M. The Effects of Frankincense Essential Oil on Stress in Rats. J Oleo Sci. 2019:68(10):1003-1009.

GRAPHICAL ABSTRACT



ABOUT AUTHORS

Ms. Paul Alan Arkin Alvarado-García
Master of Education. Professor at the Medicine School of Universidad César Vallejo. Develops research in Mental health problems, Complementary and Alternative Medicine, and natural products applicated to stress, anxiety, and depression.

Dr. Marilú Roxana Soto-Vásquez
Doctor in Pharmacy and Biochemistry, professor of the chairs of pharmacognosy, phytochemistry, pharmaceutical botany of Faculty of Pharmacy and Biochemistry of Universidad Nacional de Trujillo. Develops Research in Natural Products with antiprotozoal, antitumor, antimicrobial activities, and Complementary and Alternative Medicine.

MD. Luis Enrique Rosales-Cerquin
Gynecologist and obstetrics specialist. Professor at the Medicine School of Universidad César Vallejo. Develops research in reproductive health, natural products, and Integrative medicine.

Dr. Elda Maritza Rodrigo-Villanueva
Doctor in Pharmacy and Biochemistry, professor of the chairs of Investigation methodology. Develops Research in Natural Products.

Dr. Demetrio Rafael Jara-Aguilar
Doctor in Pharmacy and Biochemistry, professor at National University of Trujillo, section Natural Products. Develops Research in Natural Products.

Dr. Lurdes Tuesta-Collantes
Doctor in Science, professor at National University of Trujillo, Biological Science College. Develops Research in Natural Products and Environmental Sciences.

Cite this article: 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;12(1): 425-431.